

# **Recambio valvular aórtico tradicional: PARTNER 5 anos**

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## DISCLOSURE

I have no financial relationship  
to disclose

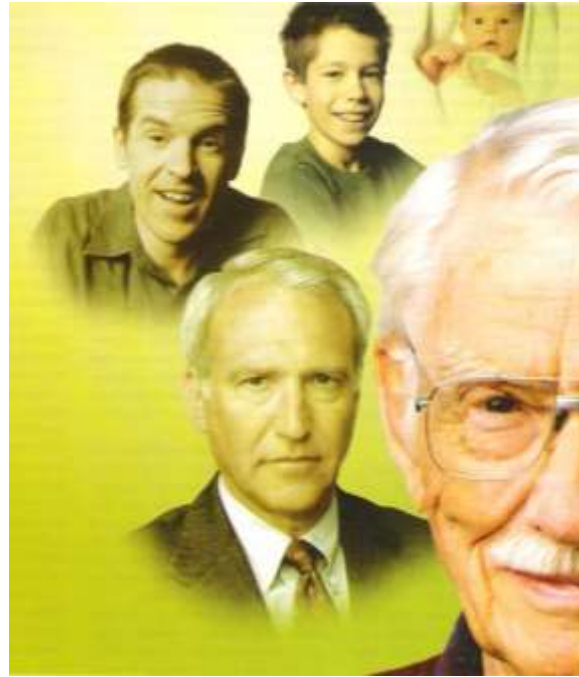
# BACKGROUND

## The elderly population in the world is growing exponentially



**80% of patients >80 years have identifiable cardiovascular disease**

Raja SG. Curr Cardiol Rev. 2012;8(1):26-36



According to the latest census, the population aged over 85 years was

**5.7 million in 2010**

The projection is that is expected to exceed **19 million in 2050**

<http://www.census.gov/population/www/projections/summarytables.html>

Brazilian life expectancy is increasing :

- 1980 – 62.5 years
- 2013 – 74.9 years
- The proportion of elderly increased from 3.9% (1999) to 5.1% (2009)

IBGE 2013

## BACKGROUND

Heart. 2011 Jan;97(2):91-3. Epub 2010 Dec 13.

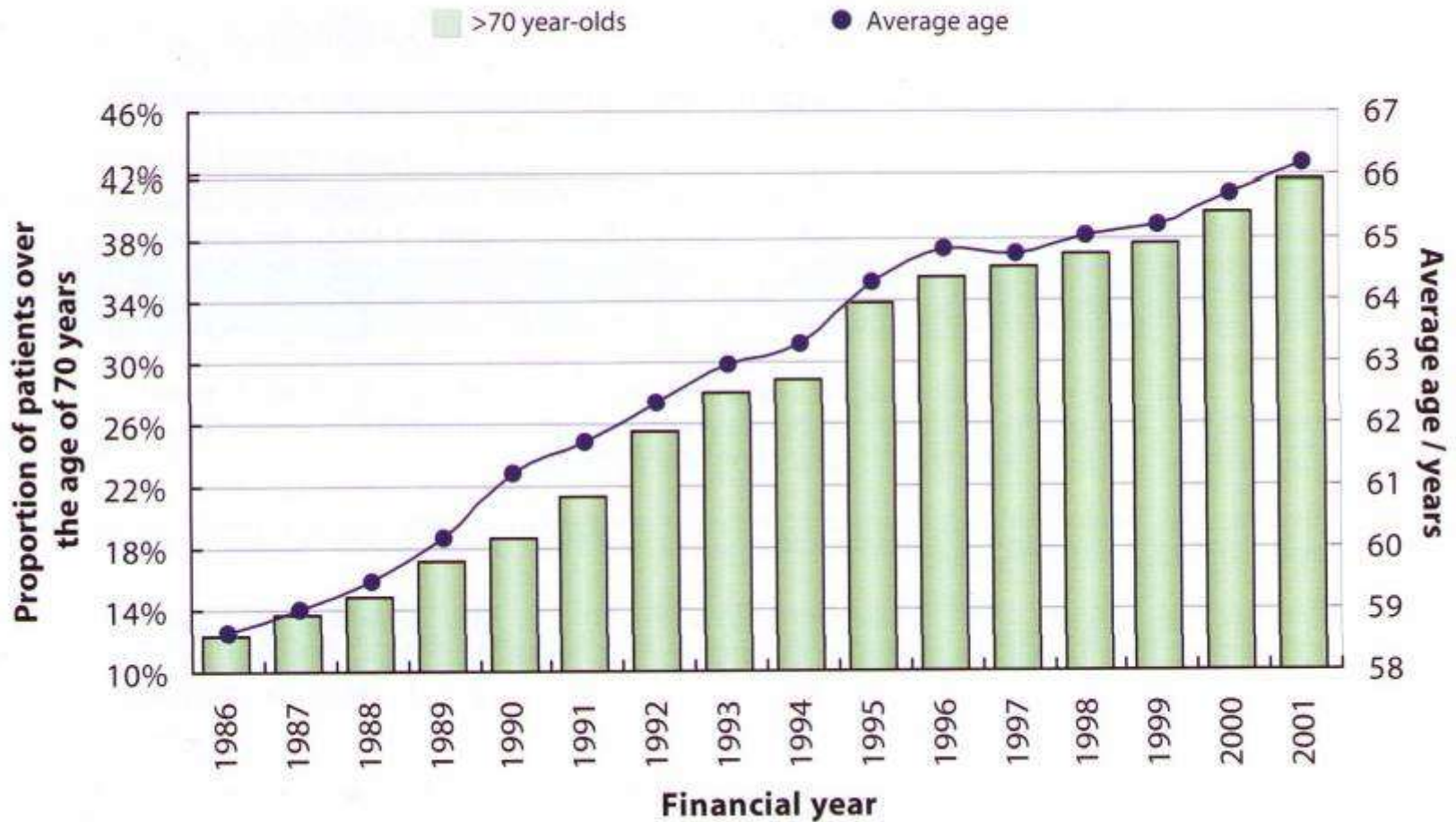
### **Valvular heart disease: the next cardiac epidemic.**

d'Arcy JL, Prendergast BD, Chambers JB, Ray SG, Bridgewater B.

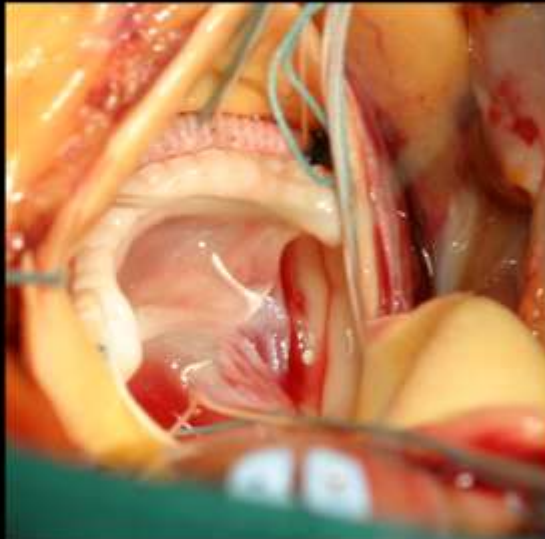
- Prevalence of valvular heart disease in the USA is 2.5%
  - 0.7% in those aged 18–44 years
  - 13.3% in those over the age of 75 years
- In UK, the situation is similar, currently
  - 120.000 pts with  $\geq$  75 years - with moderate or severe aortic stenosis
  - 60.000 pts between 65-74 years

# Data from 5th National Adult Cardiac Surgical Database Report

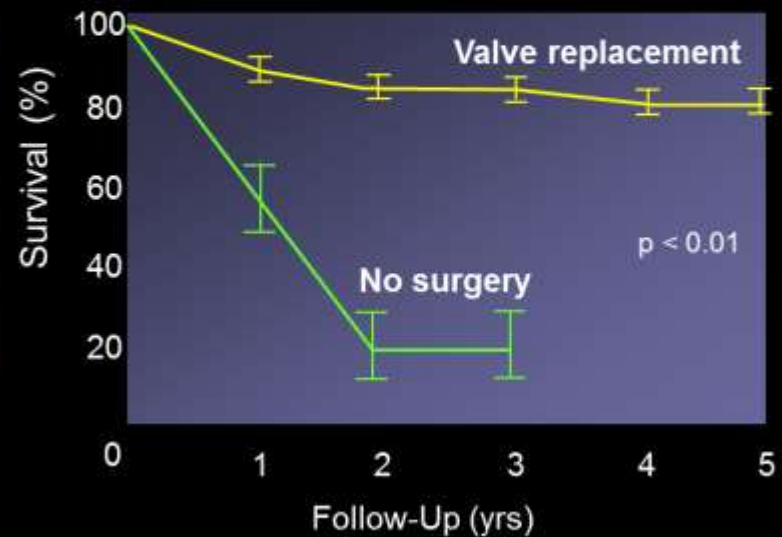
UKHVR: Age trends



# SURGICAL AORTIC VALVE REPLACEMENT

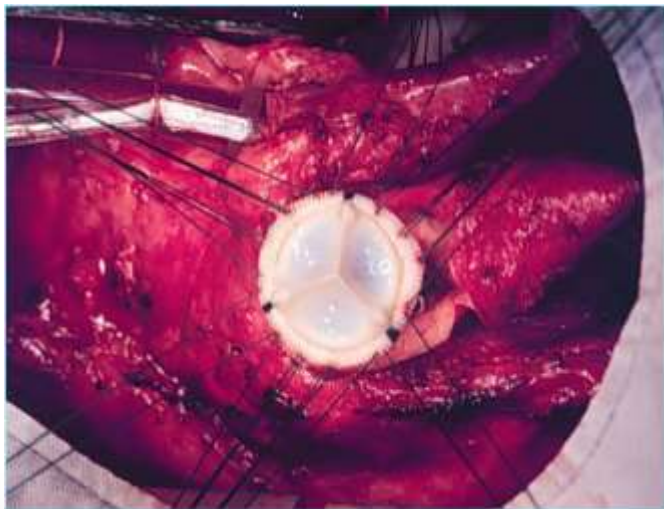
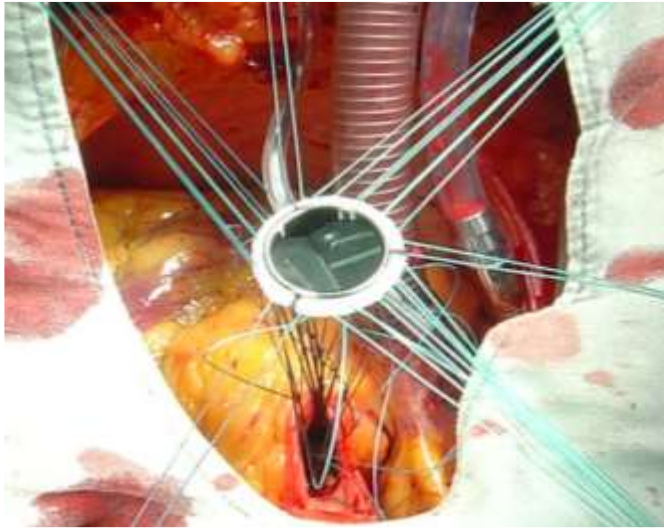


Surgery is a well established therapy that improves survival



Schwarz *Circulation* 1982;66;1105-1110

# SURGICAL AORTIC VALVE REPLACEMENT



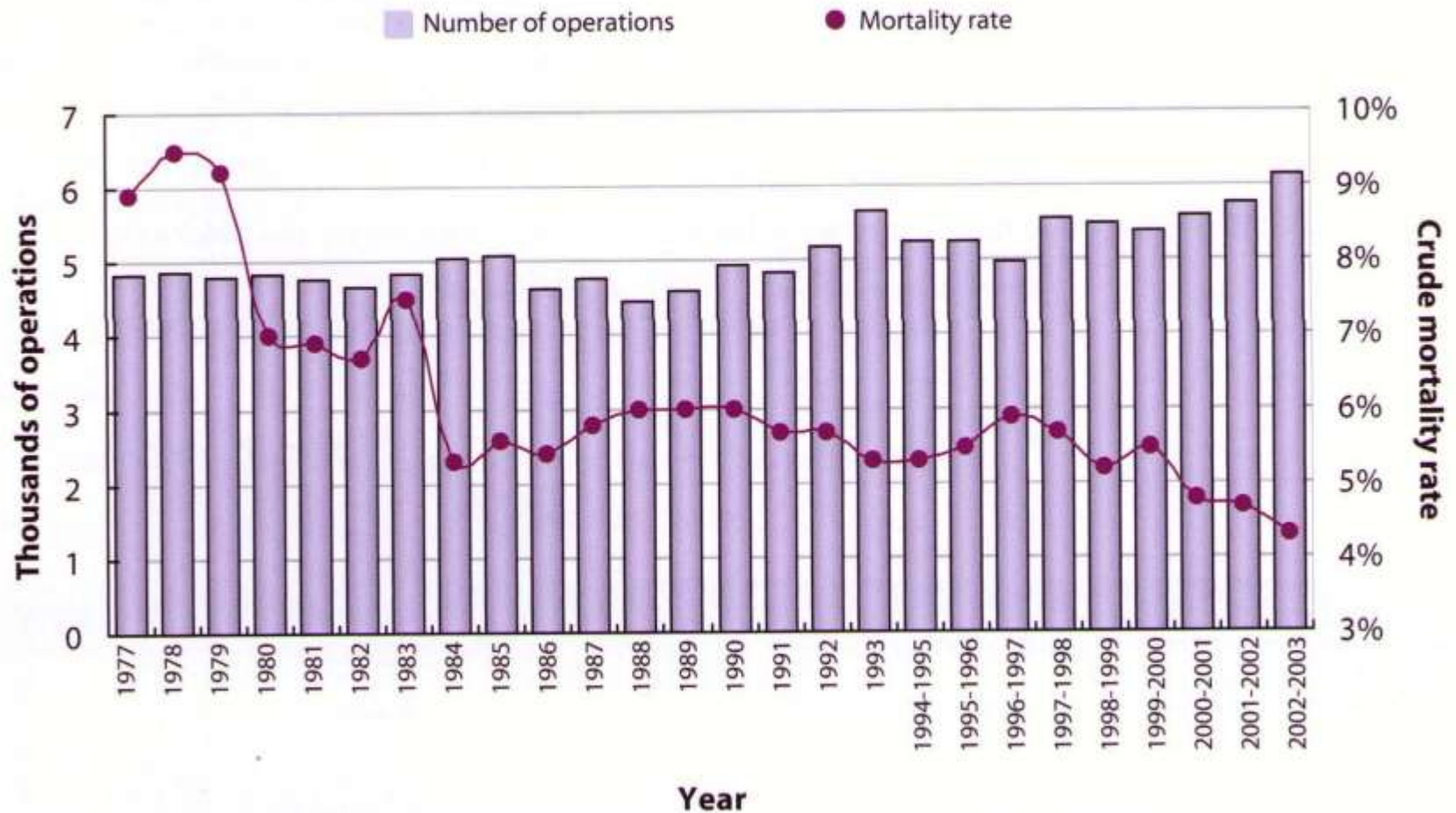
- **SAVR has been the standard of care in pts with severe aortic stenosis for the past half century.**
- About 300.000 operations/yr
- More than 40 years of clinical experience
- Prostheses are reliable
- Predictable and low risks
- Long term results available

## **SAVR InCor - FMUSP**

- **More than 700 valvar operations per year**
- **This number is increasing year by year**
- **Long waiting list for the operation**
- **The SAVR is relatively more frequent than 5 and 10 years ago**
- **Biological prosthesis is more used than mechanical ones**

# Data from 5th National Adult Cardiac Surgical Database Report

## UKCSR: Activity and mortality trends for isolated heart valve surgery (n=131,899)



# ***SURGICAL AORTIC VALVE REPLACEMENT***

<b>Patient Cohort</b>	<b>Number of Patients</b>	<b>30 day mortality</b>	<b>1 year mortality</b>
All isolated AVR	19,041	2.1%	5.5%
All AVR in patients $\geq$ 80 years	3,187	4%	10.2%

# ***SURGICAL AORTIC VALVE REPLACEMENT***

<b>Patient Cohort</b>	<b>Number of Patients</b>	<b>30 day mortality</b>	<b>1 year mortality</b>
All AVR in patients 70-80 yrs	4,783	2.4%	6.2%
All AVR in patients 60-70 yrs	5,727	1.3%	3.7%



# Sutureless Valve Systems

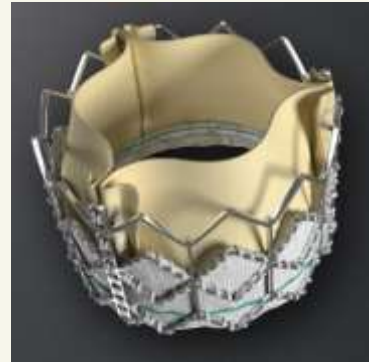
**Medtronic (ATS) Enable**



**Sorin Perceval S**

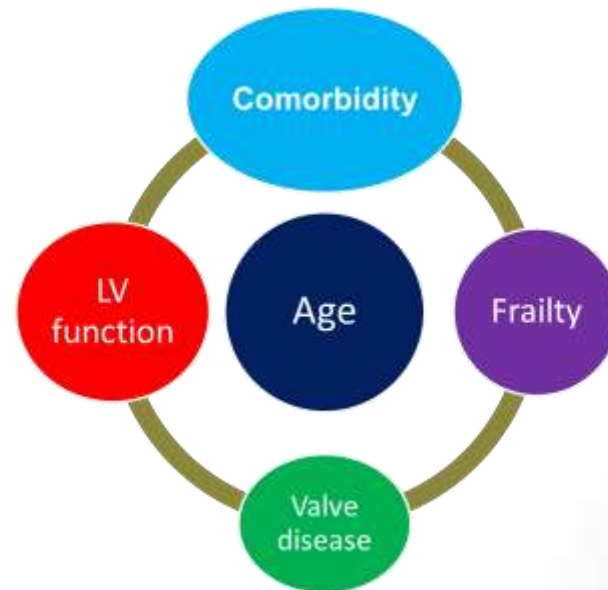
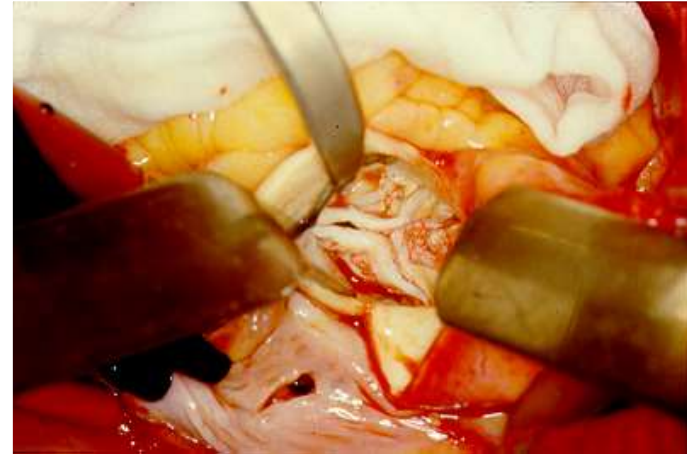


**Edwards Intuity Quick-connect System**

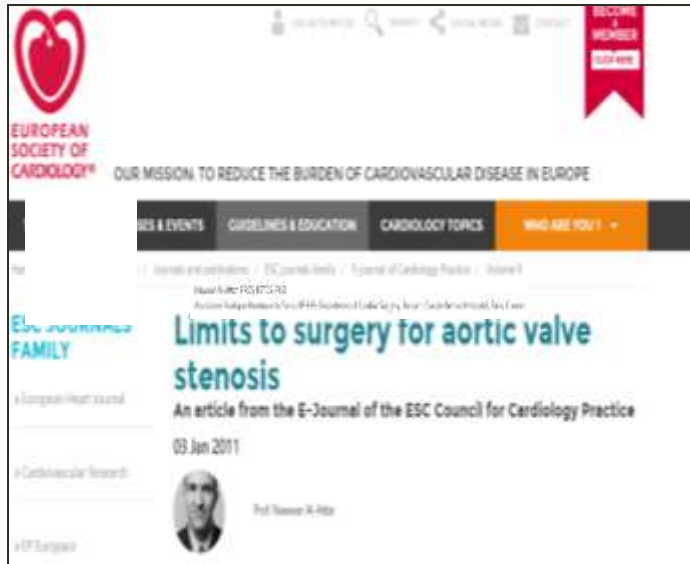


# SURGICAL AORTIC VALVE REPLACEMENT

- Despite the natural history of untreated aortic stenosis, at least 30% of symptomatic pts do not receive SAVR
- The mainly reasons for this lack of treatment are advanced age and/or other comorbidities.



# LIMITS TO SURGICAL AORTIC VALVE REPLACEMENT



## LIMITS RELATED TO

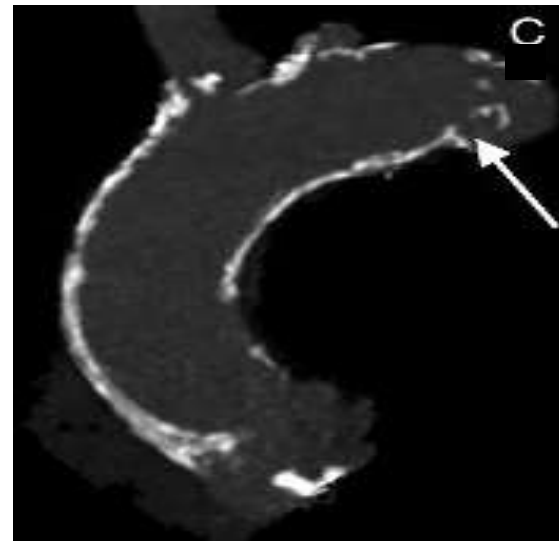
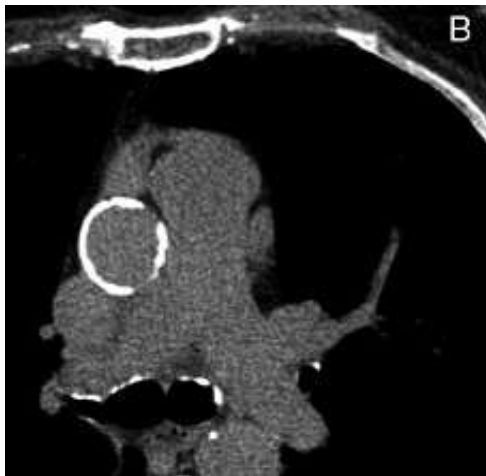
AGE

COMORBIDITY

CONCOMITANT CORONARY  
ARTERY DISEASE

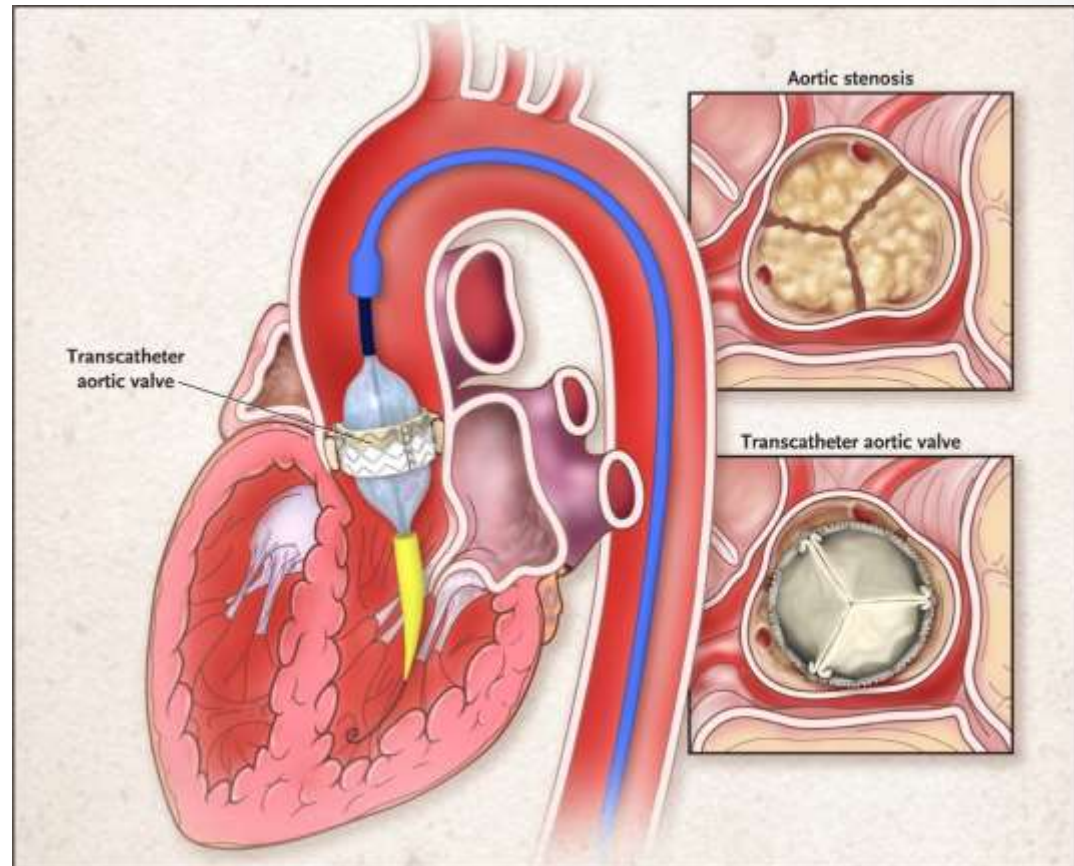
CONTRACTILE RESERVE

TECHNIQUE



# TRANSCATHETER AORTIC VALVE REPLACEMENT

Transcatheter aortic valve replacement (TAVR) is an alternative to surgical valve replacement in high-risk patients with aortic stenosis



## Conventional AVR

## TAVR

### PRO

- easy operation
- established for decades
- excellent results (no AR)

### PRO

- less invasive, fast
- no intubation (transfemoral)
- no extracorporeal circulation

### CONTRA

- invasiveness (thoracotomy)
- intubation
- use of extracorporeal circulation

### CONTRA

- in the learning phase
- suboptimal results in case of severe calcification
- designs of transcatheter heart valves not optimal yet

## TAVR use in Brazil



- **The TAVR valves are not approved in public health system patients (70% of the population)**
- **The main reason for that is the cost of the TAVI device**
- **TAVR valves are used in private health system (30% of the population)**

# TRANSCATHETER AORTIC VALVE REPLACEMENT

Several randomized studies demonstrate the efficacy and safety of transapical and Transfemoral techniques of aortic prosthesis implant

TABLE 1. Edwards Sapien transcatheter heart valve registries

Characteristic	REVIVE, REVIVAL, PARTNER EU	SOURCE	France registry	Belgium registry	Canada registry (TF)
	(N = 222)	registry (TF) (N = 920)	(N = 1137)	(N = 303)	(N = 162)
<b>Demographics</b>					
Age (y)	83	82	83	83	83
Female (%)	55	56	49	46	44
EuroSCORE (mean, %)	26	24	23	29	26
NYHA functional class III/IV (%)	89	76	75	80	93
Aortic valve area (cm <sup>2</sup> )	0.59	0.70	0.67	0.60	0.63
Mean gradient (mm Hg)	45	49	48	47	48
Prior CABG (%)	26	15	19	20	30
Ejection fraction (%)	51	52	53	50	55
<b>Outcomes</b>					
30-day mortality (%)	10.4	7.5	7.8	8	9.5
1-y mortality (%)	24	18.9	NR	NR	NR
Stroke (%)	3.3	3.5	3.5	5.0	3.0
Major vascular complications (%)	27.9	11.3	11.3	NR	13.1
Permanent pacemaker (%)	1.8	6.7	8.5	4.0	3.6

Data are derived from the Edwards Lifesciences briefing document for the U.S. Food and Drug Administration (FDA) Circulatory Devices Advisory Panel meeting on TAVR on July 21, 2011 (<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/ucm240575.htm>). CABG, Coronary artery bypass graft; NR, not reported; NYHA, New York Heart Association; TF, transfemoral.

# PARTNER TRIAL

The first randomized controlled trial to determine the safety and effectiveness of a TAVI device and delivery systems (transfemoral and transapical) in high-risk patients with severe symptomatic aortic stenosis



The PARTNER Trial represents a paradigm shift in clinical trial design and execution for high-risk pts with severe aortic stenosis:

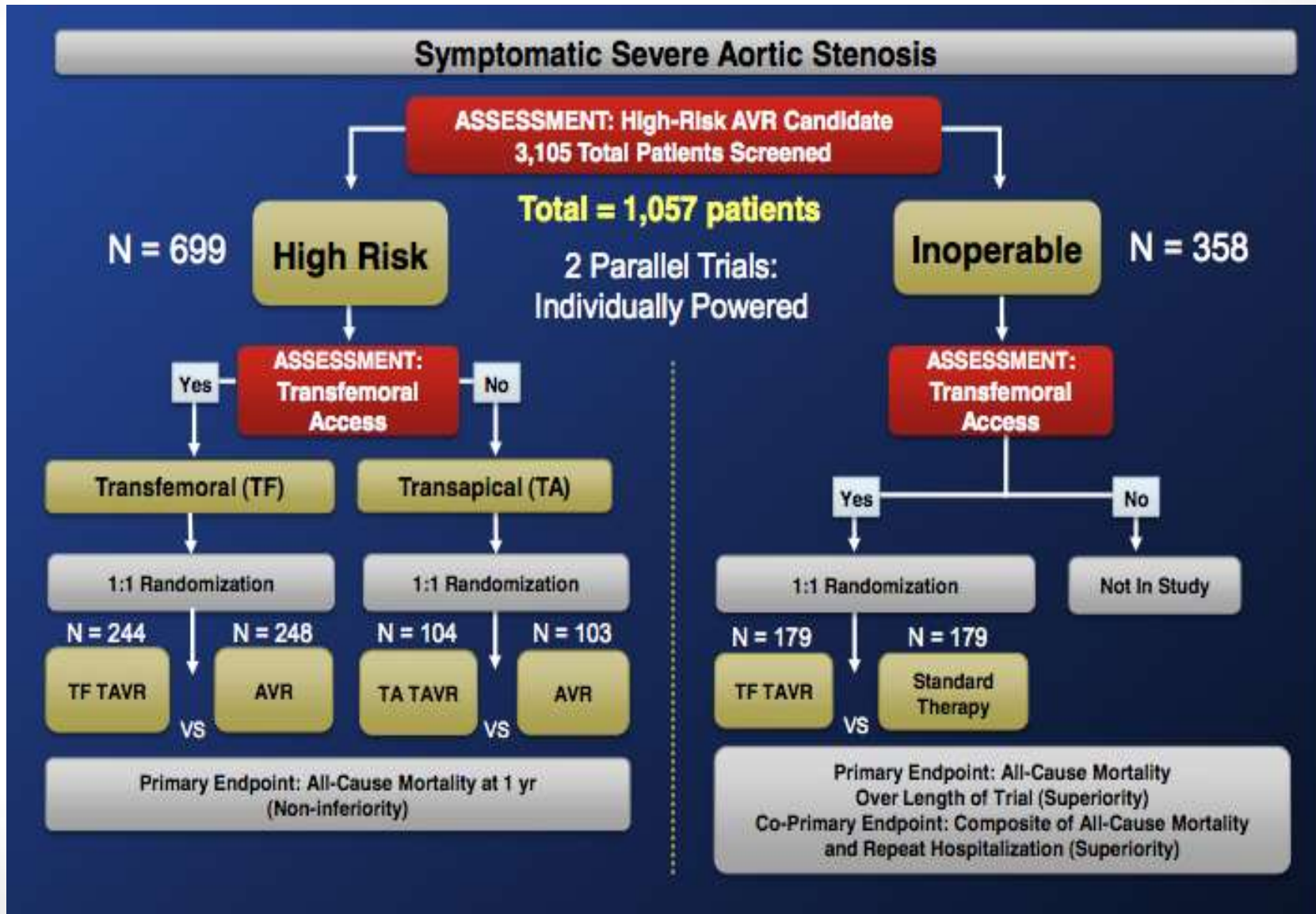
**Rigorous study protocols and management**  
**Careful patient selection**  
**Interdisciplinary in all aspects**  
**Strict site selection**

# PARTNER TRIAL SITES



**N = 1,057 patients**  
**26 investigator sites**  
**22 USA, 3 Canada, 1 Germany**

# PARTNER STUDY DESIGN



# PARTNER STUDY DESIGN

## Symptomatic Severe Aortic Stenosis

**ASSESSMENT: High-Risk AVR Candidate**  
3,105 Total Patients Screened

**Total = 1,057 patients**

2 Parallel Trials:  
Individually Powered

N = 699

**High Risk**

**ASSESSMENT:  
Transfemoral  
Access**

Yes

No

**Transfemoral (TF)**

**Transapical (TA)**

1:1 Randomization

1:1 Randomization

N = 244

N = 248

N = 104

N = 103

**TF TAVR**

**AVR**

VS

**TA TAVR**

**AVR**

VS

**Primary Endpoint: All-Cause Mortality at 1 yr  
(Non-inferiority)**

# PARTNER TRIAL

- TAVR is the recommended treatment for “inoperable” patients with severe aortic stenosis, based upon 1-year results of the PARTNER trial which demonstrated reduced mortality and improved quality of life
- These findings were maintained at 2 years and 3 years

[N Engl J Med](#). 2011 Jun 9;364(23):2187-98. doi: 10.1056/NEJMoa1103510. Epub 2011 Jun 5.

## 1-Year outcomes

### Transcatheter versus surgical aortic-valve replacement in high-risk patients.

[Smith CR](#), [Leon MB](#), [Mack MJ](#), [Miller DC](#), [Moses JW](#), [Svensson LG](#), [Tuzcu EM](#), [Webb JG](#), [Fontana GP](#), [Makkar RR](#), [Williams M](#), [Dewey T](#), [Kapadia S](#), [Babaliaros V](#), [Thourani VH](#), [Corso P](#), [Pichard AD](#), [Bavaria JE](#), [Herrmann HC](#), [Akin JJ](#), [Anderson WN](#), [Wang D](#), [Pocock SJ](#); PARTNER Trial Investigators.

⊕ Collaborators (209)

[N Engl J Med](#). 2012 May 3;366(18):1686-95. doi: 10.1056/NEJMoa1200384. Epub 2012 Mar 26.

## 2-Year outcomes

### Two-year outcomes after transcatheter or surgical aortic-valve replacement.

[Kodali SK](#), [Williams MR](#), [Smith CR](#), [Svensson LG](#), [Webb JG](#), [Makkar RR](#), [Fontana GP](#), [Dewey TM](#), [Thourani VH](#), [Pichard AD](#), [Fischbein M](#), [Szeto WY](#), [Lim S](#), [Greason KL](#), [Teirstein PS](#), [Malaisrie SC](#), [Douglas PS](#), [Hahn RT](#), [Whisenant B](#), [Zajarias A](#), [Wang D](#), [Akin JJ](#), [Anderson WN](#), [Leon MB](#); PARTNER Trial Investigators.

⊕ Collaborators (187)

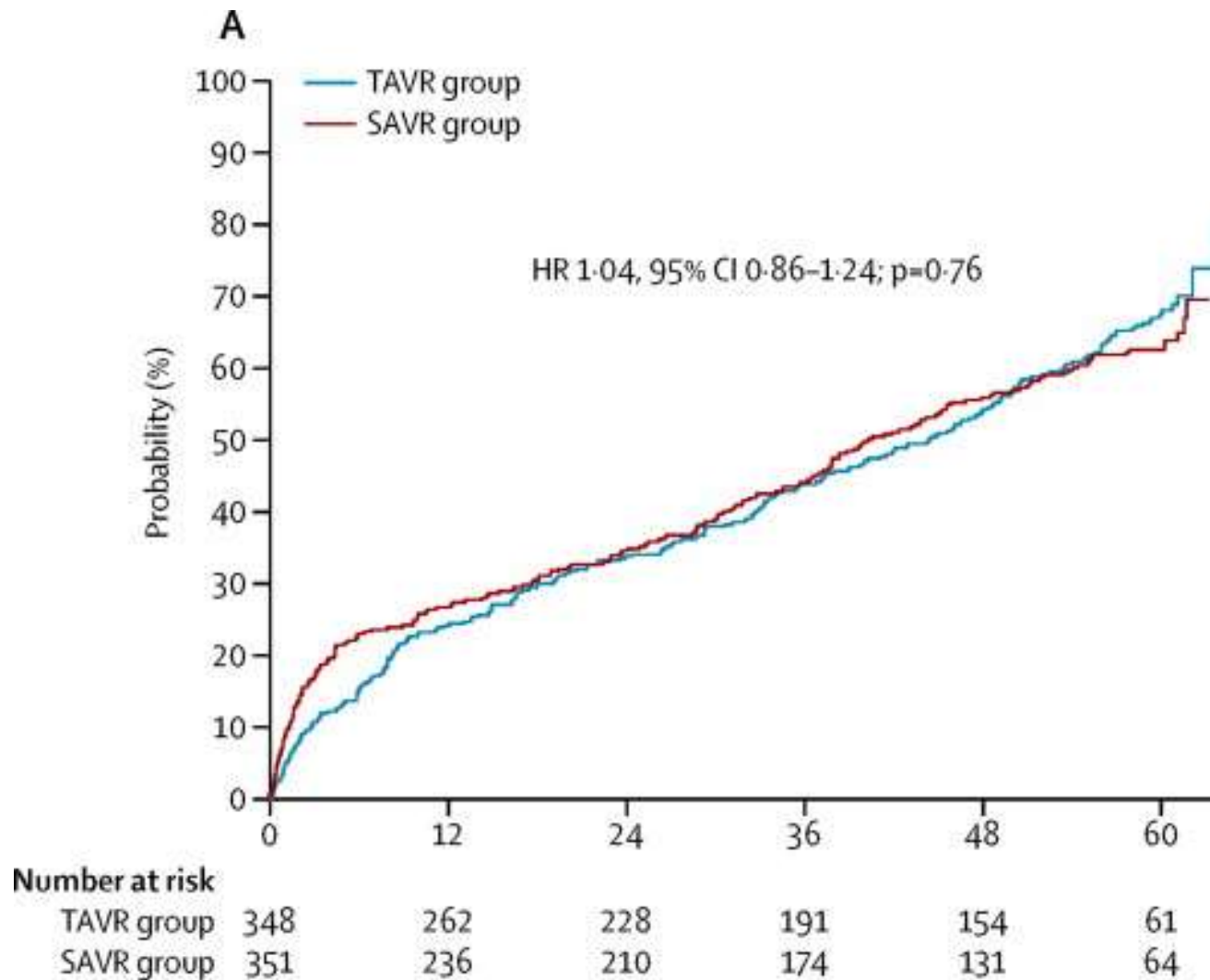
[Circulation](#). 2014 Oct 21;130(17):1483-92. doi: 10.1161/CIRCULATIONAHA.114.009834. Epub 2014 Sep 9.

## 3-Year outcomes

### Long-term outcomes of inoperable patients with aortic stenosis randomly assigned to transcatheter aortic valve replacement or standard therapy.

[Kapadia SR](#)<sup>1</sup>, [Tuzcu EM](#)<sup>2</sup>, [Makkar RR](#)<sup>2</sup>, [Svensson LG](#)<sup>2</sup>, [Aqarwal S](#)<sup>2</sup>, [Kodali S](#)<sup>2</sup>, [Fontana GP](#)<sup>2</sup>, [Webb JG](#)<sup>2</sup>, [Mack M](#)<sup>2</sup>, [Thourani VH](#)<sup>2</sup>, [Babaliaros VC](#)<sup>2</sup>, [Herrmann HC](#)<sup>2</sup>, [Szeto W](#)<sup>2</sup>, [Pichard AD](#)<sup>2</sup>, [Williams MR](#)<sup>2</sup>, [Anderson WN](#)<sup>2</sup>, [Akin JJ](#)<sup>2</sup>, [Miller DC](#)<sup>2</sup>, [Smith CR](#)<sup>2</sup>, [Leon MB](#)<sup>2</sup>.

# MORTALITY – ALL-CAUSE DEATH



## PARTNER TRIAL – 5-YEAR OUTCOMES

	At 1 year		At 5 years		Log-rank p value
	TAVR group (n=348)	SAVR group (n=351)	TAVR group (n=348)	SAVR group (n=351)	
Death					
From any cause	84 (24.2%)	89 (26.8%)	229 (67.8%)	198 (62.4%)	0.76
From cardiovascular causes	46 (14.0%)	40 (13.0%)	147 (53.1%)	123 (47.6%)	0.67
Repeat hospital admission	59 (18.5%)	51 (17.7%)	108 (42.3%)	81 (34.2%)	0.17
Death from any cause or repeat hospital admission	121 (34.9%)	125 (37.7%)	265 (77.8%)	228 (71.3%)	0.49
Stroke or transient ischaemic attack					
All	28 (8.6%)	13 (4.3%)	42 (15.9%)	33 (14.7%)	0.35
Stroke	20 (6.0%)	10 (3.2%)	29 (10.4%)	26 (11.3%)	0.61
Transient ischaemic attack	8 (2.6%)	4 (1.5%)	14 (6.3%)	8 (3.8%)	0.30
Stroke or death from any cause	95 (27.4%)	95 (28.6%)	236 (69.8%)	200 (62.9%)	0.39
Stroke or transient ischaemic attack, or death from any cause	102 (29.4%)	98 (29.5%)	242 (71.6%)	205 (64.4%)	0.35
Myocardial infarction	0 (0.0%)	2 (0.6%)	5 (2.9%)	11 (5.9%)	0.15
Major vascular complication	40 (11.6%)	13 (3.8%)	41 (11.9%)	14 (4.7%)	0.0002
Major bleeding	52 (15.7%)	88 (26.7%)	75 (26.6%)	103 (34.4%)	0.003
Endocarditis	2 (0.6%)	3 (1.0%)	5 (2.0%)	6 (2.5%)	0.65
Renal failure	18 (5.4%)	20 (6.5%)	24 (8.6%)	24 (8.5%)	0.69
New pacemaker	21 (6.4%)	17 (5.3%)	28 (9.7%)	23 (9.1%)	0.64

# PARTNER TRIAL – 5-YEAR OUTCOMES

## 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial



Michael J Mack, Martin B Leon, Craig R Smith, D Craig Miller, Jeffrey W Moses, E Murat Tuzcu, John G Webb, Pamela S Douglas, William N Anderson, Eugene H Blackstone, Susheel K Kodali, Raj R Makkar, Gregory P Fontana, Samir Kapadia, Joseph Bavaria, Rebecca T Hahn, Vinod H Thourani, Vasilis Babaliaros, Augusto Pichard, Howard C Herrmann, David L Brown, Mathew Williams, Jodi Akin\*, Michael J Davidson†, Lars G Svensson, for the PARTNER 1 trial investigators

### Summary

**Background** The Placement of Aortic Transcatheter Valves (PARTNER) trial showed that mortality at 1 year, 2 years, and 3 years is much the same with transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR) for high-risk patients with aortic stenosis. We report here the 5-year outcomes.

**Methods** We did this randomised controlled trial at 25 hospitals, in Canada (two), Germany (one), and the USA (23). We used a computer-generated randomisation sequence to randomly assign high-risk patients with severe aortic stenosis to either SAVR or TAVR with a balloon-expandable bovine pericardial tissue valve by either a transfemoral or transapical approach. Patients and their treating physicians were not masked to treatment allocation. The primary outcome of the trial was all-cause mortality in the intention-to-treat population at 1 year, we present here predefined outcomes at 5 years. The study is registered with ClinicalTrials.gov, number NCT00530894.

**Findings** We screened 3105 patients, of whom 699 were enrolled (348 assigned to TAVR, 351 assigned to SAVR). Overall mean Society of Thoracic Surgeons Predicted Risk of Mortality score was 11·7%. At 5 years, risk of death was 67·8% in the TAVR group compared with 62·4% in the SAVR group (hazard ratio 1·04, 95% CI 0·86–1·24;  $p=0\cdot76$ ). We recorded no structural valve deterioration requiring surgical valve replacement in either group. Moderate or severe aortic regurgitation occurred in 40 (14%) of 280 patients in the TAVR group and two (1%) of 228 in the SAVR group ( $p<0\cdot0001$ ), and was associated with increased 5-year risk of mortality in the TAVR group (72·4% for moderate or severe aortic regurgitation vs 56·6% for those with mild aortic regurgitation or less;  $p=0\cdot003$ ).

**Interpretation** Our findings show that TAVR as an alternative to surgery for patients with high surgical risk results in similar clinical outcomes.

**Funding** Edwards Lifesciences.

*Lancet* 2015; 385: 2477–84

Published Online

March 15, 2015

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See [Comment](#) page 2439

See [Articles](#) page 2485

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Stanford University School of

Medicine, Department of

Cardiovascular Surgery, Falk CV

Research Center, Stanford, CA,

USA (Prof D C Miller MD);

Cleveland Clinic, Cleveland, OH,

USA (Prof E M Tuzcu MD,

E H Blackstone MD,

# PARTNER 5-YEAR

[Lancet. 2015 Jun 20;385\(9986\):2439-41. doi: 10.1016/S0140-6736\(15\)60568-2. Epub 2015 Mar 15.](#)

## **PARTNERS in the future of surgical aortic valve replacement.**

[Kappetein AP<sup>1</sup>.](#)

### **⊖ Author information**

<sup>1</sup>Department of Cardio-Thoracic Surgery, Erasmus University Medical Center, 3000 CA Rotterdam, Netherlands. Electronic address: [a.kappetein@erasmusmc.nl](mailto:a.kappetein@erasmusmc.nl).

**Surgery is associated and often described with a higher short-term probability of discomfort or mortality, however, the most patients will not consider the likelihood of a long-term benefit but instead choose the less invasive option.**

## FINAL REMARKS - PARTNER TRIAL – 5-YEAR OUTCOMES

- PARTNER Trial - consistent results
- TAVR is safe and effective
- Inoperable patients: TAVR is superior to medical treatment
- High risk patients: TAVR is similar to SAVR
- Durability of the prostheses over five years remains uncertain
- Other patient groups could be included in the near future in this new treatment



**What the  
guidelines say?**

# GUIDELINES

J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132. doi: 10.1016/j.jtcvs.2014.05.014. Epub 2014 May 9.

## 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.

Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Creager MA, Curtis LH, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Ohman EM, Pressler SJ, Sellke FW, Shen WK, Stevenson WG, Yancy CW; American College of Cardiology; American College of Cardiology/American Heart Association; American Heart Association

**TABLE 10. Summary of recommendations for AS: Choice of surgical or transcatheter intervention**

Recommendations	COR	LOE	References
Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.2.3) with low or intermediate surgical risk	I	A	74,148
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C	N/A
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival >12 mo	I	B	169,170
TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.2.3) and who have high surgical risk (Section 2.5)	IIa	B	171,172
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C	N/A
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No Benefit	B	169

## FINAL REMARKS - SAVR

- Very well established operation
- Very safe and consistent results
- The number of operations is still high and we have waiting list for the operation
- The number of TAVR is increasing in private patients in Brazil for non operable and high risk patients
- No TAVR in public health system in Brazil

Hybrid operating room with the support of a multidisciplinary team (surgery, cardiology, anesthesia, echocardiography, CPB support)



# HEART TEAM



**GRACIAS**



# CHANGES IN BRAZILIAN POPULATION PYRAMID

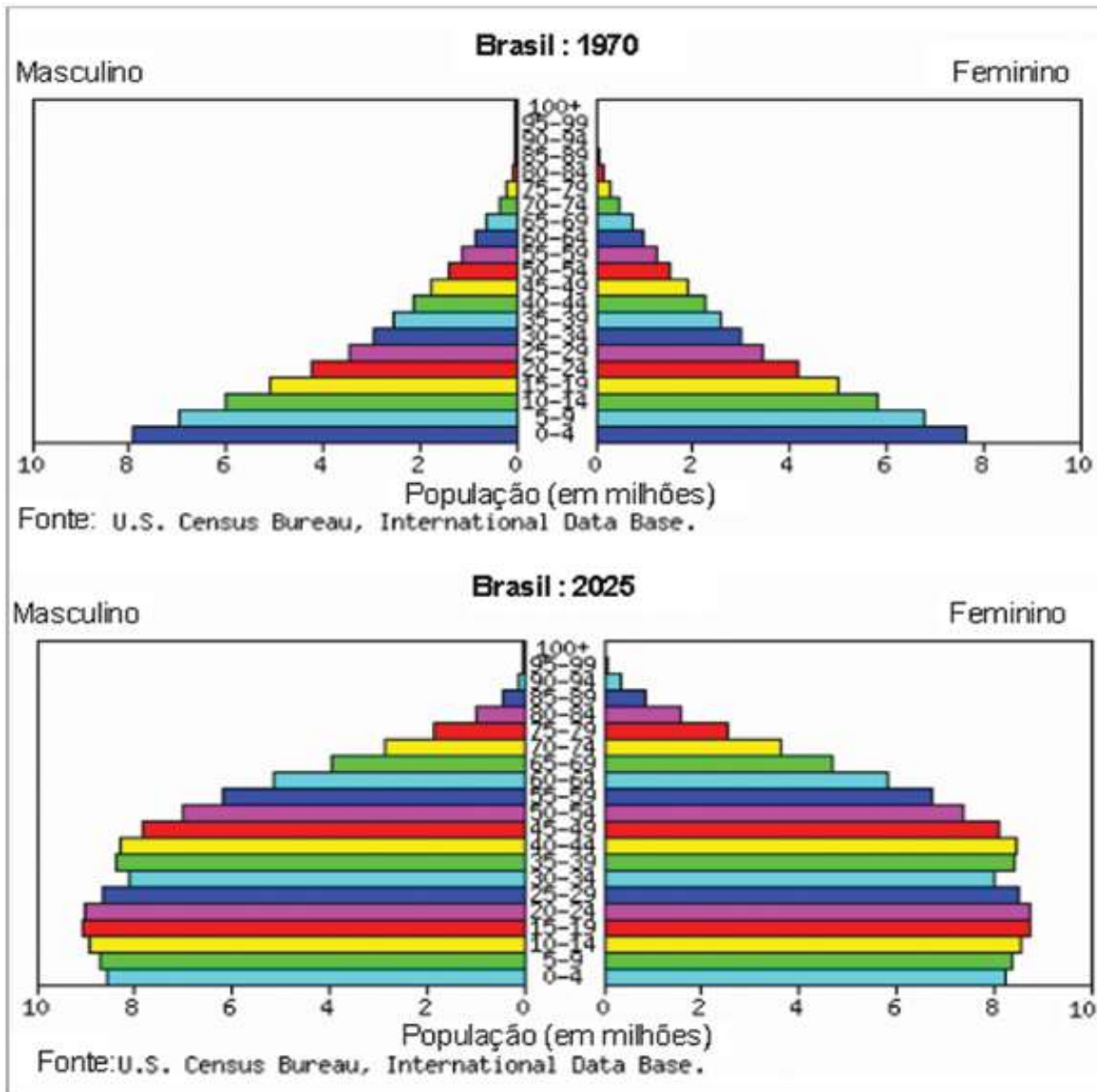
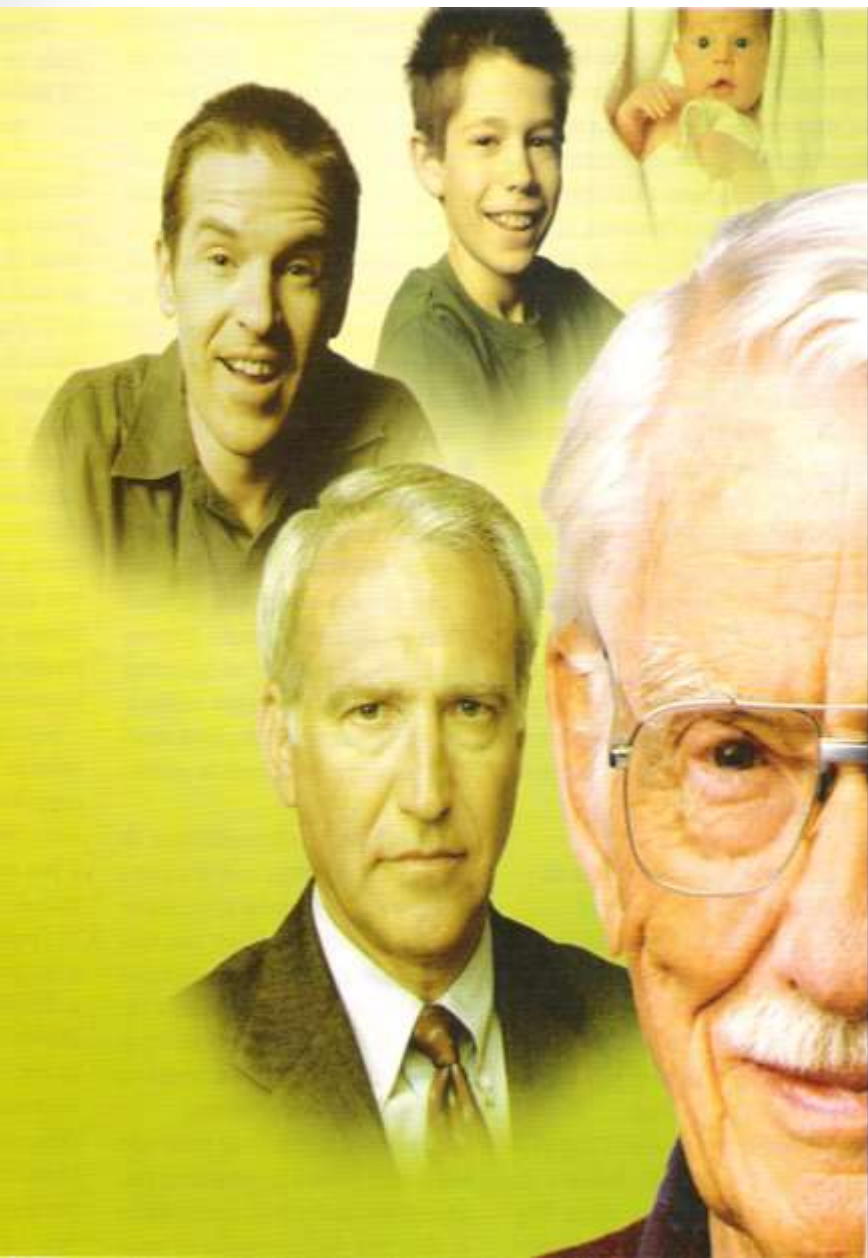


Fig 1 - Mudança da pirâmide populacional brasileira conforme 1970 para a forma trapezoidal prevista para 2025.

## BACKGROUND



## The elderly population in the world is growing exponentially

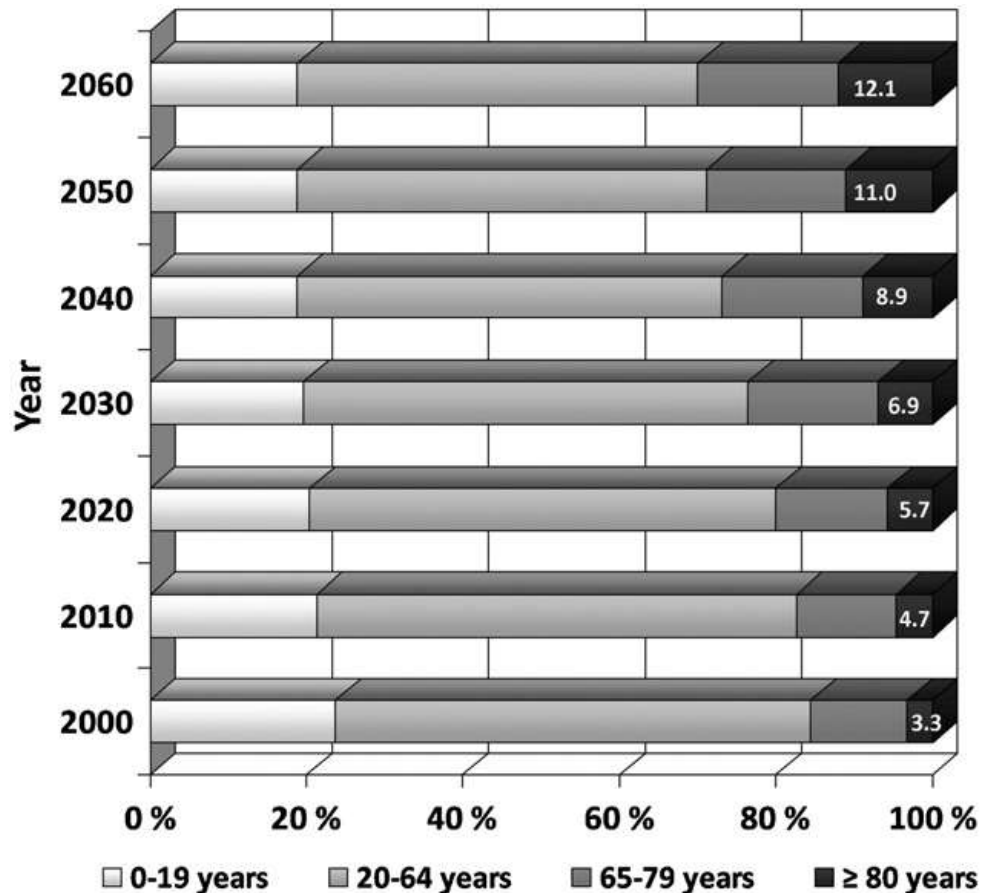
Brazilian life expectancy is increasing :

- 1980 – 62.5 years
  - 2000 – 70.5 years
  - 2003 – 71.3 years
  - 2010 – 73.8 years
  - 2013 – 74.9 years
- 
- Today we have about 15 million over 65 years - a number that will double in the next 2 decades
  - The proportion of elderly increased from 3.9% (1999) to 5.1% (2009)

IBGE /2013

## BACKGROUND

### Estimated changes in population structure by major age in the European Community



# AORTIC VALVE DISEASE - PROBLEM SIZE

## Moderate or severe valve disease

- 2.5% of the adult population (USA)

## Aortic Stenosis

- 4% of the population (> 65 years)

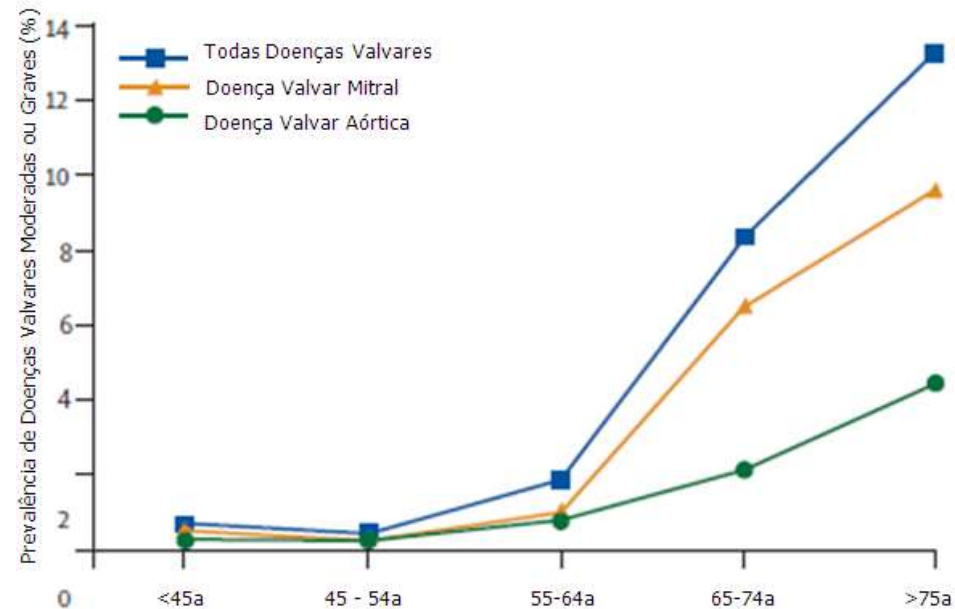
## Rheumatic fever

- World prevalence: 12 million people
- 3-4% of children with pharyngitis untreated
- Epidemiology – Brazil (12th in incidence)

## Aortic Valve Bicuspid

- 2% of the population (USA)
- High-risk aortic stenosis
- 4: 1 male

## PREVALENCE



# AORTIC STENOSIS - ETIOLOGY

- **Congenital**
- **Acquired**
  - Rheumatic
  - Degenerative
  - Atherosclerotic
  - Calcification (Paget's disease)
  - Rheumatoid arthritis



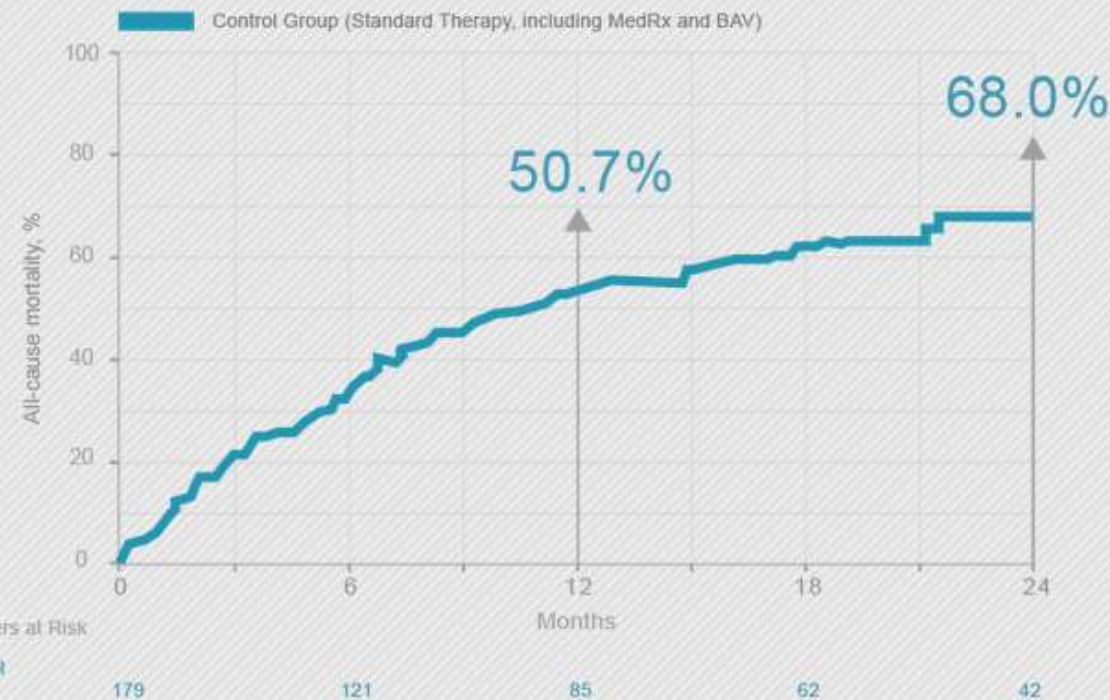
Freeman et al. *Circulation* 2005;111:3316-26; Nkomo et al. *Lancet* 2006;368:1005-11;  
Brien et al. *Ann Thorac Surg* 2009;88:S23-42; WHO Statistics – 2005

# AORTIC STENOSIS

## Cohort B - The PARTNER Trial

*Standard Therapies Are Inadequate for Severe Aortic Stenosis*

Cohort B - The PARTNER Trial

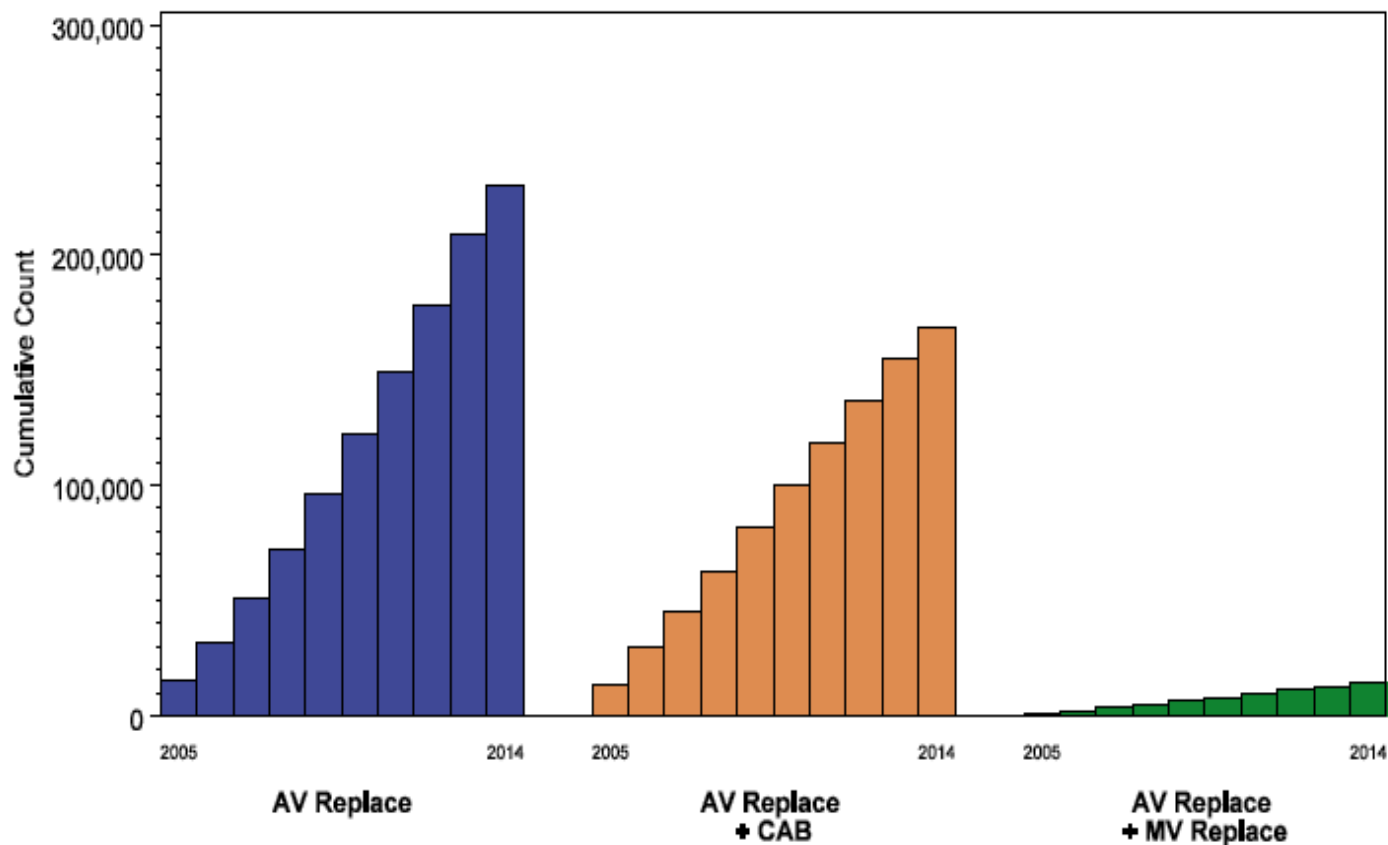


- In inoperable patients with severe aortic stenosis who did not receive a valve replacement, 50% died within one year.
- Despite the frequent utilization of balloon aortic valvuloplasty, standard therapy did not do much to alter the dismal course of disease for inoperable patients with severe aortic stenosis.

# Adult Cardiac Surgery Database Executive Summary 10 Years

STS Period Ending 09/30/2014

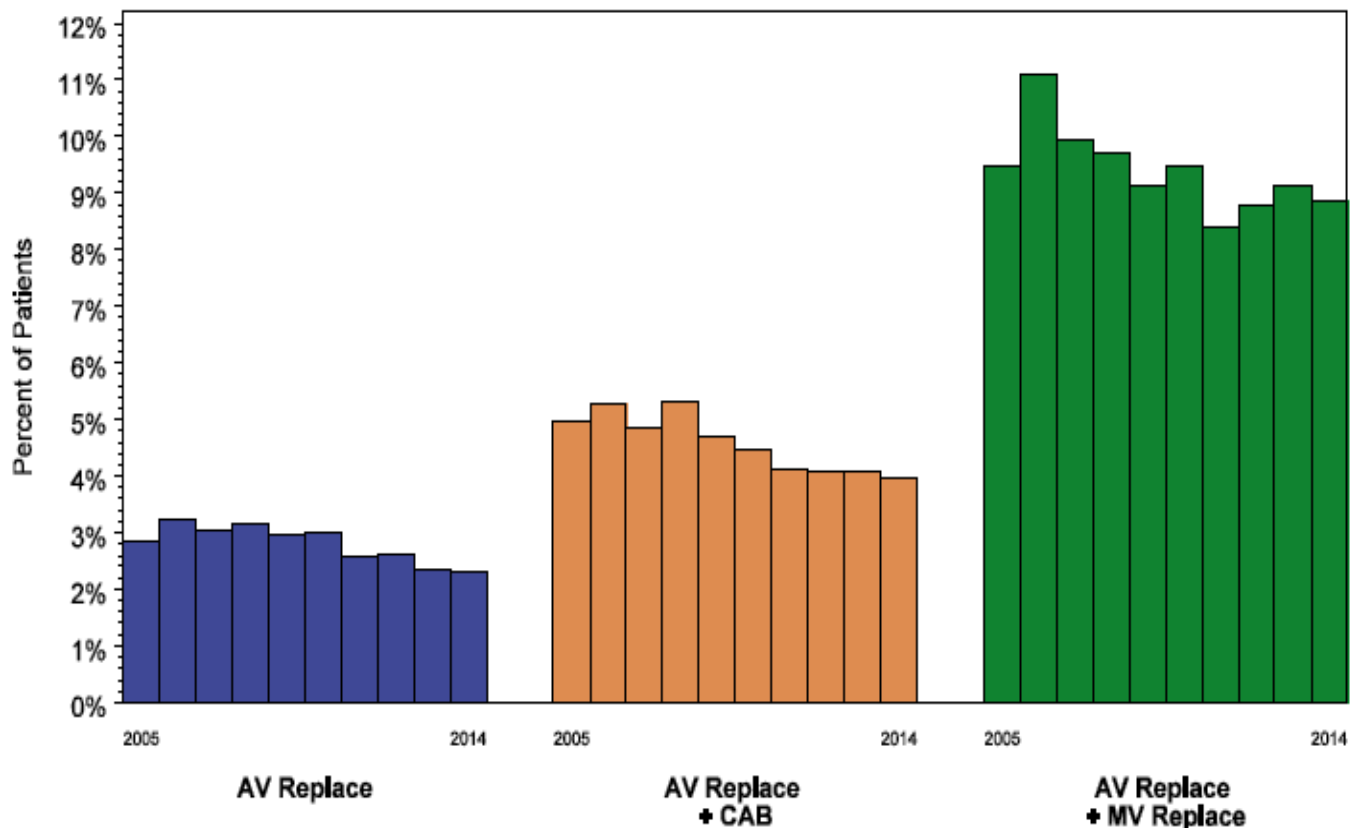
## Number of Aortic Valve Procedures Cumulative over last 10 years



# Adult Cardiac Surgery Database Executive Summary 10 Years

STS Period Ending 09/30/2014

## Unadjusted Aortic Valve Operative Mortality Yearly over last 10 years



# SURGICAL AORTIC VALVE REPLACEMENT

**“despite severe AS and severe symptoms, intervention was denied in as many as 33% of patients”**



European Heart Journal (2005) 26, 2714–2720  
doi:10.1093/eurheartj/ehi471

Clinical research

## Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery?

Bernard Iung<sup>1\*</sup>, Agnès Cachier<sup>1</sup>, Gabriel Baron<sup>2</sup>, David Messika-Zeitoun<sup>1</sup>, François Delahaye<sup>3</sup>, Pilar Tornos<sup>4</sup>, Christa Gohlke-Bärwolf<sup>5</sup>, Eric Boersma<sup>6</sup>, Philippe Ravaud<sup>2</sup>, and Alec Vahanian<sup>1</sup>

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Received 6 May 2005; revised 4 July 2005; accepted 4 August 2005; online publish-ahead-of-print 1 September 2005

### KEYWORDS

Aortic stenosis;  
Elderly;  
Aortic valve replacement

**Aims** To analyse decision-making in elderly patients with severe, symptomatic aortic stenosis (AS).

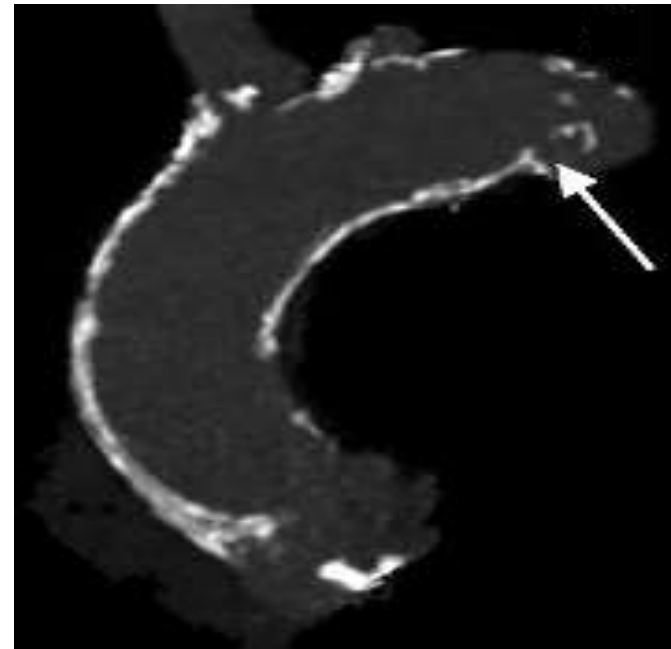
**Methods and results** In the Euro Heart Survey on valvular heart disease, 216 patients aged  $\geq 75$  had severe AS (valve area  $\leq 0.6$  cm<sup>2</sup>/m<sup>2</sup> body surface area or mean gradient  $\geq 50$  mmHg) and angina or New York Heart Association class III or IV. Patient characteristics were analysed according to the decision to operate or not. A decision not to operate was taken in 72 patients (33%). In multivariable analysis, left ventricular (LV) ejection fraction [OR = 2.27, 95% CI (1.32–3.97) for ejection fraction 30–50, OR = 5.15, 95% CI (1.73–15.35) for ejection fraction  $\leq 30$  vs.  $>50\%$ ,  $P = 0.003$ ] and age [OR = 1.84, 95% CI (1.18–2.89) for 80–85 years, OR = 3.38, 95% CI (1.38–8.27) for  $\geq 85$  vs. 75–80 years,  $P = 0.008$ ] were significantly associated with the decision not to operate; however, the Charlson comorbidity index was not [OR = 1.72, 95% CI (0.83–3.50),  $P = 0.14$  for index  $\geq 2$  vs.  $<2$ ]. Neurological dysfunction was the only comorbidity significantly linked with the decision not to operate.

**Conclusion** Surgery was denied in 33% of elderly patients with severe, symptomatic AS. Older age and LV dysfunction were the most striking characteristics of patients who were denied surgery, whereas comorbidity played a less important role.

# LIMITS TO SURGICAL AORTIC VALVE REPLACEMENT

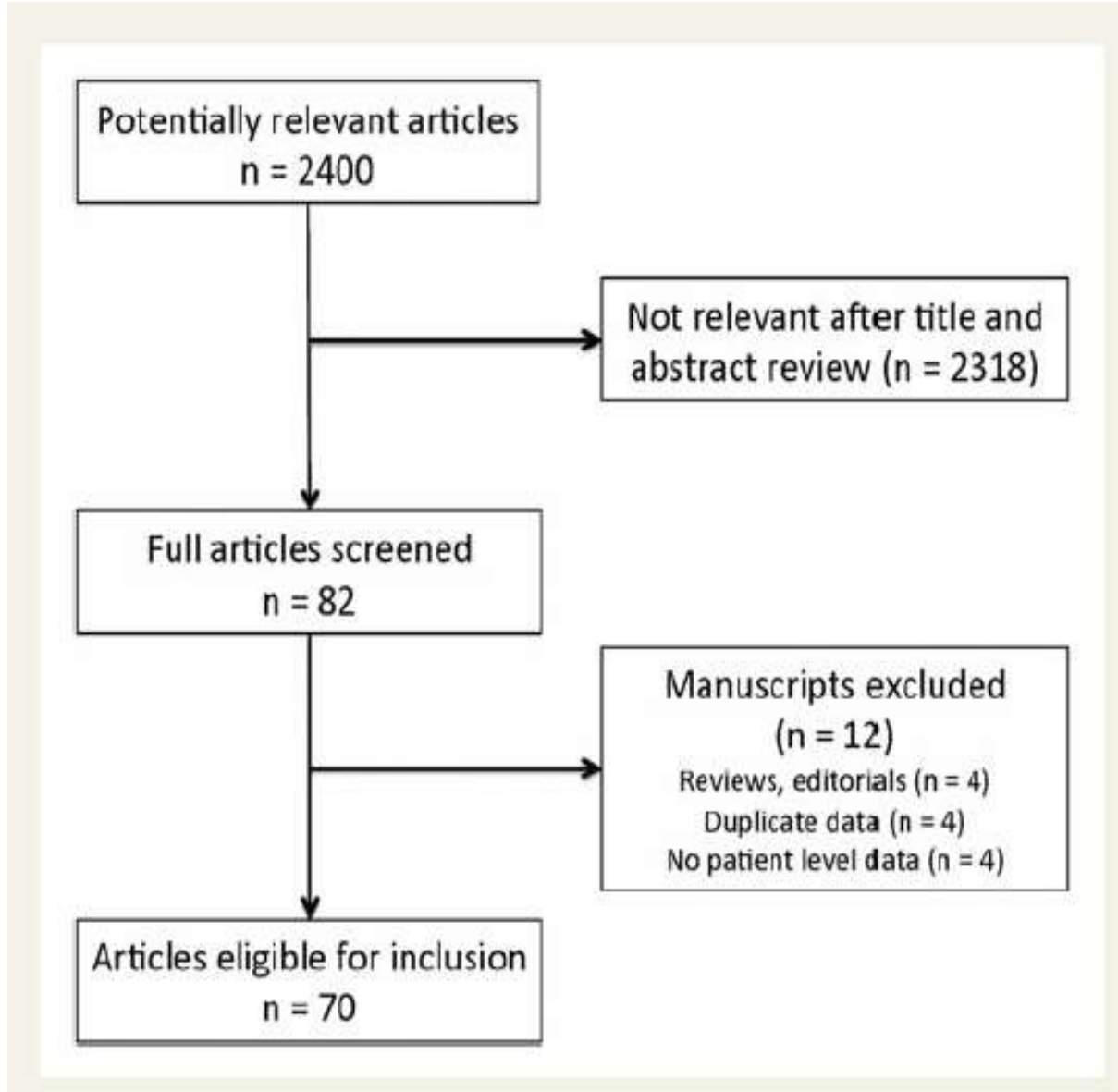
LIMITS RELATED TO	CONSIDERATIONS
AGE	<ul style="list-style-type: none"><li>• Elderly patients experience increased operative mortality and also are at higher risk for valve-related events in several reports.</li><li>• However in current guidelines, age is not a contraindication to AVR</li></ul>
COMORBIDITY	<ul style="list-style-type: none"><li>• General condition of the patient, such as neurological dysfunction, chronic lung disease, liver cirrhosis and renal insufficiency are additional predictors of poor outcome</li></ul>
CONCOMITANT CORONARY ARTERY DISEASE	<ul style="list-style-type: none"><li>• CAD may negatively affect prognosis in patients with AS due to the presence of a concomitant cardiac pathology and impaired LV function from an ischaemic myocardium</li><li>• The operative mortality of AVR doubles with the addition of a concomitant CABG procedure</li></ul>
CONTRACTILE RESERVE	<ul style="list-style-type: none"><li>• When hypertrophy fails to normalize wall stress, the abnormal afterload leads to reduced ventricular ejection, reducing cardiac output, adding to the heart failure syndrome</li></ul>
TECHNIQUE	<ul style="list-style-type: none"><li>• Redo surgery with patent coronary artery bypass grafts, previous mediastinal radiotherapy and radiation damage to the myocardium, in the presence of a heavily calcified and atheromatous ascending aorta (porcelain aorta)</li></ul>

## PORCELAIN AORTA

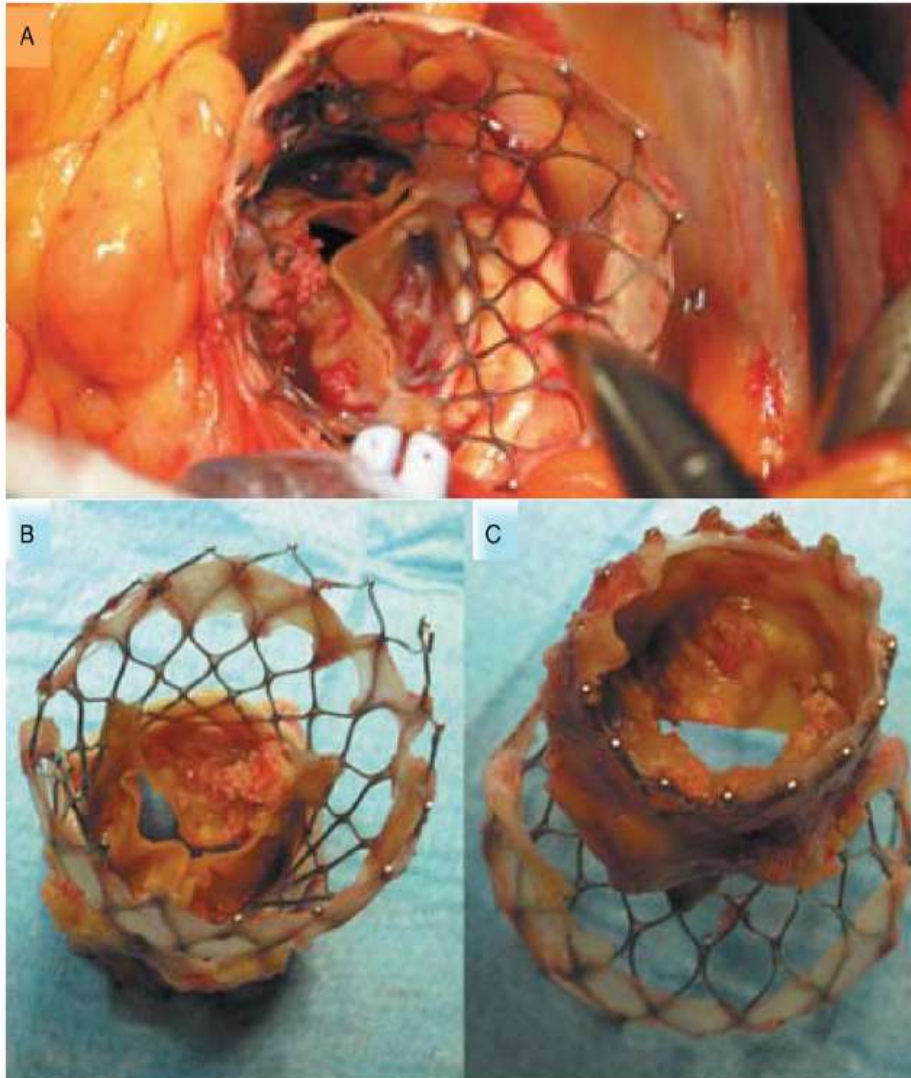


Multislice CT scan illustrating porcelain aorta, heavily calcified ascending thoracic aorta with plaque protrusion (arrow)

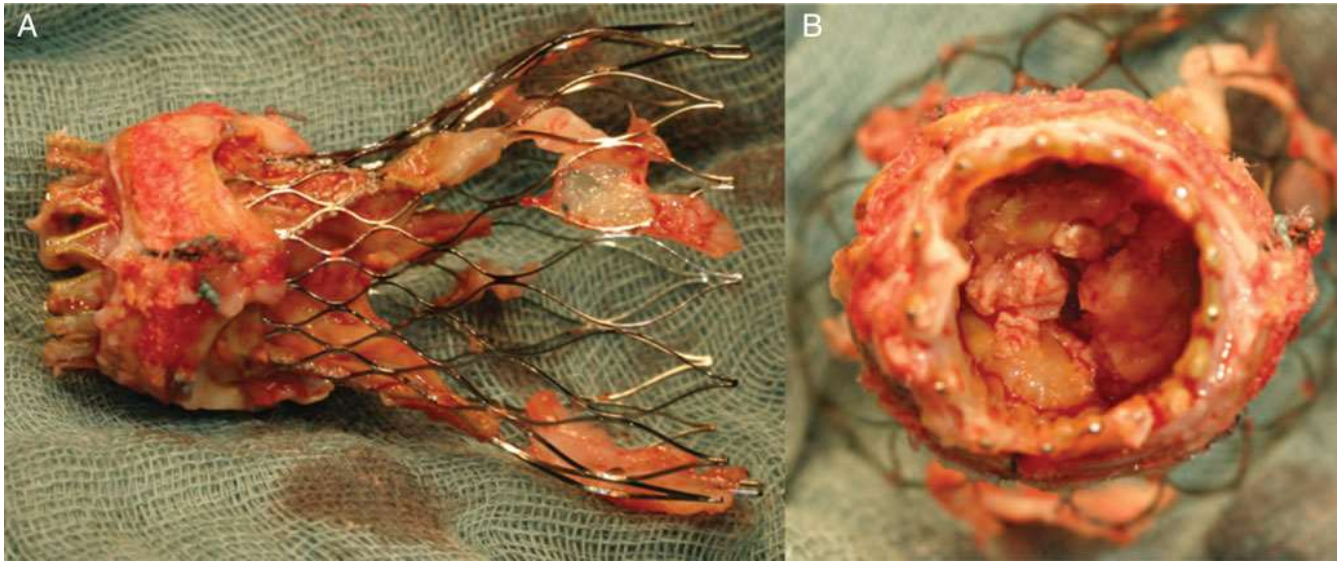
# LITERATURE SEARCH RESULTS



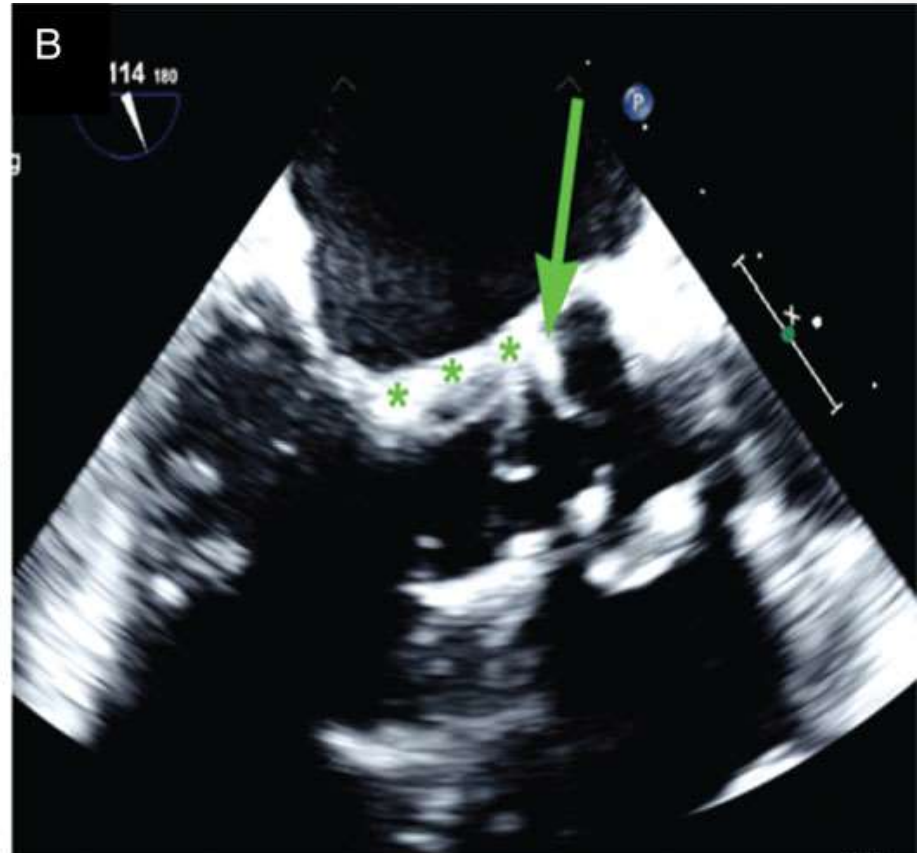
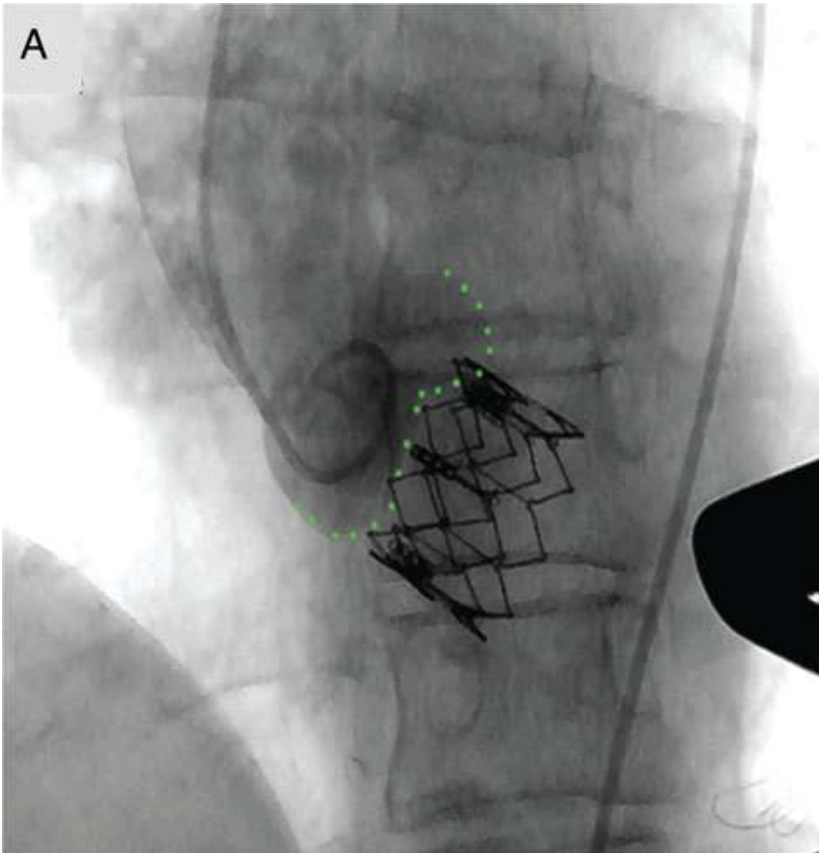
# EXTENSIVE LEAFLET CALCIFICATION



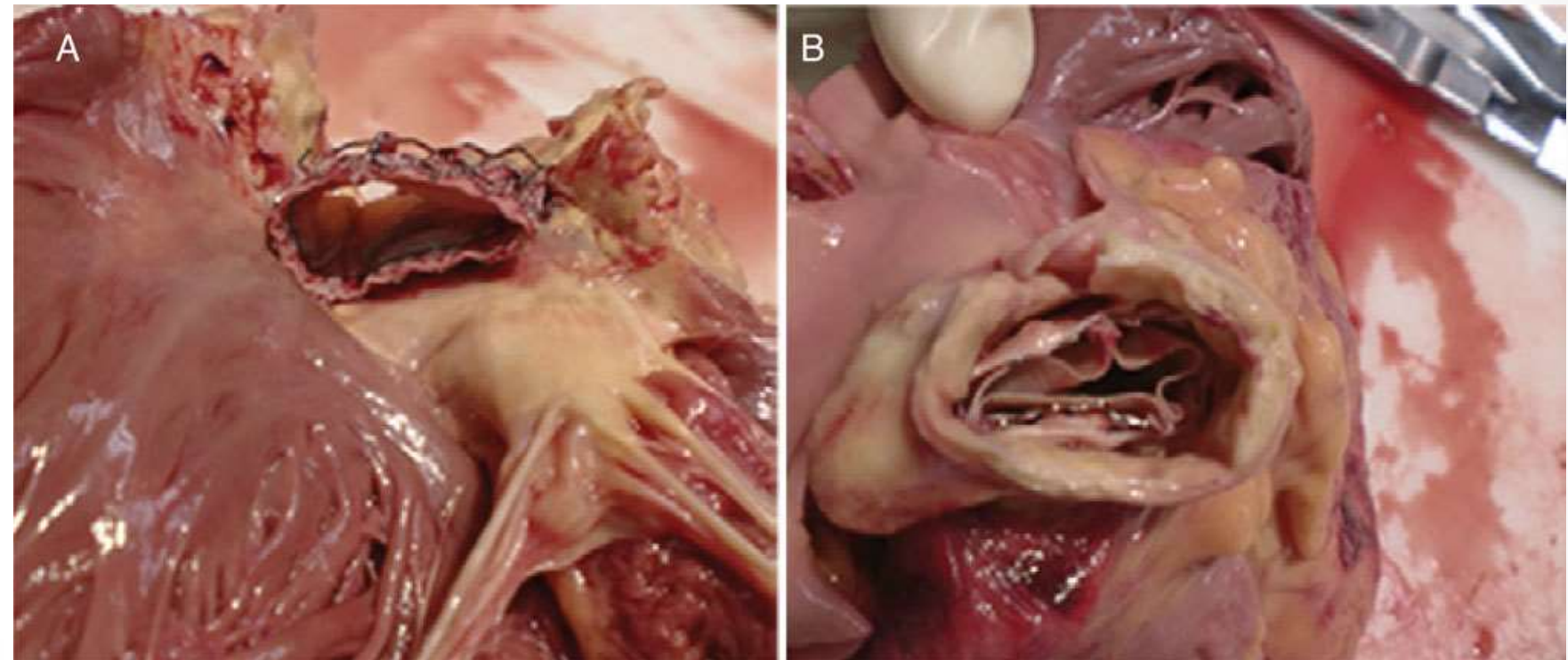
# VALVE ENDOCARDITIS



# LATE TRANSCATHETER HEART VALVE EMBOLIZATION



# TRANSCATHETER HEART VALVE COMPRESSION



# Transcatheter heart valve failure: a systematic review

Darren Mylotte<sup>1,2</sup>, Ali Andalib<sup>1</sup>, Pascal Thériault-Lauzier<sup>1</sup>, Magdalena Dorfmeister<sup>3</sup>, Mina Girgis<sup>1</sup>, Waleed Alharbi<sup>1</sup>, Michael Chetrit<sup>1</sup>, Christos Galatas<sup>1</sup>, Samuel Mamane<sup>1</sup>, Igal Sebag<sup>4</sup>, Jean Buithieu<sup>1</sup>, Luc Bilodeau<sup>1</sup>, Benoit de Varennes<sup>5</sup>, Kevin Lachapelle<sup>5</sup>, Ruediger Lange<sup>3</sup>, Giuseppe Martucci<sup>1</sup>, Renu Virmani<sup>6</sup>, and Nicolo Piazza<sup>1,3\*</sup>

<sup>1</sup>Department of Interventional Cardiology, McGill University Health Centre, Montreal, QC, Canada; <sup>2</sup>Department of Cardiology, Galway University Hospital, Galway, Ireland;

<sup>3</sup>Department of Cardiac Surgery, German Heart Center, Munich, Germany; <sup>4</sup>Department of Cardiology, Mortimer Davis, Jewish General Hospital, Montreal, QC, Canada;

<sup>5</sup>Department of Cardiovascular Surgery, McGill University Health Centre, Montreal, QC, Canada; and <sup>6</sup>CVPath Institute, Gaithersburg, MD, USA

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See page 1284 for the editorial comment on this article (doi:10.1093/eurheartj/ehu459)

## Aims

A comprehensive description of transcatheter heart valve (THV) failure has not been performed. We undertook a systematic review to investigate the aetiology, diagnosis, management, and outcomes of THV failure.

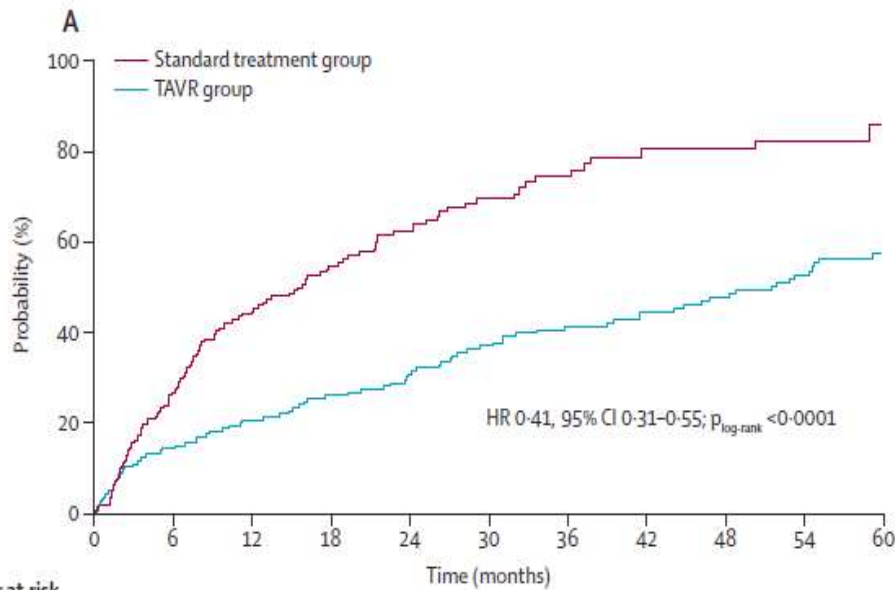
## Methods and results

The systematic review was performed in accordance with the PRISMA guidelines using EMBASE, MEDLINE, and Scopus. Between December 2002 and March 2014, 70 publications reported 87 individual cases of transcatheter aortic valve implantation (TAVI) failure. Similar to surgical bioprosthetic heart valve failure, we observed cases of prosthetic valve endocarditis (PVE) ( $n = 34$ ), structural valve failure ( $n = 13$ ), and THV thrombosis ( $n = 15$ ). The microbiological profile of THV PVE was similar to surgical PVE, though one-quarter had satellite mitral valve endocarditis, and surgical intervention was required in 40% (75% survival). Structural valve failure occurred most frequently due to leaflet calcification and was predominantly treated by redo-THV (60%). Transcatheter heart valve thrombosis occurred at a mean  $9 \pm 7$  months post-implantation and was successfully treated by prolonged anticoagulation in three-quarters of cases. Two novel causes of THV failure were identified: late THV embolization ( $n = 18$ ); and THV compression ( $n = 7$ ) following cardiopulmonary resuscitation (CPR). These failure modes have not been reported in the surgical literature. Potential risk factors for late THV embolization include low prosthesis implantation, THV undersizing/underexpansion, bicuspid, and non-calcified anatomy. Transcatheter heart valve embolization mandated surgery in 80% of patients. Transcatheter heart valve compression was noted at post-mortem in most cases.

## Conclusion

Transcatheter heart valves are susceptible to failure modes typical to those of surgical bioprostheses and unique to their specific design. Transcatheter heart valve compression and late embolization represent complications previously unreported in the surgical literature.

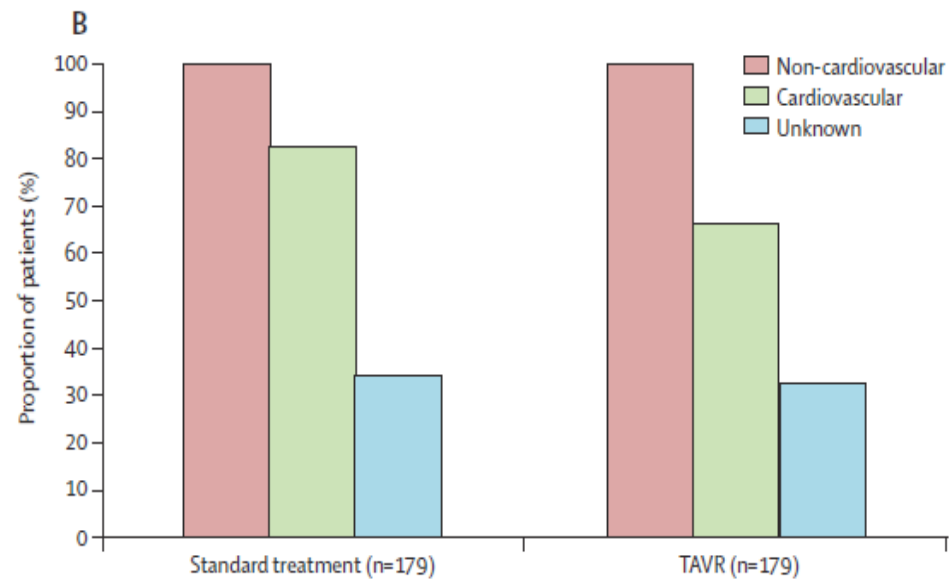
## CARDIOVASCULAR MORTALITY



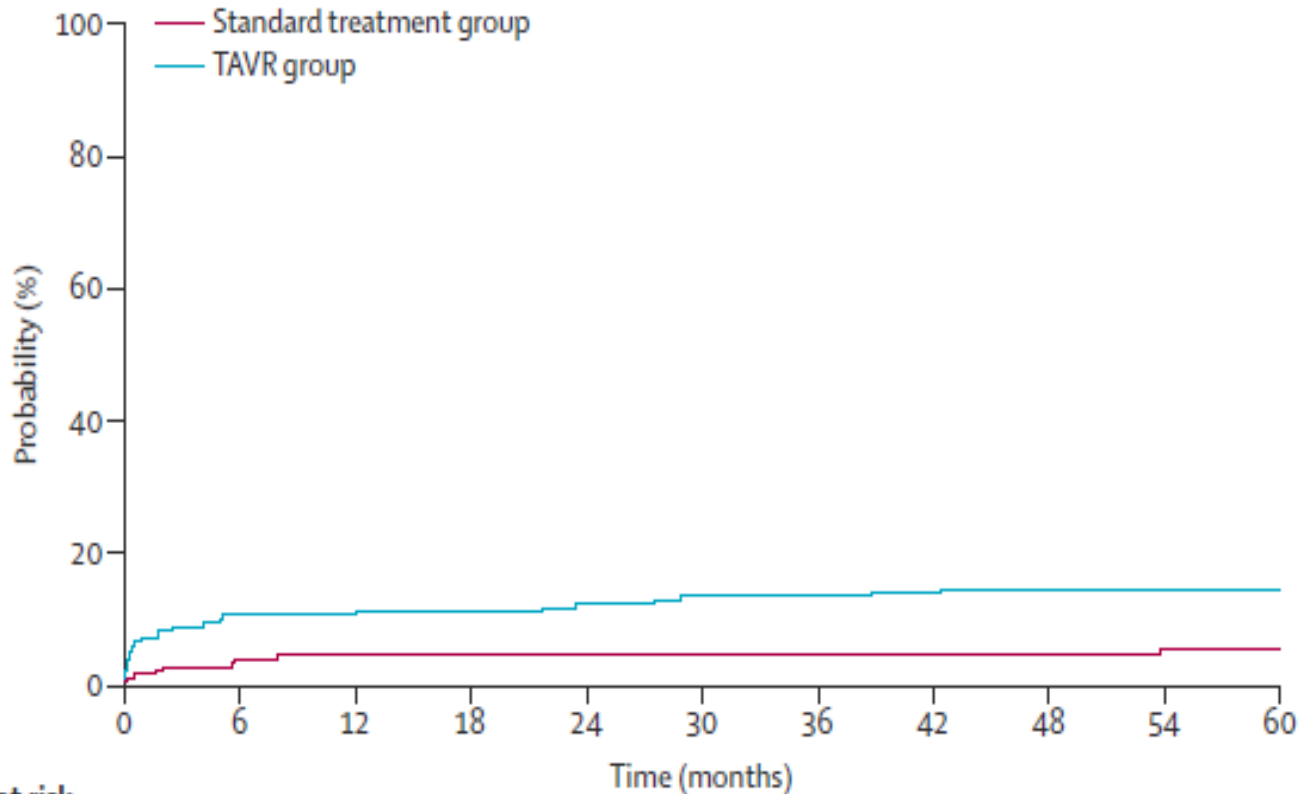
Number at risk

	0	6	12	18	24	30	36	42	48	54	60
Standard treatment group	179	121	85	62	46	27	19	11	11	9	3
TAVR group	179	138	124	110	101	89	81	72	63	53	35

## CAUSES OF DEATH



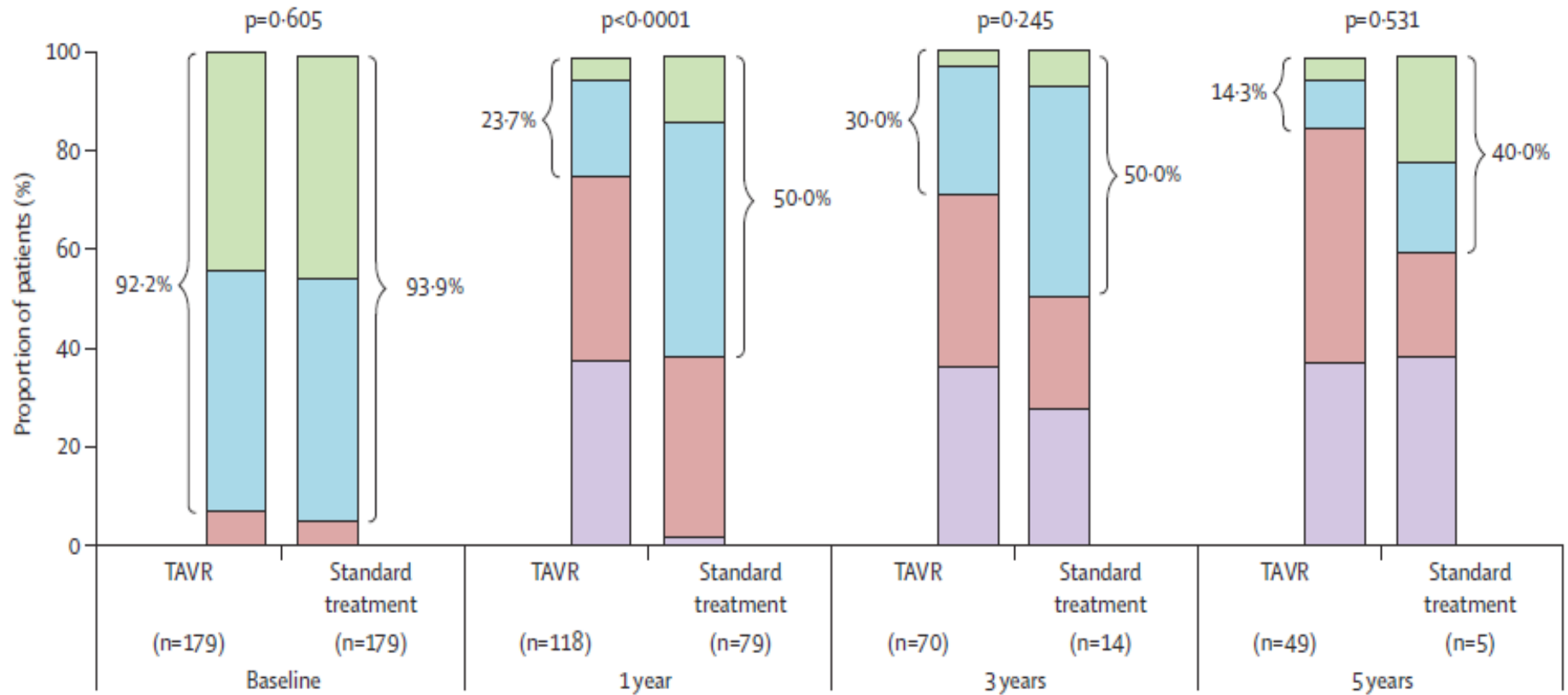
# RISK OF STROKE



## Number at risk

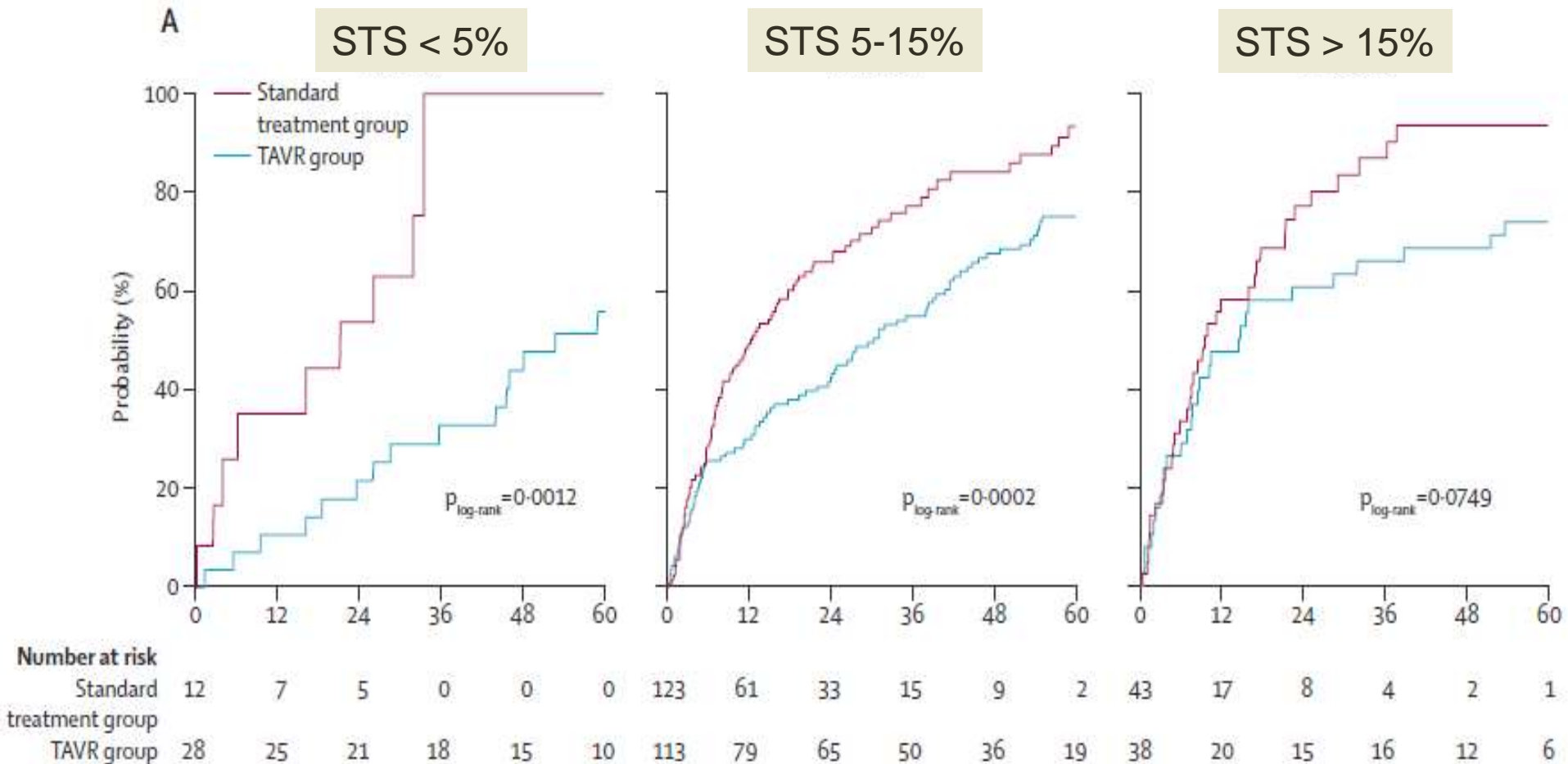
Standard treatment group	179	118	84	62	46	27	19	11	11	8	3
TAVR group	179	128	116	105	96	83	75	65	56	48	34

# NYHA FUNCTIONAL CLASS OF THE SURVIVORS



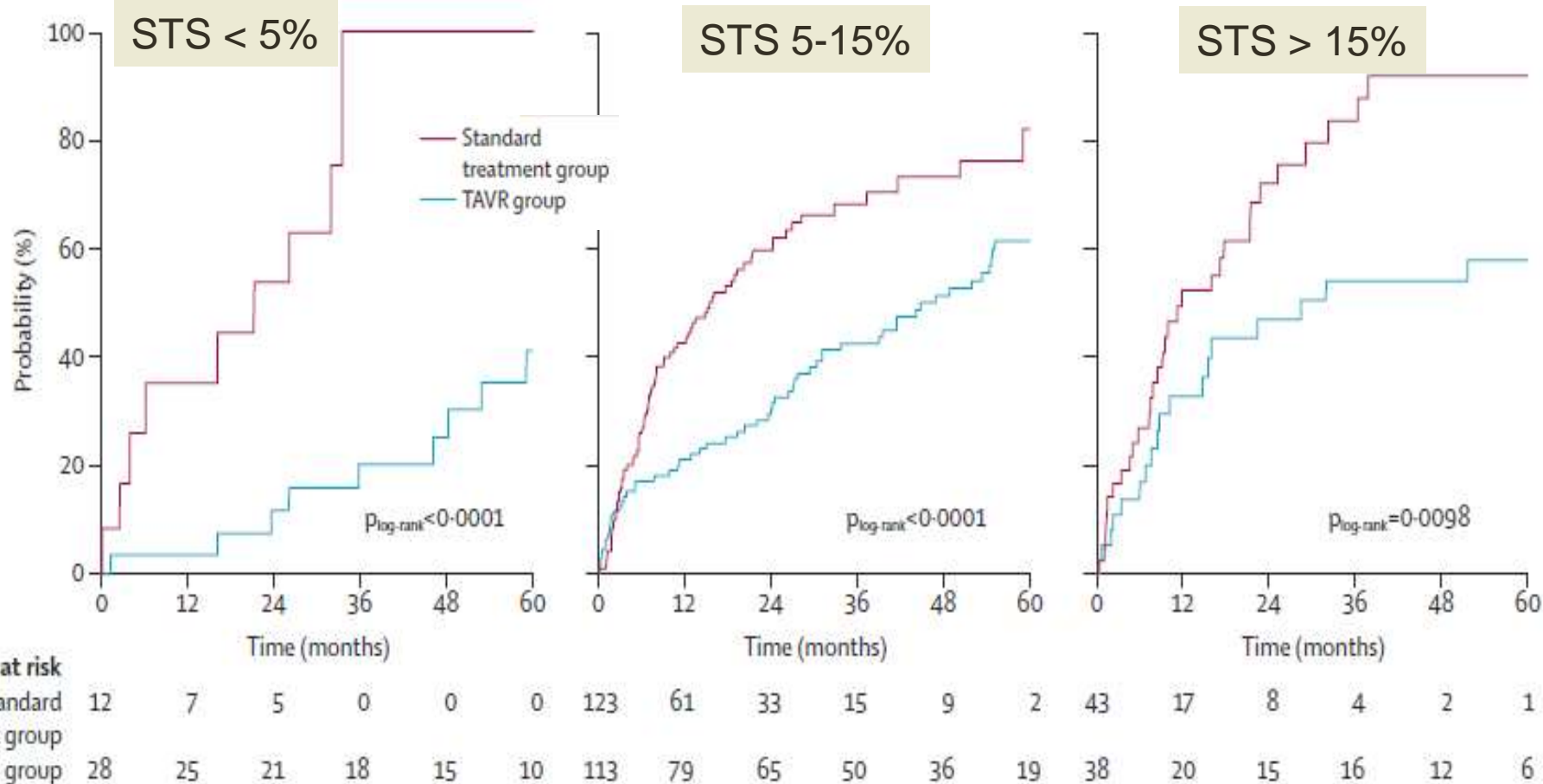
# MORTALITY OUTCOMES STRATIFIED BY STS SCORE

## ALL-CAUSE MORTALITY

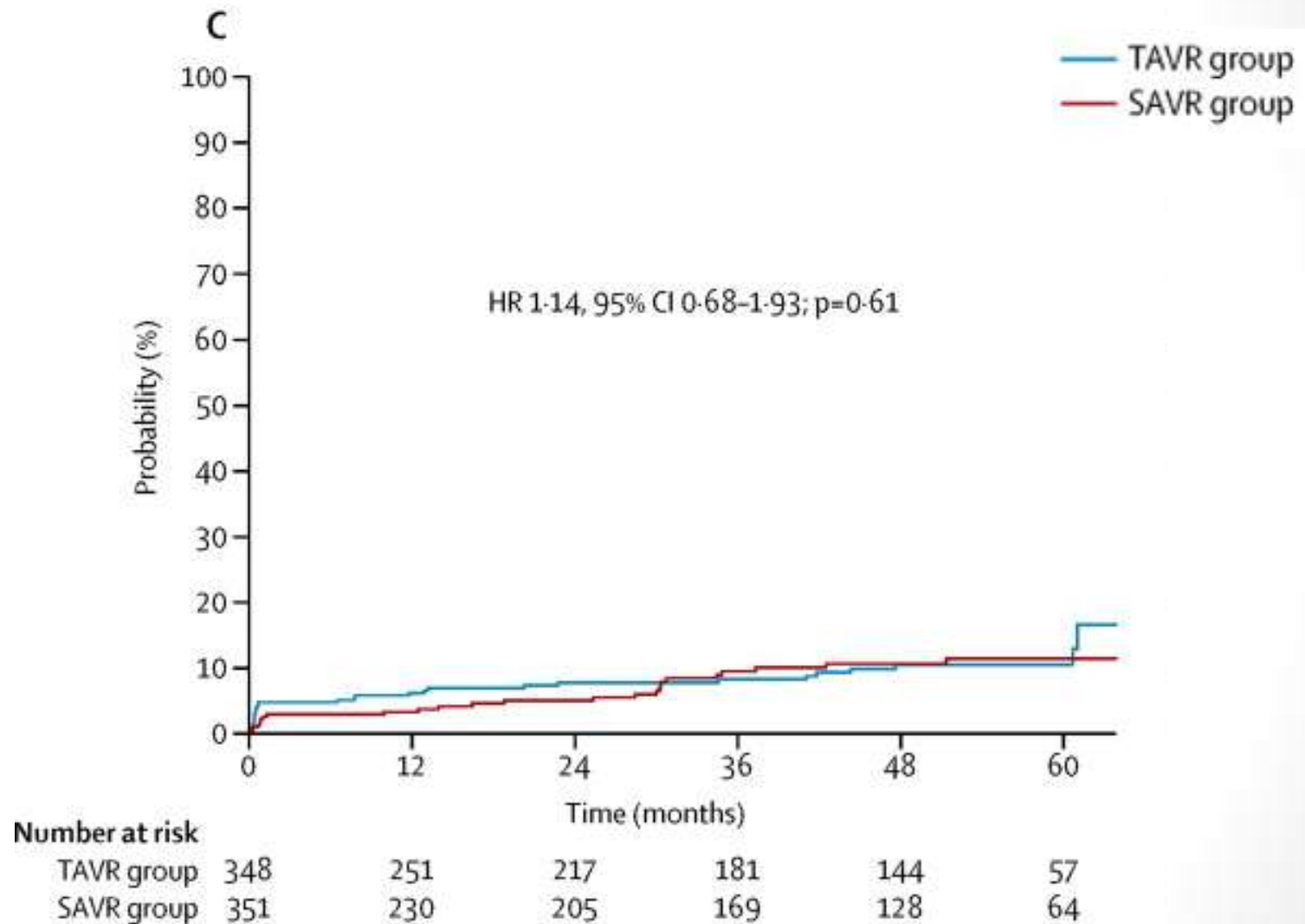


# MORTALITY OUTCOMES STRATIFIED BY STS SCORE

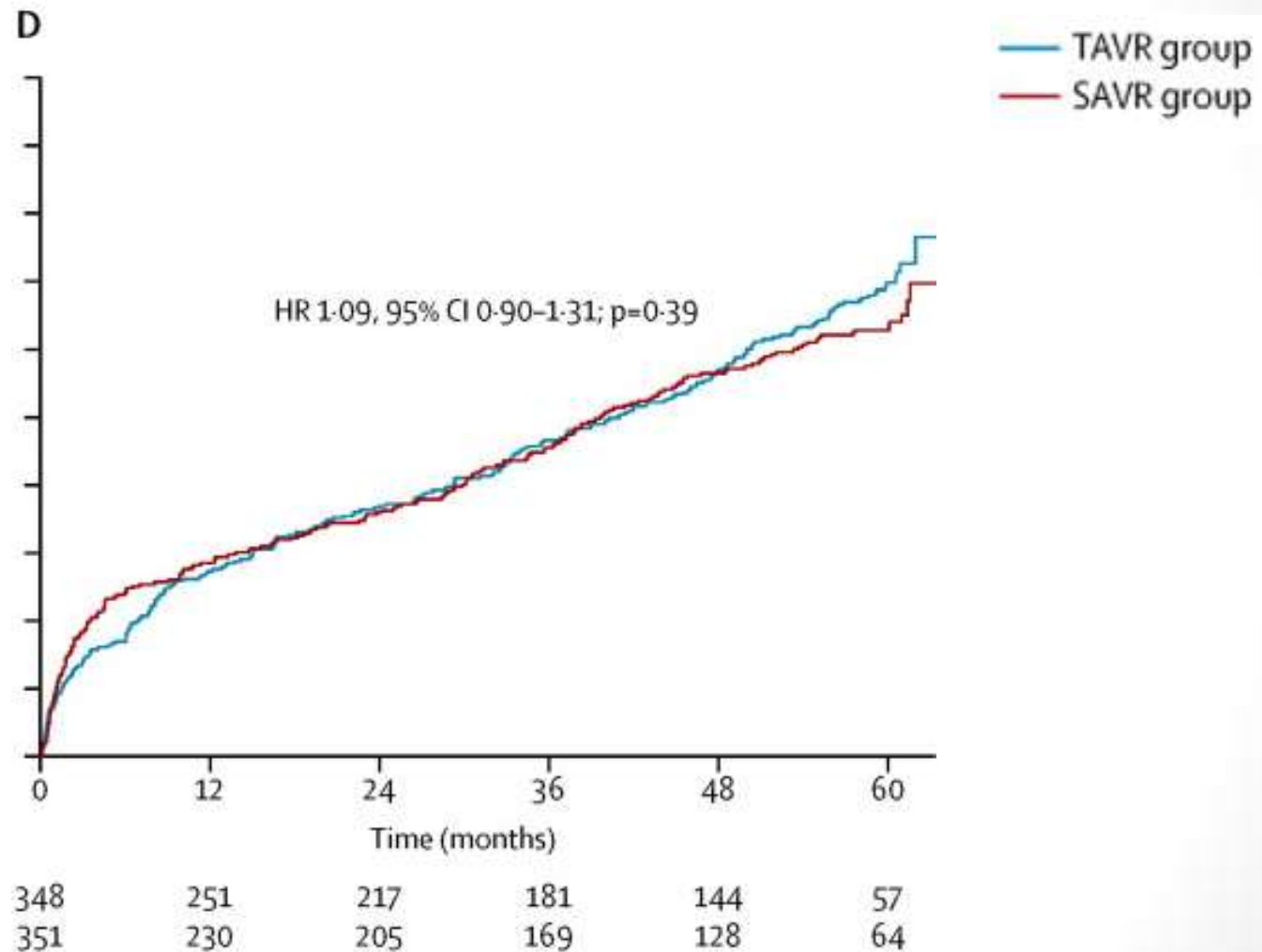
## CARDIOVASCULAR MORTALITY



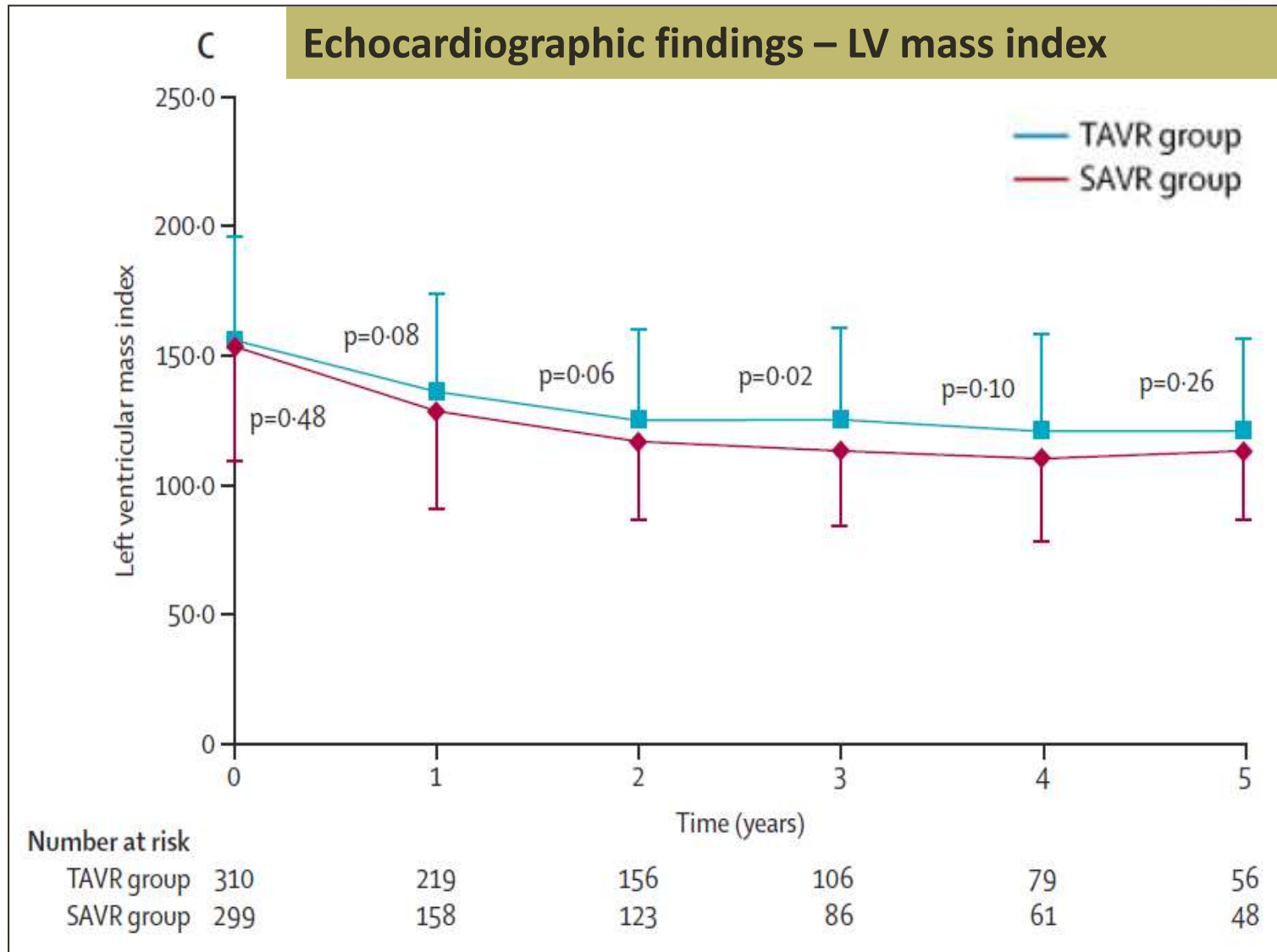
# STROKE OR TRANSIENT ISCHAEMIC ATTACK



# STROKE, TRANSIENT ISCHAEMIC ATTACK, OR DEATH FROM ANY CAUSE



# PARTNER TRIAL – 5-YEAR OUTCOMES

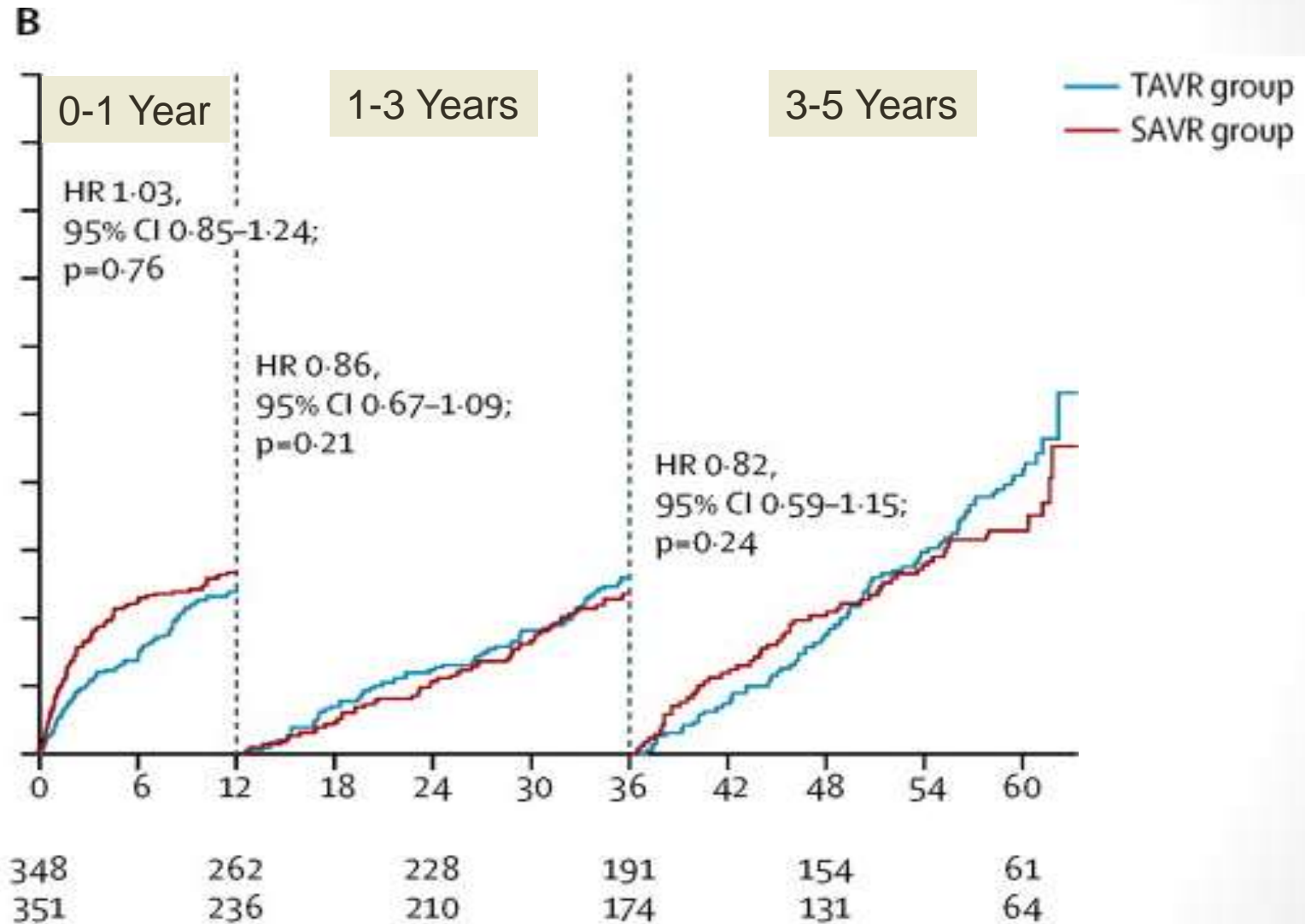


# PARTNER TRIAL

**The PARTNER Trial represents a paradigm shift in clinical trial design and execution for high-risk pts with severe aortic stenosis:**

- Rigorous study protocols and management
- Careful patient selection
- Interdisciplinary in all aspects
- Strict site selection

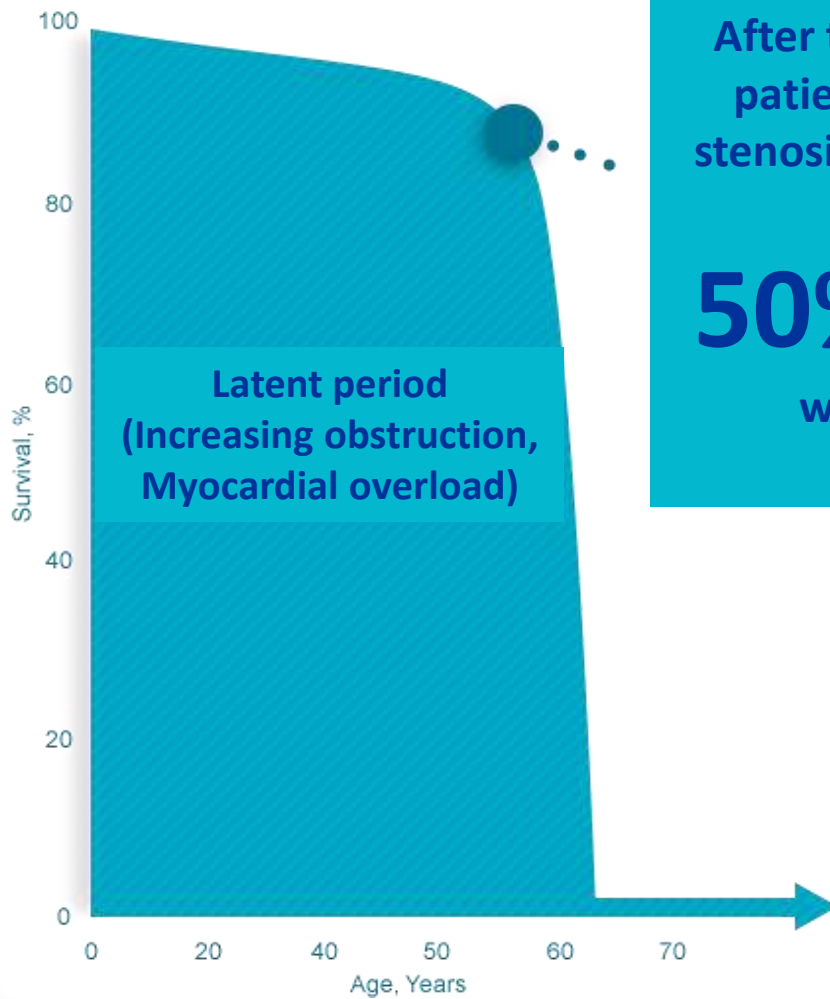
# MORTALITY – ALL-CAUSE DEATH BY LANDMARK



## PARTNER 5-YEAR OUTCOMES - LIMITATIONS

- **This trial includes an extremely high-risk cohort, with a mean STS of 12%. Other trials have had lower mean STS scores and the initial clinical experience of commercial TAVR with the Sapien and Sapien XT valves in the USA for high-risk and inoperable patients showed a mean STS of 7%**

# AORTIC STENOSIS

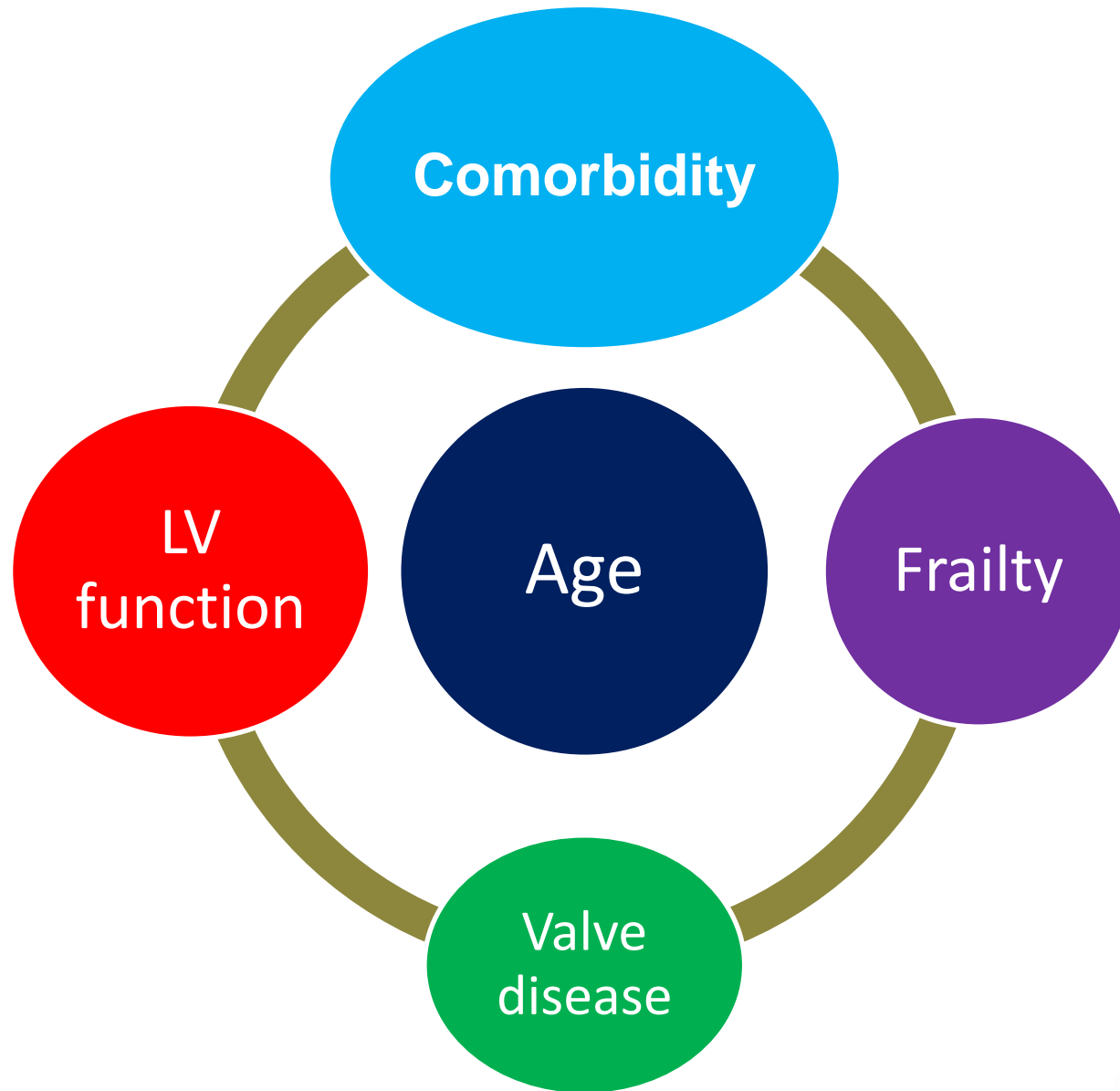


After the onset of symptoms  
patients with severe aortic  
stenosis have a survival rate as  
low as

**50% at 2 yrs**

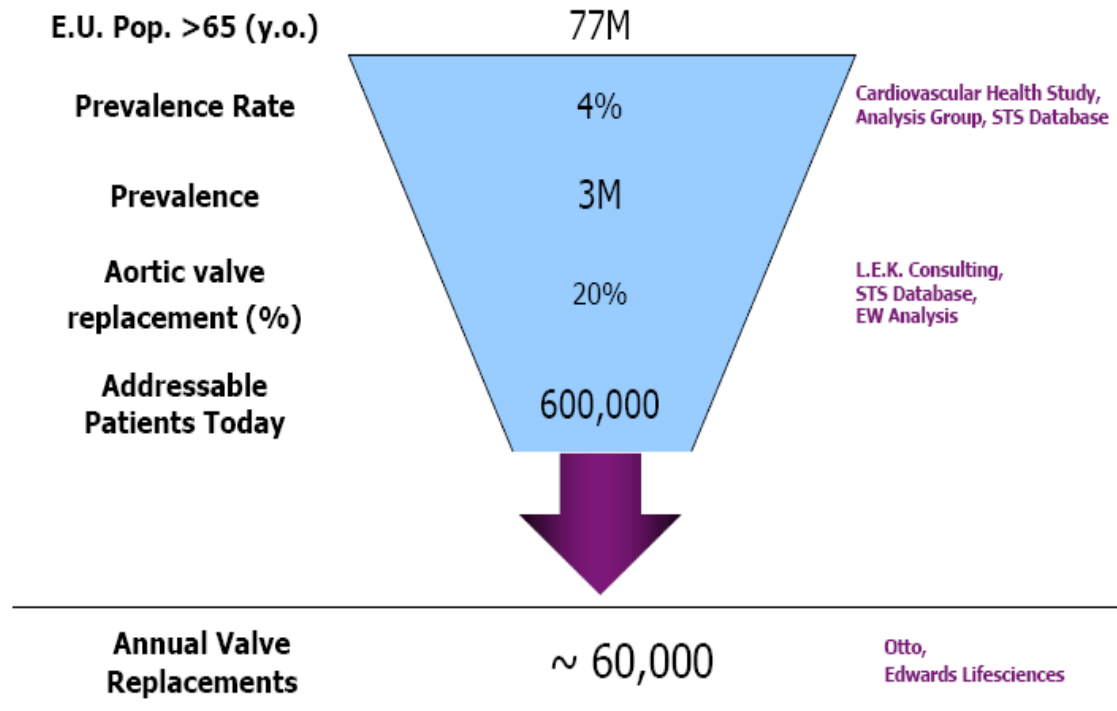
without aortic valve  
replacement

# AORTIC STENOSIS



# AORTIC STENOSIS

## Prevalence of Aortic Stenosis European Union 2008



# PARTNER TRIAL – 5-YEAR OUTCOMES

## 5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomised controlled trial



Samir R Kapadia, Martin B Leon, Raj R Makkar, E Murat Tuzcu, Lars G Svensson, Susheel Kodali, John G Webb, Michael J Mack, Pamela S Douglas, Vinod H Thourani, Vasilis C Babaliaros, Howard C Herrmann, Wilson Y Szeto, Augusto D Pichard, Mathew R Williams, Gregory P Fontana, D Craig Miller, William N Anderson, Jodi J Akin\*, Michael J Davidson†, Craig R Smith, for the PARTNER trial investigators

### Summary

**Background** Based on the early results of the Placement of Aortic Transcatheter Valves (PARTNER) trial, transcatheter aortic valve replacement (TAVR) is an accepted treatment for patients with severe aortic stenosis who are not suitable for surgery. However, little information is available about the late clinical outcomes in such patients.

**Methods** We did this randomised controlled trial at 21 experienced valve centres in Canada, Germany, and the USA. We enrolled patients with severe symptomatic inoperable aortic stenosis and randomly assigned (1:1) them to transfemoral TAVR or to standard treatment, which often included balloon aortic valvuloplasty. Patients and their treating physicians were not masked to treatment allocation. The randomisation was done centrally, and sites learned of the assignment only after a patient had been screened, consented, and entered into the database. The primary outcome of the trial was all-cause mortality at 1 year in the intention-to-treat population, here we present the prespecified findings after 5 years. This study is registered with ClinicalTrials.gov, number NCT00530894.

**Findings** We screened 3015 patients, of whom 358 were enrolled (mean age 83 years, Society of Thoracic Surgeons Predicted Risk of Mortality 11·7%, 54% female). 179 were assigned to TAVR treatment and 179 were assigned to standard treatment. 20 patients crossed over from the standard treatment group and ten withdrew from study, leaving only six patients at 5 years, of whom five had aortic valve replacement treatment outside of the study. The risk of all-cause mortality at 5 years was 71·8% in the TAVR group versus 93·6% in the standard treatment group (hazard ratio 0·50, 95% CI 0·39–0·65;  $p < 0·0001$ ). At 5 years, 42 (86%) of 49 survivors in the TAVR group had New York Heart Association class 1 or 2 symptoms compared with three (60%) of five in the standard treatment group. Echocardiography after TAVR showed durable haemodynamic benefit (aortic valve area 1·52 cm<sup>2</sup> at 5 years, mean gradient 10·6 mm Hg at 5 years), with no evidence of structural valve deterioration.

**Interpretation** TAVR is more beneficial than standard treatment for treatment of inoperable aortic stenosis. TAVR should be strongly considered for patients who are not surgical candidates for aortic valve replacement to improve their survival and functional status. Appropriate selection of patients will help to maximise the benefit of TAVR and reduce mortality from severe comorbidities.

**Funding** Edwards Lifesciences.

*Lancet* 2015; 385: 2485–91

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See Comment page 2439

See *Articles* page 2477

\*J J Akin MS has no affiliations  
†M J Davidson MD died in January, 2015

Cleveland Clinic, Cleveland, OH, USA (Prof S R Kapadia MD, Prof E M Tuzcu MD, Prof L G Svensson MD);

Columbia University Medical Center/New York Presbyterian Hospital, New York, NY, USA (Prof M B Leon MD, S Kodali MD, Prof C R Smith MD); Cedars

Sinai Medical Center, Los Angeles, CA, USA (R R Makkar MD); St Paul's

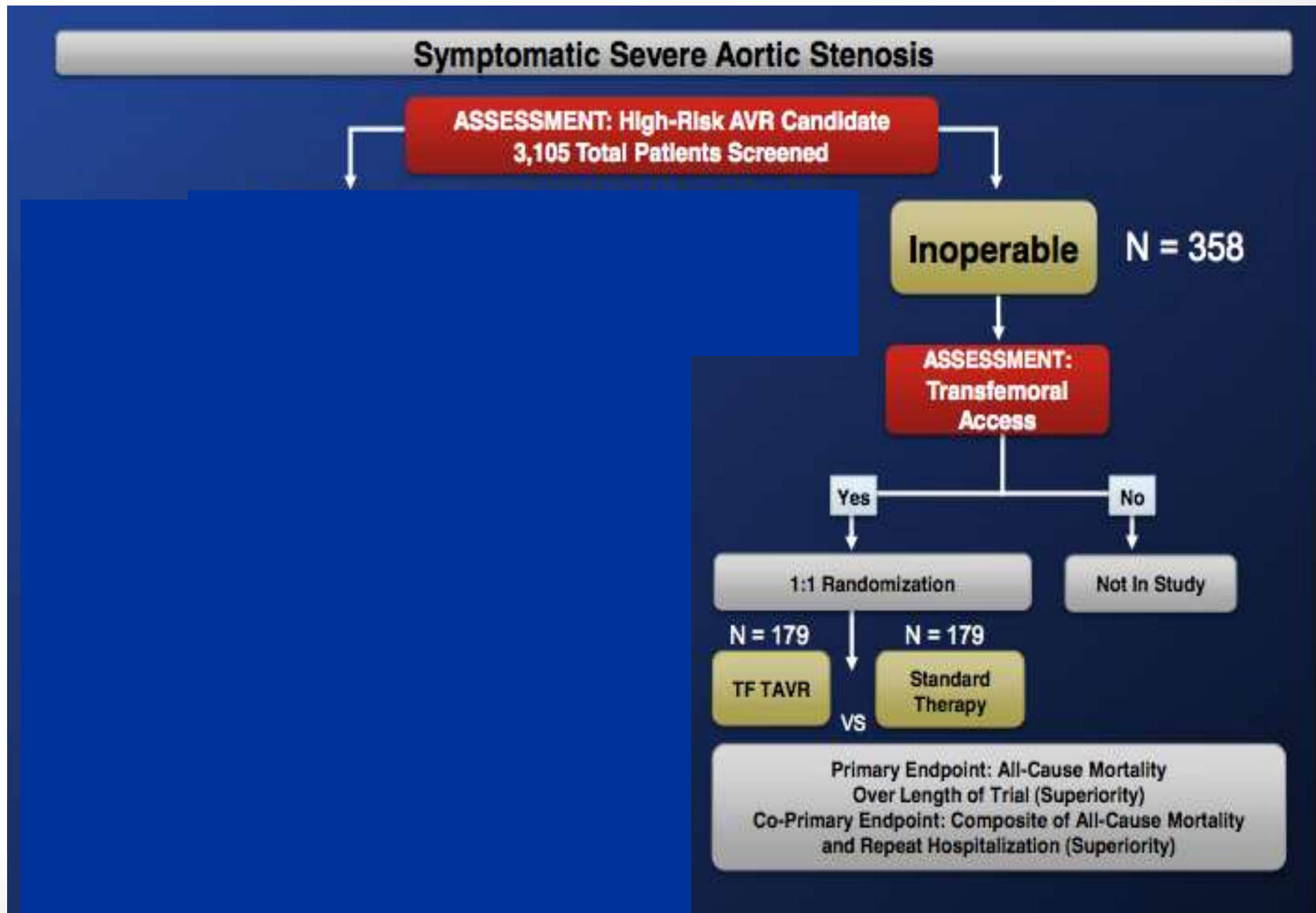
Hospital, Vancouver, BC, Canada (Prof J G Webb MD); Baylor Scott & White Health,

Plano, TX, USA (Prof M J Mack MD); Duke

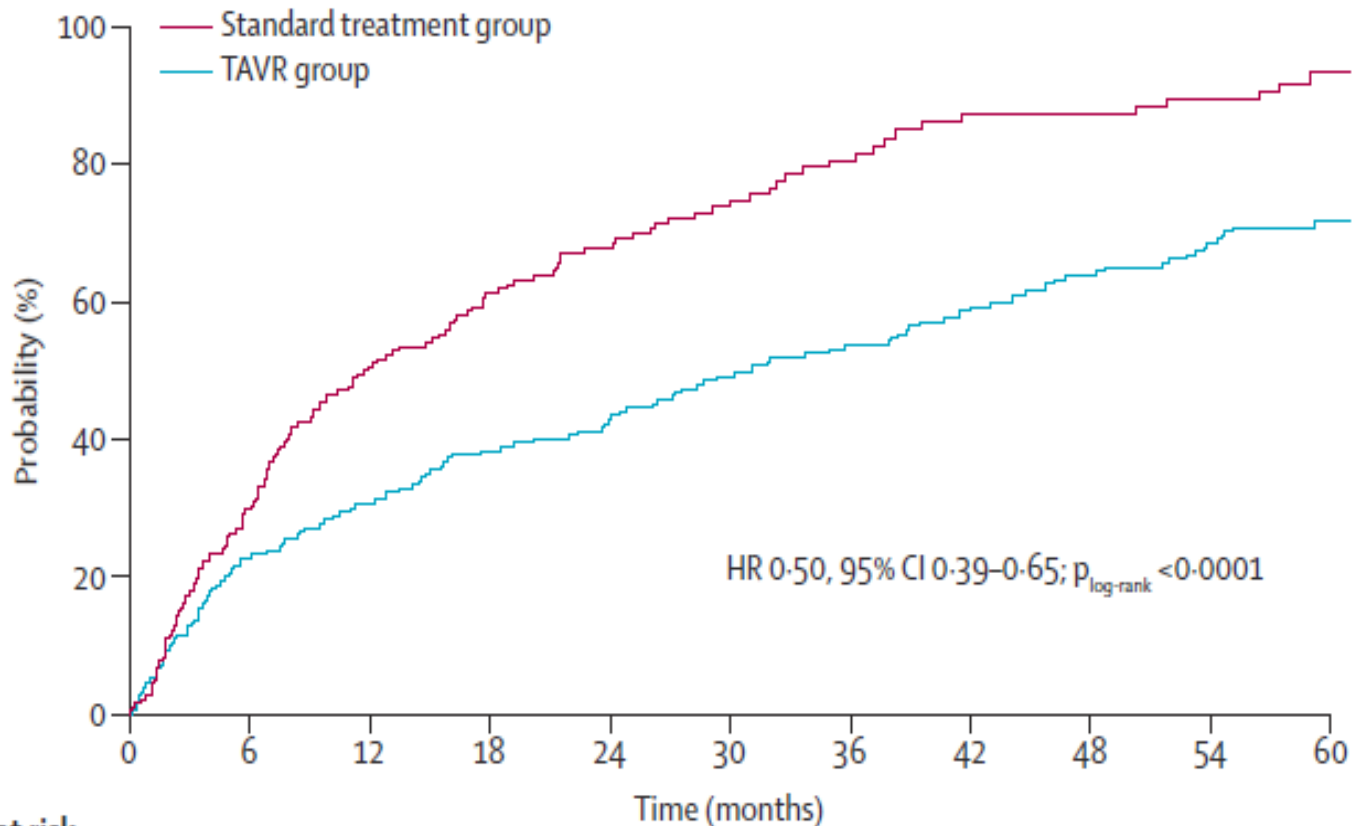
Clinical Research Institute/Duke University Medical Center, Durham, NC, USA (Prof P S Douglas MD); Emory

University School of Medicine, Atlanta, GA, USA

# PARTNER STUDY DESIGN



# PARTNER TRIAL – ALL CAUSE MORTALITY



Number at risk												
		0	6	12	18	24	30	36	42	48	54	60
Standard treatment group		179	121	85	62	46	27	19	11	11	9	3
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# RESEARCH IN CONTEXT

## Research in context

### Systematic review

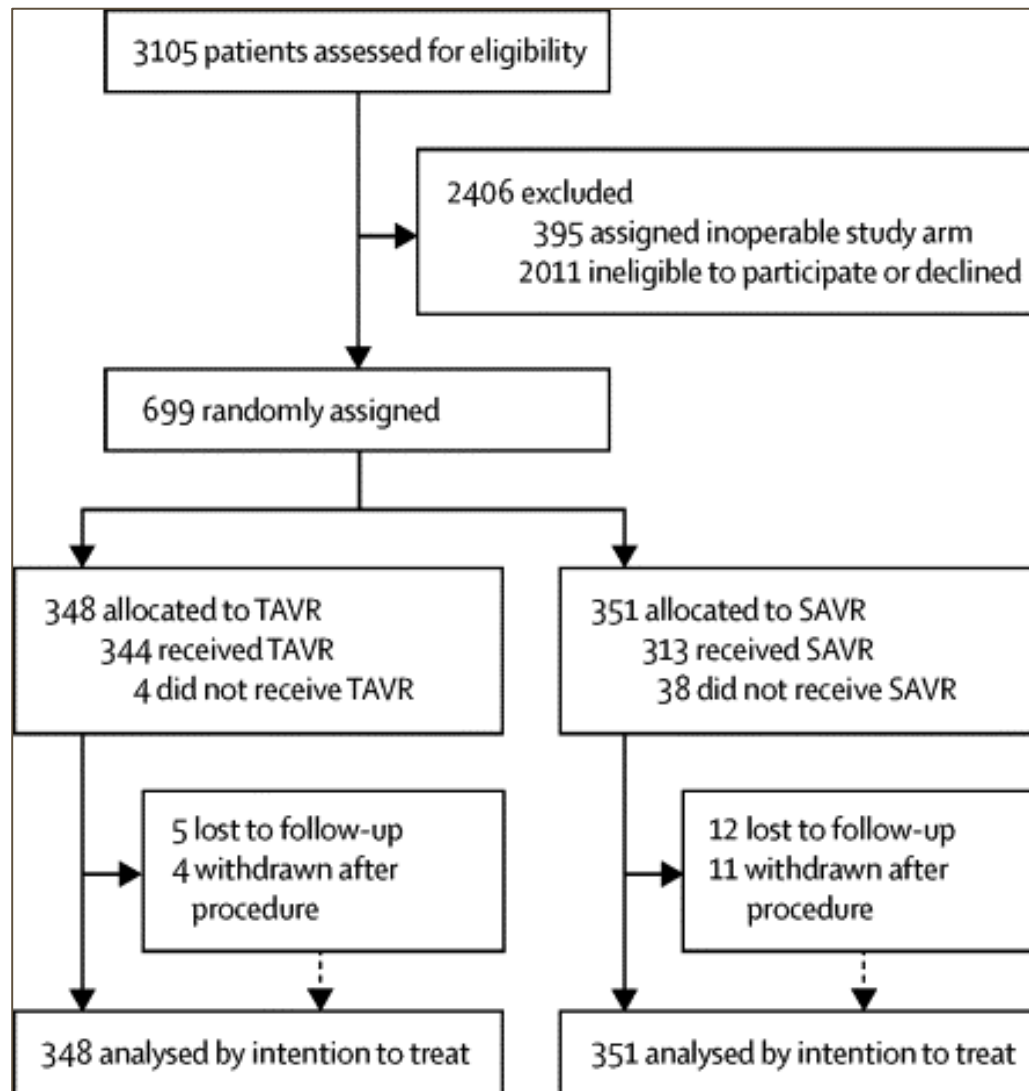
We searched Medline on March 7, 2015, with the terms “transcatheter aortic valve replacement” or “transcatheter aortic valve implantation”, which returned 3300 results, of which 284 were filtered “clinical trials”. We reviewed these citations and found no other randomised study comparing transcatheter aortic valve replacement with treatment without aortic valve replacement. The Placement of Aortic Transcatheter Valves (PARTNER) 1B trial is the only randomised trial published to date comparing outcomes of percutaneous aortic valve replacement with contemporary standard treatment (without aortic valve replacement) in surgically inoperable patients.

### Interpretation

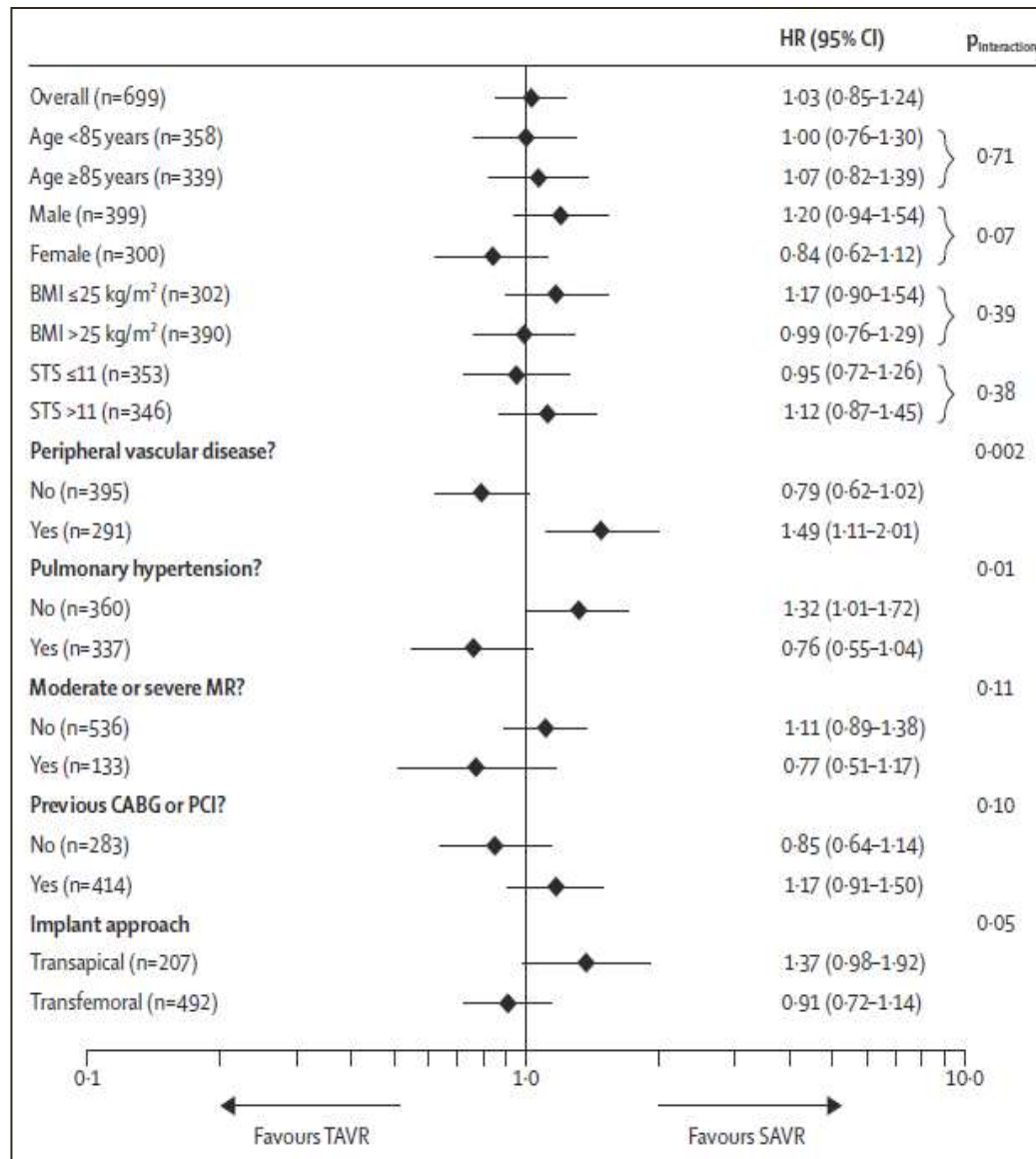
Although other technologies (either newer iterations of approved valves or new valve designs) have been and are

being tested in extreme risk patients, this study is the only randomised trial with a standard treatment control arm. This report describes the crucial 5-year (end of study) follow-up data from this study. This study shows sustained benefit of TAVR as measured by all-cause mortality, cardiovascular mortality, repeat hospital admission, and functional status compared with standard treatment. By contrast, long-term outcomes of patients with severe symptomatic aortic stenosis treated with standard treatment are dismal. Furthermore, this study confirmed transcatheter valve durability over 5 years of follow-up. This rigorous trial with comparative effectiveness analyses of adjudicated endpoints provides the benchmark for TAVR benefit compared with standard treatment.

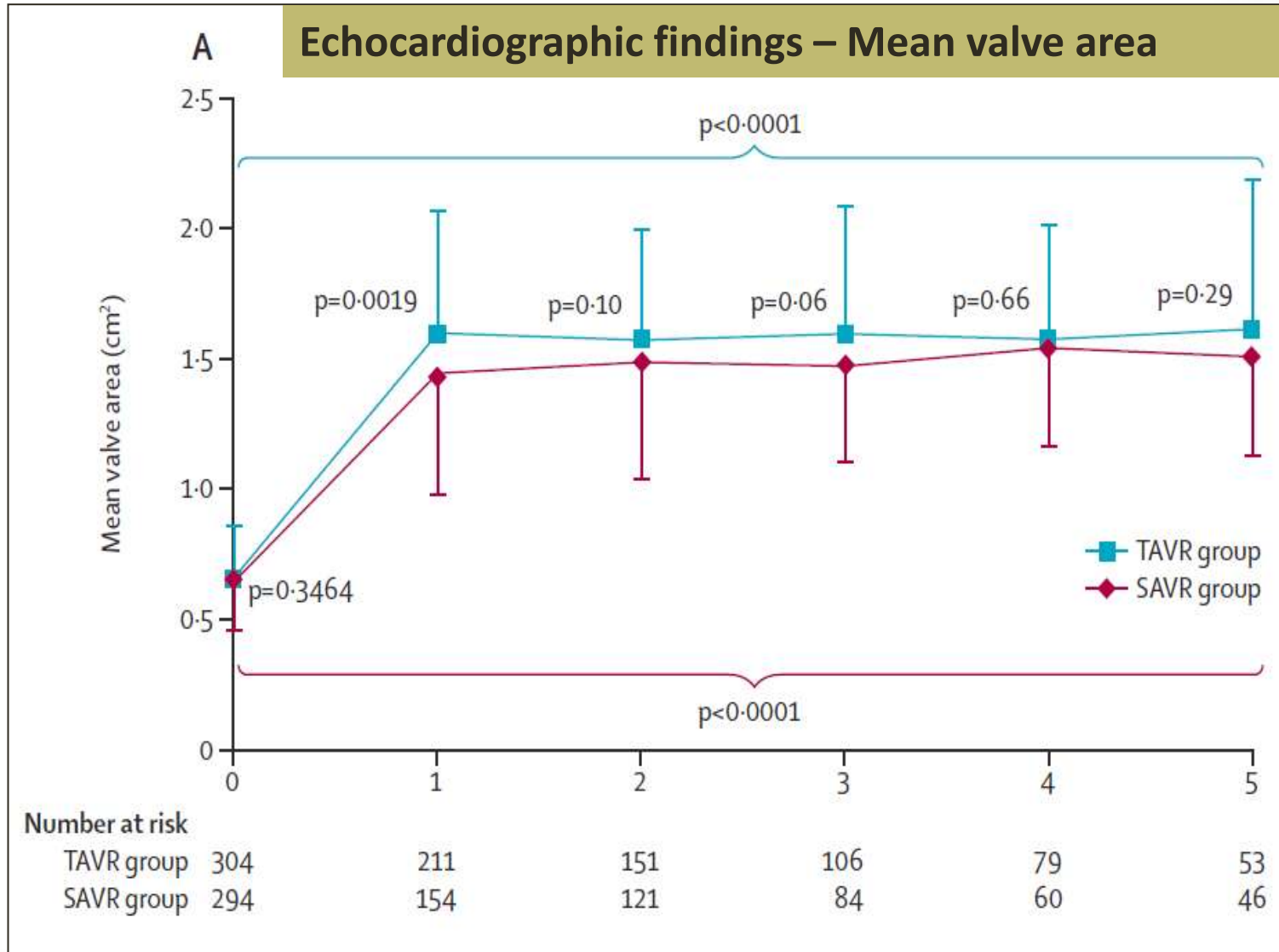
# TRIAL PROFILE



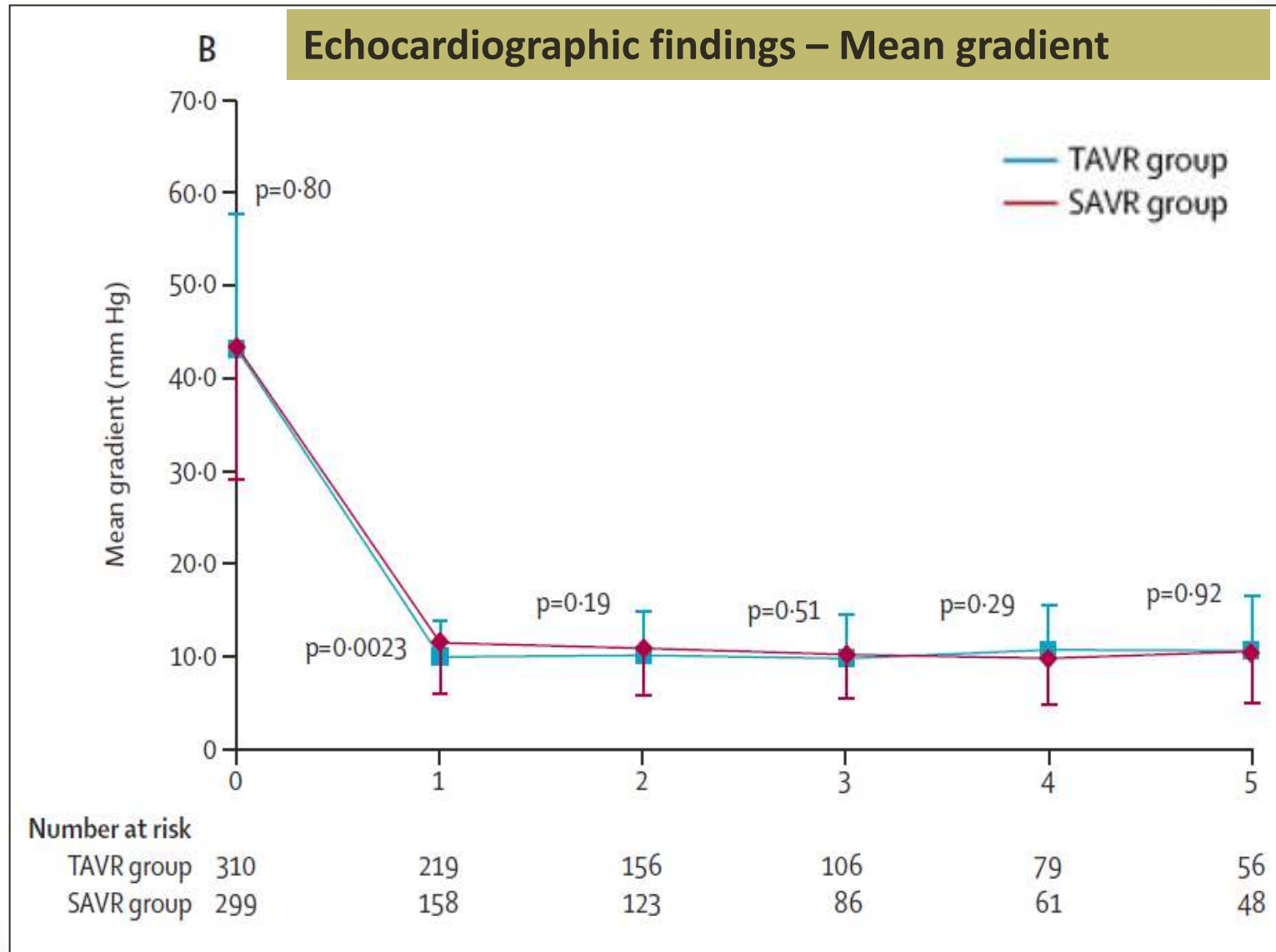
# PARTNER TRIAL – 5-YEAR OUTCOMES



# PARTNER TRIAL – 5-YEAR OUTCOMES



# PARTNER TRIAL – 5-YEAR OUTCOMES



# RESEARCH IN CONTEXT

## Research in context

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## **PARTNER 5-YEAR OUTCOMES - LIMITATIONS**

- **TAVR was done with a first-generation device requiring a large sheath-delivery system in a very high surgical risk population; major advances in devices have since occurred, and the Sapien device used in the trial is no longer being implanted.**
- **This trial is the first TAVR experience of most sites in the USA. A learning curve was undoubtedly present, which affected TAVR outcomes early in the trial, especially with the transapical approach**
- **This trial includes an extremely high-risk cohort, with a mean STS of 12%. Other trials have had lower mean STS scores and the initial clinical experience of commercial TAVR with the Sapien and Sapien XT valves in the USA for high-risk and inoperable patients showed a mean STS of 7%**

# TAVR is free of complications?



## Transcatheter heart valve failure: a systematic review

Darren Mylotte<sup>1,2</sup>, Ali Andalib<sup>1</sup>, Pascal Thériault-Lauzier<sup>1</sup>, Magdalena Dorfmeister<sup>3</sup>, Mina Girgis<sup>1</sup>, Waleed Alharbi<sup>1</sup>, Michael Chetrit<sup>1</sup>, Christos Galatas<sup>1</sup>, Samuel Mamane<sup>1</sup>, Igal Sebag<sup>4</sup>, Jean Buithieu<sup>1</sup>, Luc Bilodeau<sup>1</sup>, Benoit de Varennes<sup>5</sup>, Kevin Lachapelle<sup>5</sup>, Ruediger Lange<sup>3</sup>, Giuseppe Martucci<sup>1</sup>, Renu Virmani<sup>6</sup>, and Nicolo Piazza<sup>1,3\*</sup>

<sup>1</sup>Department of Interventional Cardiology, McGill University Health Centre, Montreal, QC, Canada; <sup>2</sup>Department of Cardiology, Galway University Hospital, Galway, Ireland; <sup>3</sup>Department of Cardiac Surgery, German Heart Center, Munich, Germany; <sup>4</sup>Department of Cardiology, Montmirail David, Jewish General Hospital, Montreal, QC, Canada; <sup>5</sup>Department of Cardiovascular Surgery, McGill University Health Centre, Montreal, QC, Canada; and <sup>6</sup>CVPath Institute, Gaithersburg, MD, USA

Received 30 January 2014; revised 20 August 2014; accepted 28 August 2014; online publication ahead of print 29 September 2014

See page 1284 for the editorial comment on this article (doi:10.1093/eurheartj/ehu459)

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A comprehensive description of transcatheter heart valve (THV) failure has not been performed. We undertook a systematic review to investigate the aetiology, diagnosis, management, and outcomes of THV failure.

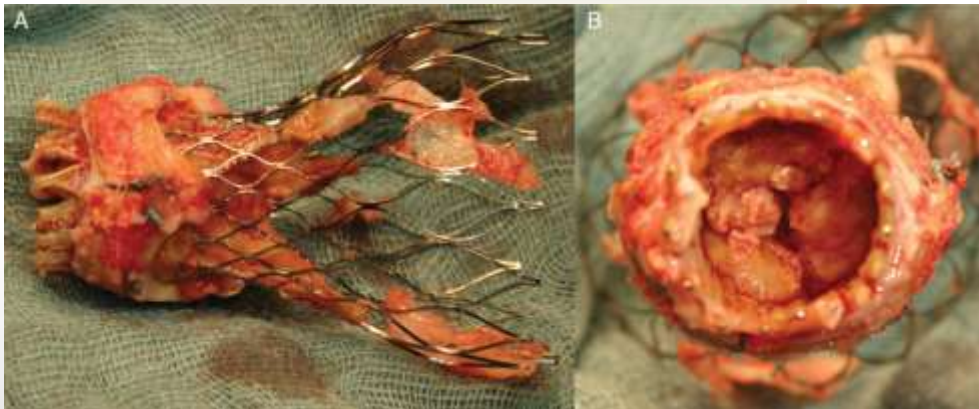
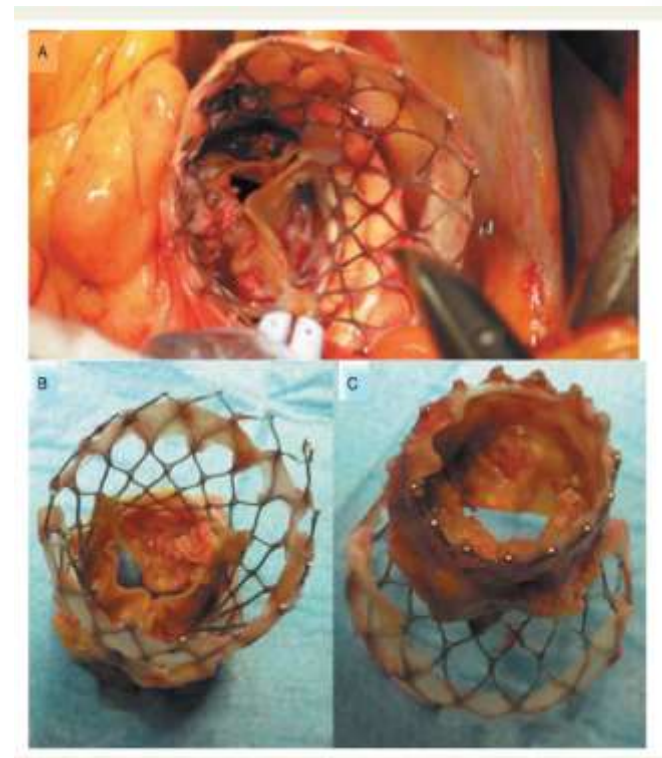
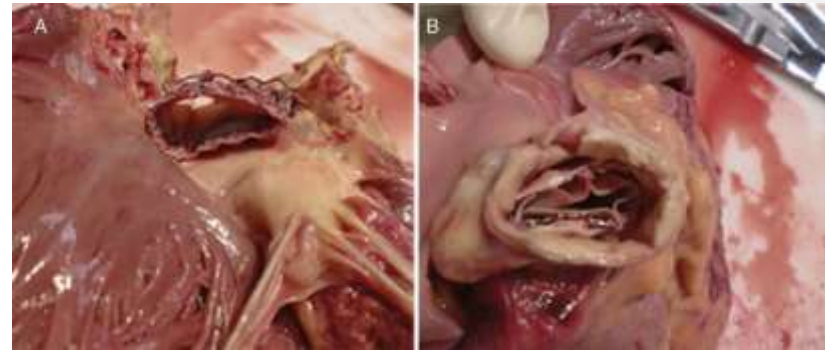
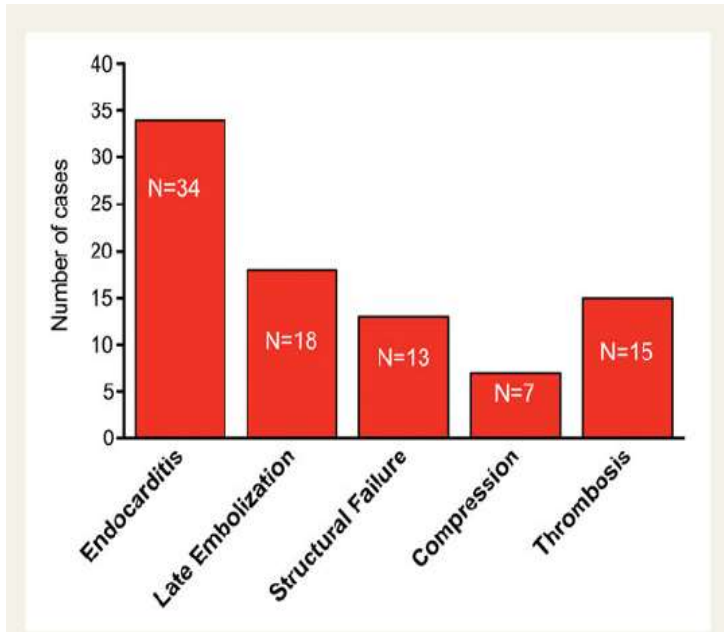
### Methods and results

The systematic review was performed in accordance with the PRISMA guidelines using EMBASE, MEDLINE, and Scopus. Between December 2002 and March 2014, 70 publications reported 87 individual cases of transcatheter aortic valve implantation (TAVI) failure. Similar to surgical bioprosthetic heart valve failure, we observed cases of prosthetic valve endocarditis (PVE) ( $n = 34$ ), structural valve failure ( $n = 13$ ), and THV thrombosis ( $n = 15$ ). The microbiological profile of THV PVE was similar to surgical PVE, though one-quarter had satellite mitral valve endocarditis, and surgical intervention was required in 40% (75% survival). Structural valve failure occurred most frequently due to leaflet calcification and was predominantly treated by redo-THV (60%). Transcatheter heart valve thrombosis occurred at a mean  $9 \pm 7$  months post-implantation and was successfully treated by prolonged anticoagulation in three-quarters of cases. Two novel causes of THV failure were identified: late THV embolization ( $n = 18$ ); and THV compression ( $n = 7$ ) following cardiopulmonary resuscitation (CPR). These failure modes have not been reported in the surgical literature. Potential risk factors for late THV embolization include low prosthesis implantation, THV undersizing/underexpansion, bicuspid, and non-calcified anatomy. Transcatheter heart valve embolization mandated surgery in 80% of patients. Transcatheter heart valve compression was noted at post-mortem in most cases.

### Conclusion

Transcatheter heart valves are susceptible to failure modes typical to those of surgical bioprostheses and unique to their specific design. Transcatheter heart valve compression and late embolization represent complications previously unreported in the surgical literature.

# TRANSCATHETER HEART VALVE FAILURE



## 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement

*Developed in collaboration with the American Heart Association, American Society of Echocardiography, European Association for Cardio-Thoracic Surgery, Heart Failure Society of America, Mended Hearts, Society of Cardiovascular Anesthesiologists, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance*

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# GUIDELINES

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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.	Ia	B

## Class I:

- Heart Team required
- On-site cardiac surgery
- Pts not suitable for AVR

## Class Ia:

- High-risk operable as an alternative to surgery; determined by heart team and case-based decisions

# GUIDELINES

J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132. doi: 10.1016/j.jtcvs.2014.05.014. Epub 2014 May 9.

## 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.

Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Creager MA, Curtis LH, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Ohman EM, Pressler SJ, Sellke FW, Shen WK, Stevenson WG, Yancy CW; American College of Cardiology; American College of Cardiology/American Heart Association; American Heart Association.

**TABLE 9. Summary of recommendations for AS: timing of intervention**

Recommendations	COR	LOE	References
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B	9,91,134,135
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B	136,137
AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B	108,138
AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity $\geq 5.0$ m/s) and low surgical risk	IIa	B	139,140
AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	IIa	B	25,47
AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity $\geq 4.0$ m/s (or mean pressure gradient $\geq 40$ mm Hg) with a valve area $\leq 1.0$ cm <sup>2</sup> at any dobutamine dose	IIa	B	43,141,142
AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF $\geq 50\%$ if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa	C	N/A
AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery	IIa	C	N/A
AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C	N/A