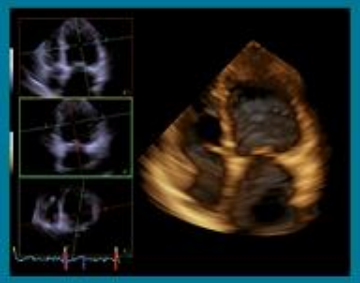


EuroValve

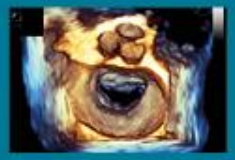
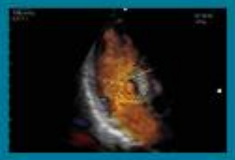
October 24-25, 2014

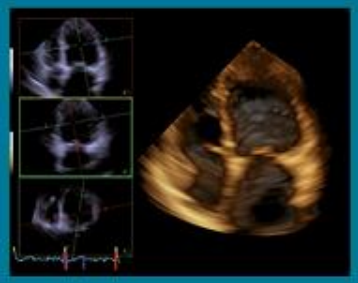
Measuring the risk in valve patients
Lessons learnt from the TAVI story?

Bernard Iung

Bichat Hospital, Paris, France





EuroValve

October 24-25, 2014

Faculty disclosure

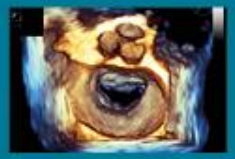
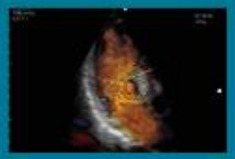
Bernard Iung

I disclose the following financial relationships:

Consultant for Abbott, Boehringer Ingelheim, Valtech

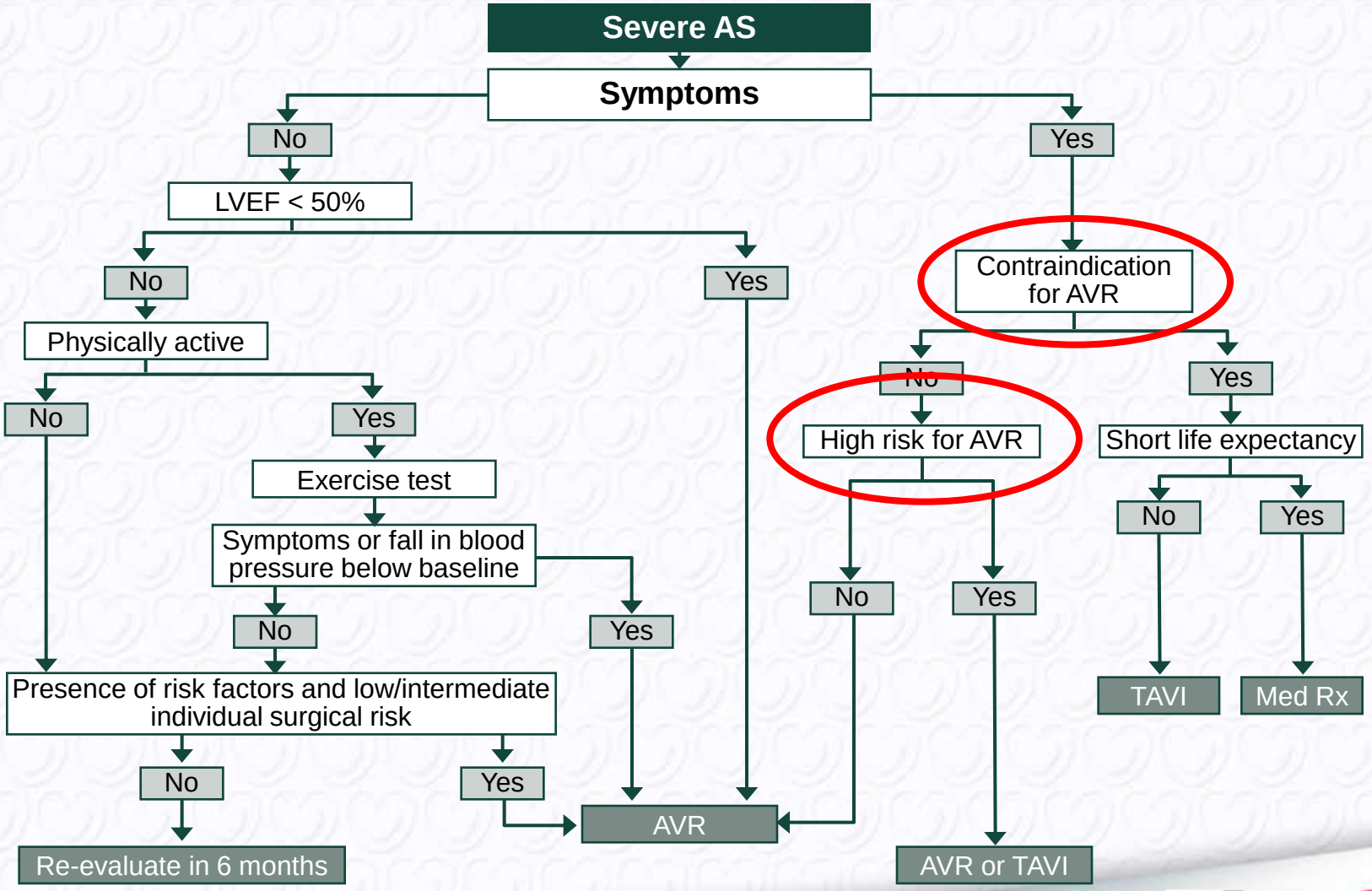
Paid speaker for Edwards Lifesciences



www.eurovalvecongress.com

Management of severe aortic stenosis



European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 & European Journal of Cardio-Thoracic Surgery 2012 - doi:10.1093/ejcts/ezs455).

www.escardio.org/guidelines

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Risk scores and contraindication for surgery

- **Contraindication for surgery (Partner B)**
  - 358 patients
  - Logistic Euroscore: 28%
  - STS score: 12%

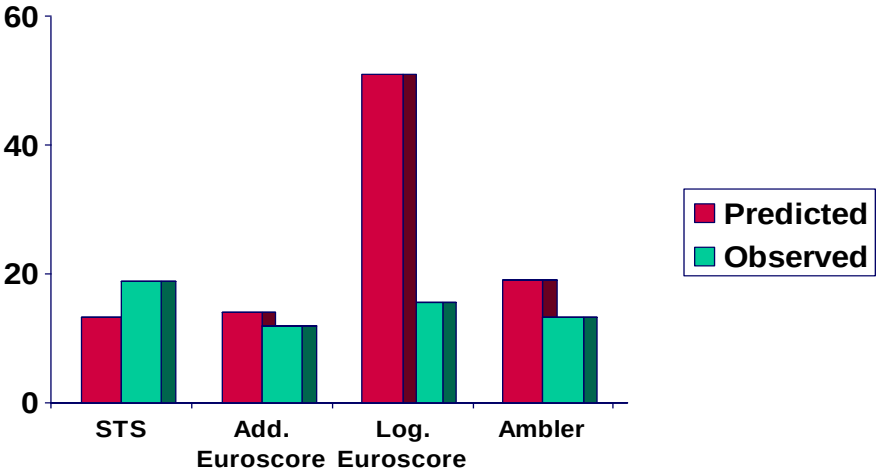
  (Leon et al. N Engl J Med 2010;363:1597-607)

- **High risk for surgery, but operable (Partner A)**
  - 699 patients
  - Logistic Euroscore: 29%
  - STS score: 12%

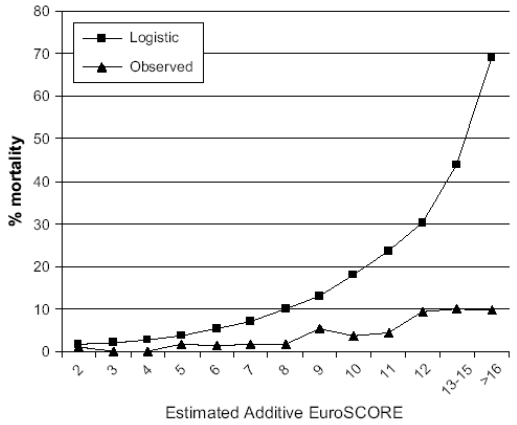
  (Smith et al. N Engl J Med 2011;364:2187-98)

Risk scores in valve surgery

- Good discrimination (low vs. high risk)
  C-index 0.75-0.80
- But poor calibration (predicted vs. observed risk)



(Dewey et al. JTCS 2008;135:180-7

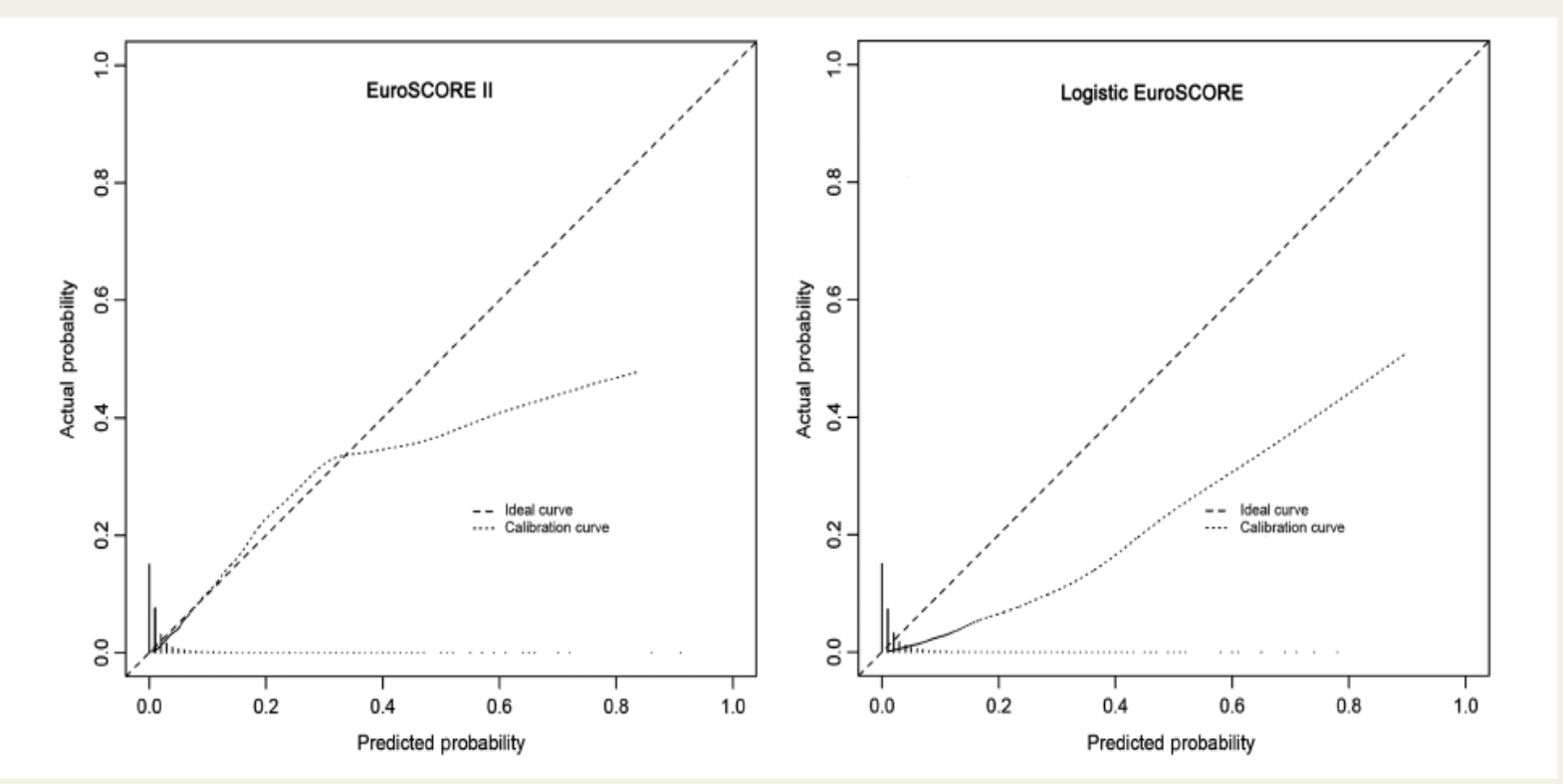


(Brown et al. JTCS 2008;136:566-71)

- Euroscore II
  improved calibration, but no specific data in high-risk patients
  (Nashef et al. Eur J Cardiothorac Surg 2012;41:734-45)

EuroSCORE I and II: external validation

- Good discrimination (c-index 0.82)

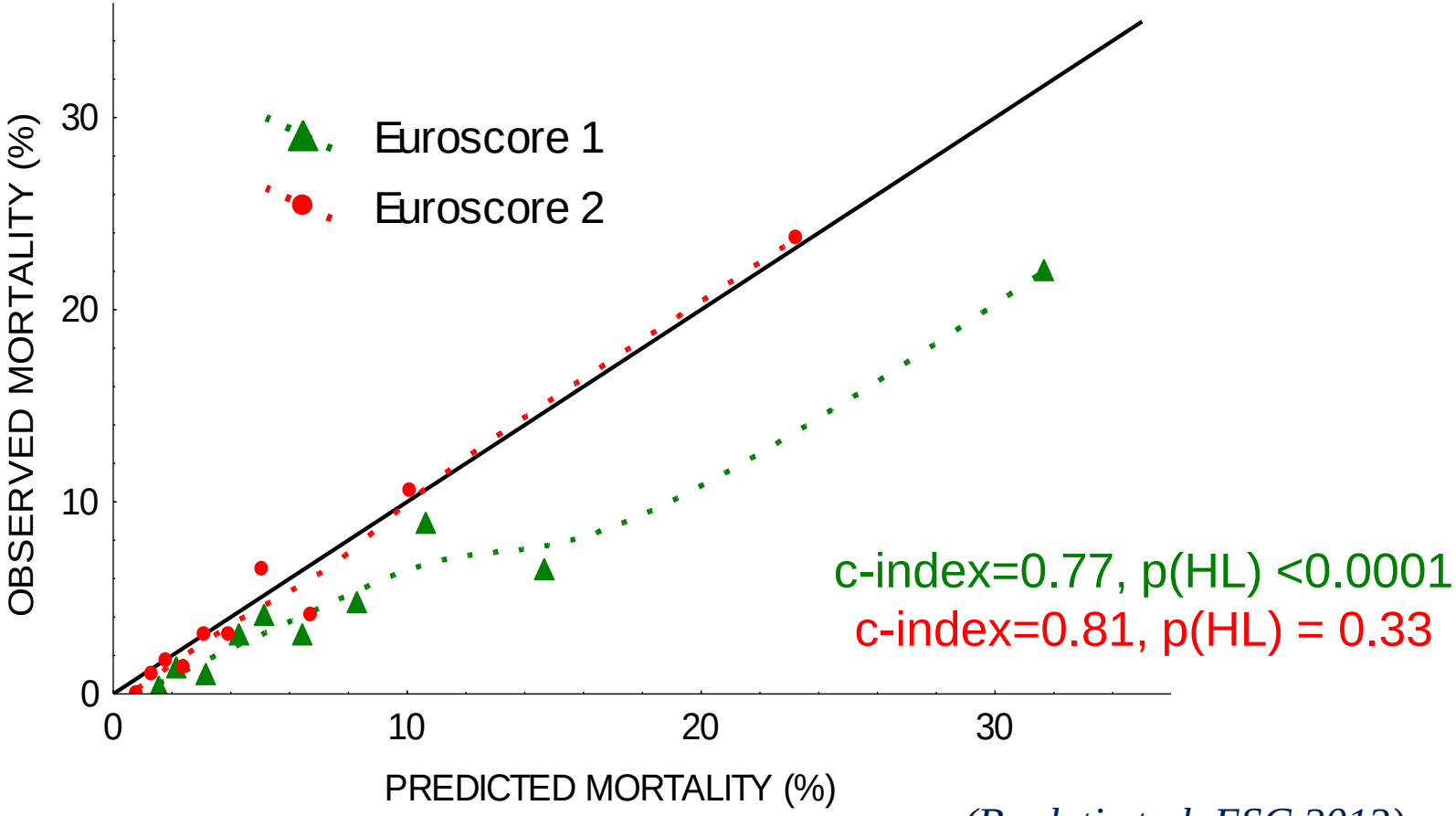


- Better calibration than Euroscore I only for low and intermediate risks

(Barili et al. Eur Heart J 2013;34:22-9)

EuroSCORE II: validation in valvular diseases

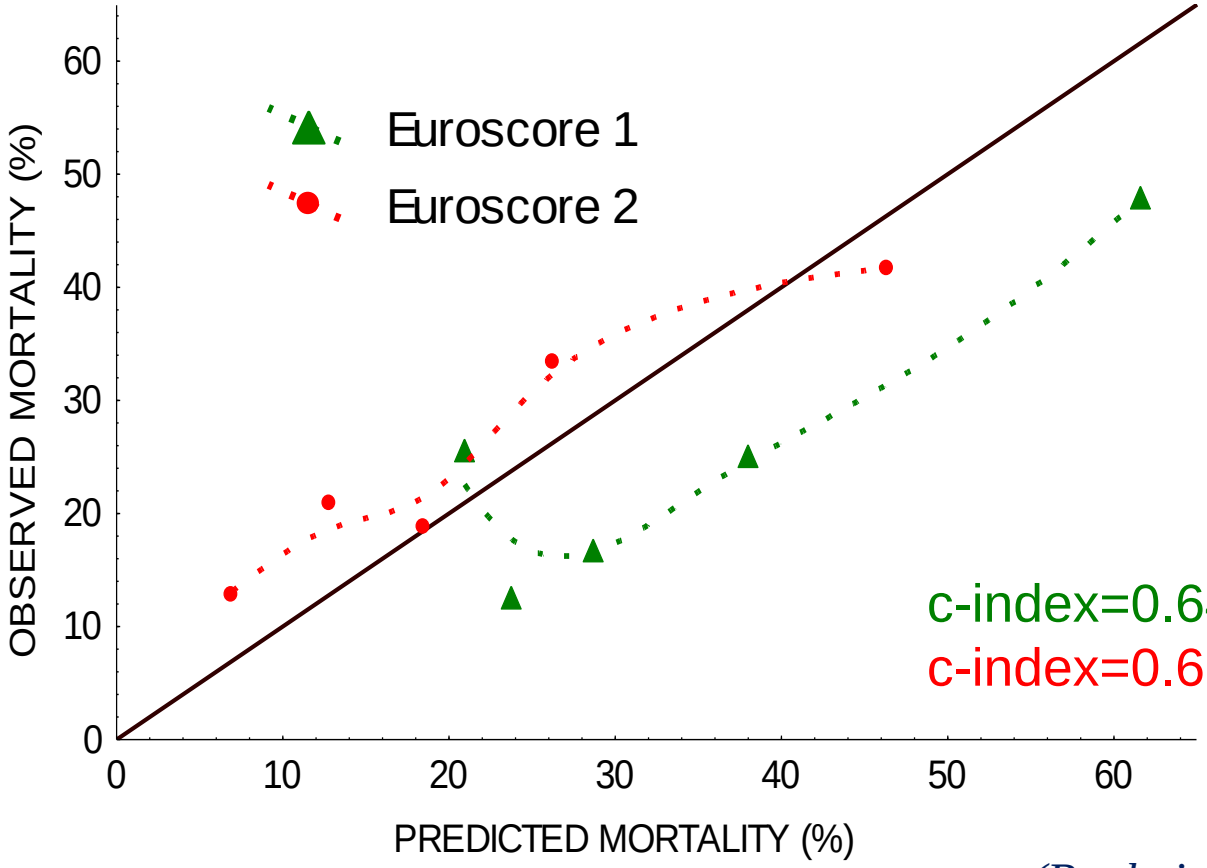
- 2931 consecutive patients operated on for valvular surgery in Bichat Hospital during a 5-year period
- 30-day mortality: 5.5%



(Bouleti et al. ESC 2013)

EuroSCORE II: validation in valvular diseases

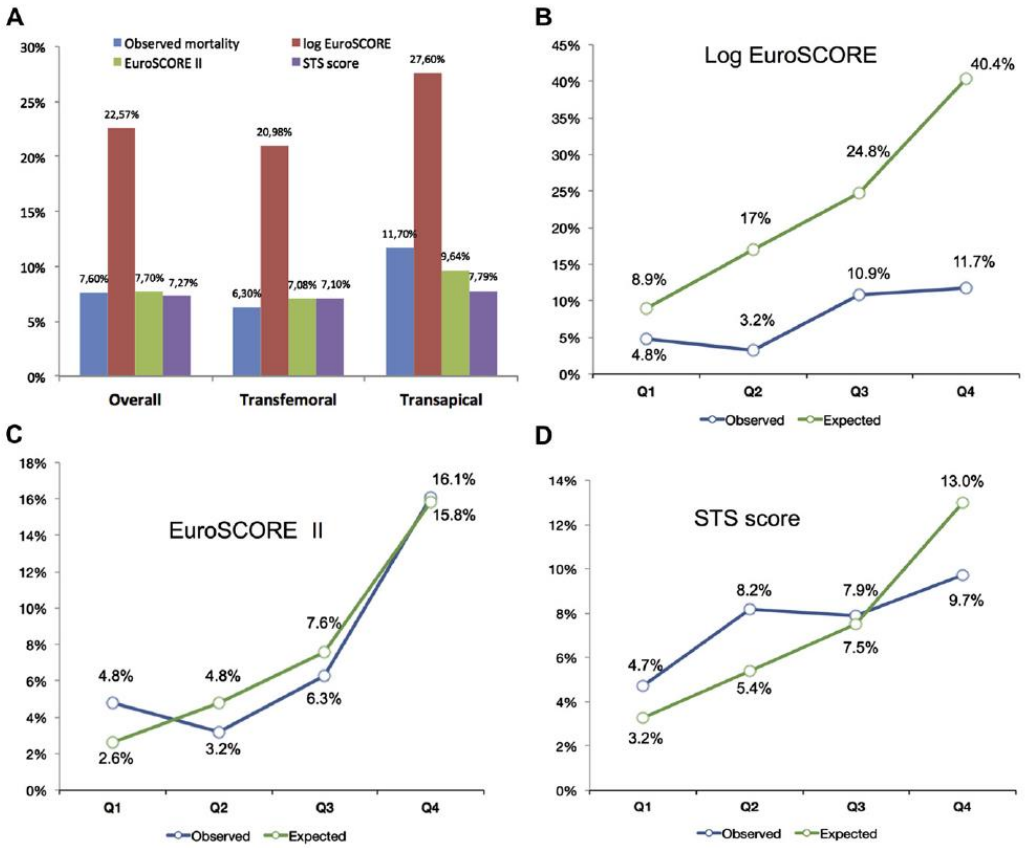
- 239 patients operated on for valvular surgery with Euroscore I ≥ 20% (mean 35±16)
- 30-day mortality : 25%



(Bouleti et al. ESC 2013)

Euroscore and TAVI

- 250 patients treated with TAVI
- Mean age 83±7 years
- 190 transfemoral,
  60 transapical
- 30-day mortality 7.6%
- c-index
  - ES I 0.63
  - ES II 0.66
  - STS 0.58



(Durand et al. Am J Cardiol 2013;111:891-7)

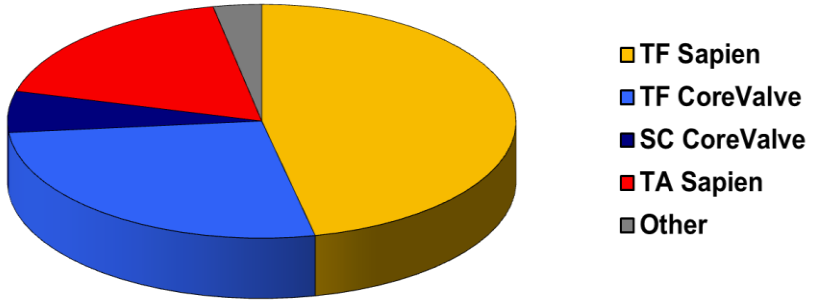
Risk Score for TAVI

- France 2 registry (01 Jan 2010 - 31 Dec 2011)
- 3933 patients in 34 centres
- Exclusion of 100 patients
  (missing procedure data or valve-in-valve)

➢ 3833 patients

Random sampling

– Derivation cohort: 2552 patients
– Validation cohort: 1281 patients



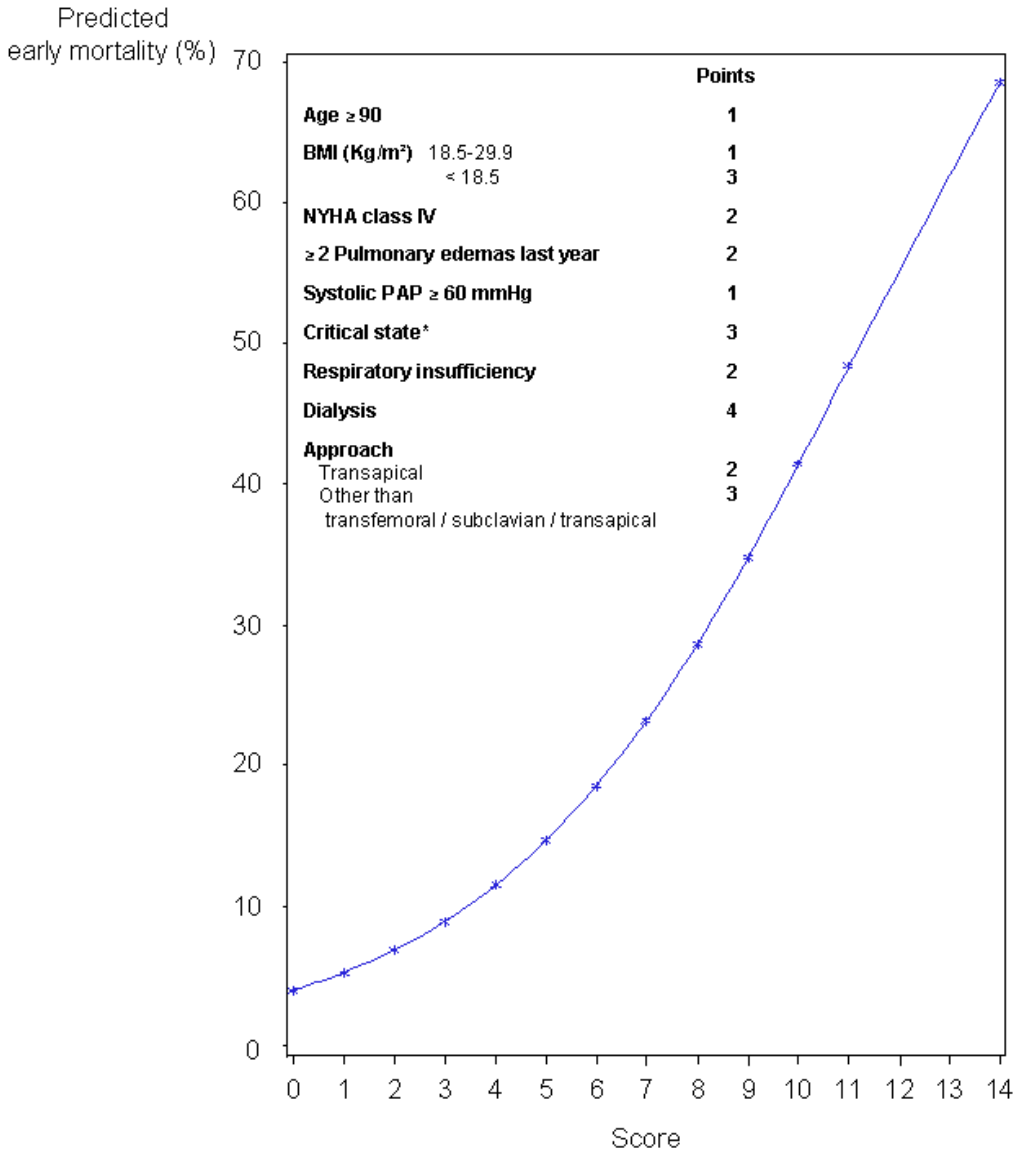
- 382 deaths at 30 days or in hospital (10%)

(Iung et al. Heart 2014;100:1016-23)

Predictive model and score

	Adjusted odds-ratio [95% CI]	*p*	Points for score
Age (years)			
< 90	1		0
≥ 90	1.53 [1.02-2.30]	0.04	1
Body mass index			
≥ 30	1		0
18.5-30	1.51 [1.01-2.27]	0.05	1
<18.5	2.27 [1.09-4.74]	0.03	3
NYHA class IV	1.79 [1.26-2.54]	0.001	2
≥2 acute pulmonary edemas last year	1.61 [1.12-2.30]	0.01	2
Pulmonary hypertension (sPAP ≥60 mmHg)	1.45 [1.08-1.94]	0.01	1
Critical state (Euroscore)	2.39 [1.42-4.02]	0.001	3
Respiratory insufficiency	1.64 [1.22-2.20]	0.001	2
Dialysis	2.88 [1.46-5.66]	0.002	4
Approach			
Transfemoral or subclavian	1		0
Transapical	2.02 [1.47-2.78]	<0.0001	2
Other	2.18 [1.11-4.28]	0.02	3

Prediction and Calibration

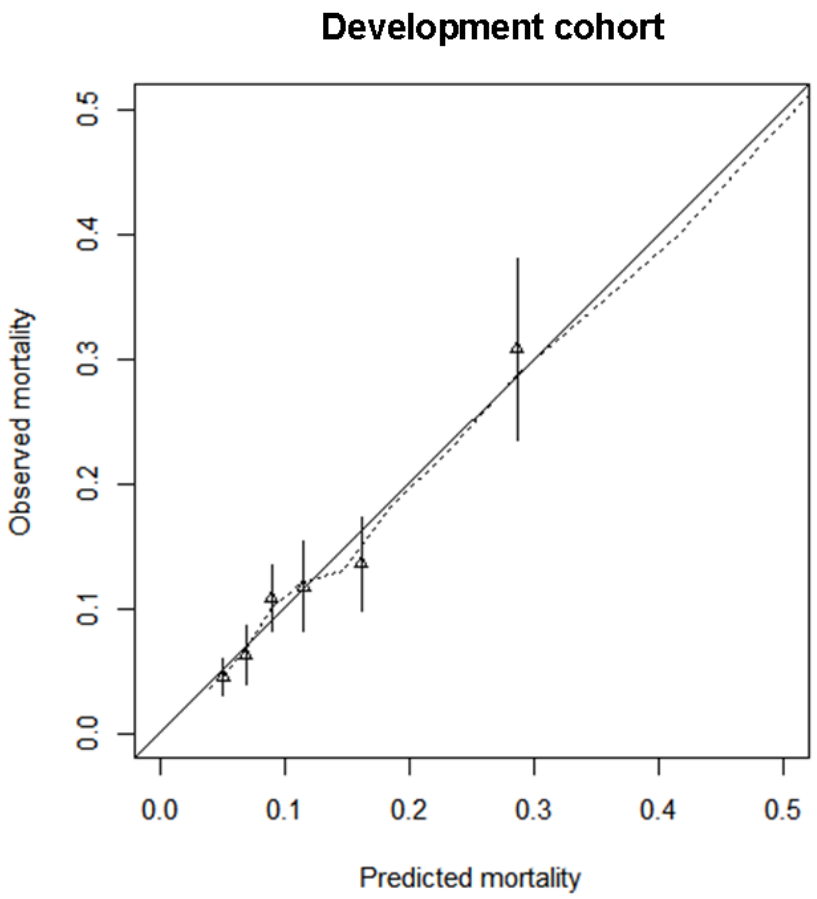


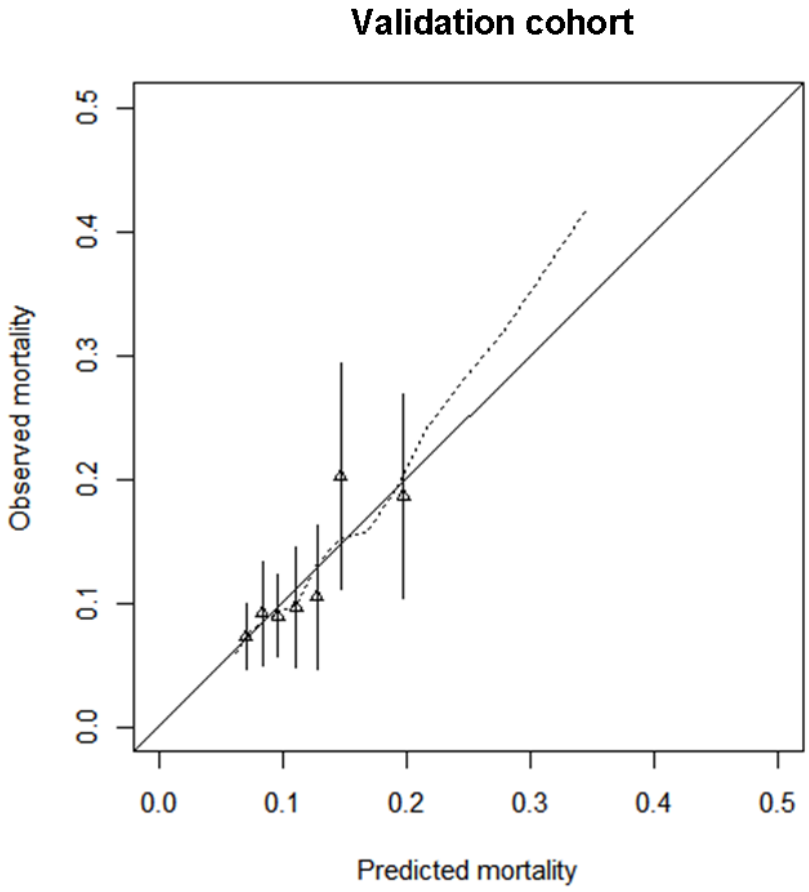
C-index

Derivation cohort
0.67 [0.64-0.71]

Validation cohort
0.59 [0.54-0.64]

Calibration
(Predicted vs. Observed Mortality)



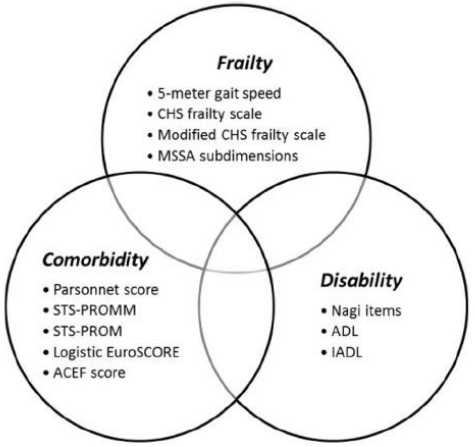


Frailty in patients with aortic stenosis

- Prevalence in patients undergoing TAVI
  - 25% in a multicentre Canadian series of 339 patients
    (Rodés-Cabau et al. J Am Coll Cardiol 2010;55:1080-90)
  - 17% in the TAVI German Registry (697 patients)
    (Zahn et al. Eur Heart J 2011, 32:198-204)
  - 23% in the Partner B Cohort (358 patients)
    (Leon et al. N Engl J Med 2010;363:1597-607)
- Impact of indices of functional performance / frailty
  - Karnofsy index was predictive of 30-day MACCE/death
    (Buellesfeld et al. Eur Heart J 2010:31:984-91)
  - Independent predictor of 5-year survival
    (Rodes Cabau et al. J Am Coll Cardiol 2012;60:1864-75)

Impact of Frailty / Diasability Indices

- 152 patients aged ≥70 undergoing CABG and/or valve surgery (mean Euroscore I 10.4%)
- 37 (24%) in-hospital mortality or major morbidity (STS)
- Discrimination (c-index)
  - Euroscore I 0.65
  - STS PROM 0.67
  - STS PROMM 0.68
- C-index of STS PROMM increased from 0.68 to 0.73 when adding:
  - Nagi scale
  - 5-meter gait speed



(Afilalo et al. Circ Cardiovasc Qual Outcomes 2012;5:222-8)

Impact of Frailty / Diasbility Indices

- 2137 patients from the PARTNER trial/registry
- 6-month poor outcome (death or impaires Qol as assessed by the Kansas city Cardiomyopathy Questionnaire)
- 33% poor outcome at 6 months
- 10 predictive factors, inclusding MMSE and 6-min walk test
- Discrimination (c-index)
  - Derivation sample 0.66
  - Validation sample 0.64

(Arnold et al. Circulation 2014;129:2682-90)

Indications for transcatheter aortic valve implantation

	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.	IIa	B

« In the absence of a perfect quantitative score, the risk assessment should mostly rely on the clinical judgement of the ‘heart team’, in addition to the combination of scores. »

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 & European Journal of Cardio-Thoracic Surgery 2012 - doi:10.1093/ejcts/ezs455).

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High Surgical Risk?
Decision between TAVI and AVR?

EuroScore ≥ 20%

STS score > 10%

Frailty

Ch[illegible]diation

[illegible]rcelain aorta

Re-operation

HEART TEAM DECISION

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

2.5. Evaluation of Surgical and Interventional Risk

See Table 5 for risk assessment combining STS risk estimate, frailty, major organ system dysfunction, and procedure-specific impediments.

Table 5. Risk Assessment Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

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

Conclusion

- Risk-stratification faces limitations when applied to TAVI.
- This is mainly due to a moderate discrimination of predictive models of short and mid-term outcome.
- The same findings apply to valvular surgery when performed in high-risk patients.
- No score threshold can be used to reliably identify patients who will not benefit from TAVI.
- The inclusion of indices of cognitive or functional capacity may improve the performance of future scores.
- Current guidelines therefore privilege the heart team approach in decision-making.

Frailty

« A syndrome of decreased reserve and resistance to stressors, resulting from multiple declines across multiple physiologic systems leading to vulnerability to adverse outcomes »

≥ 3 criteria among: weakness, weight loss, exhaustion, low physical activity, and slowed walking speed

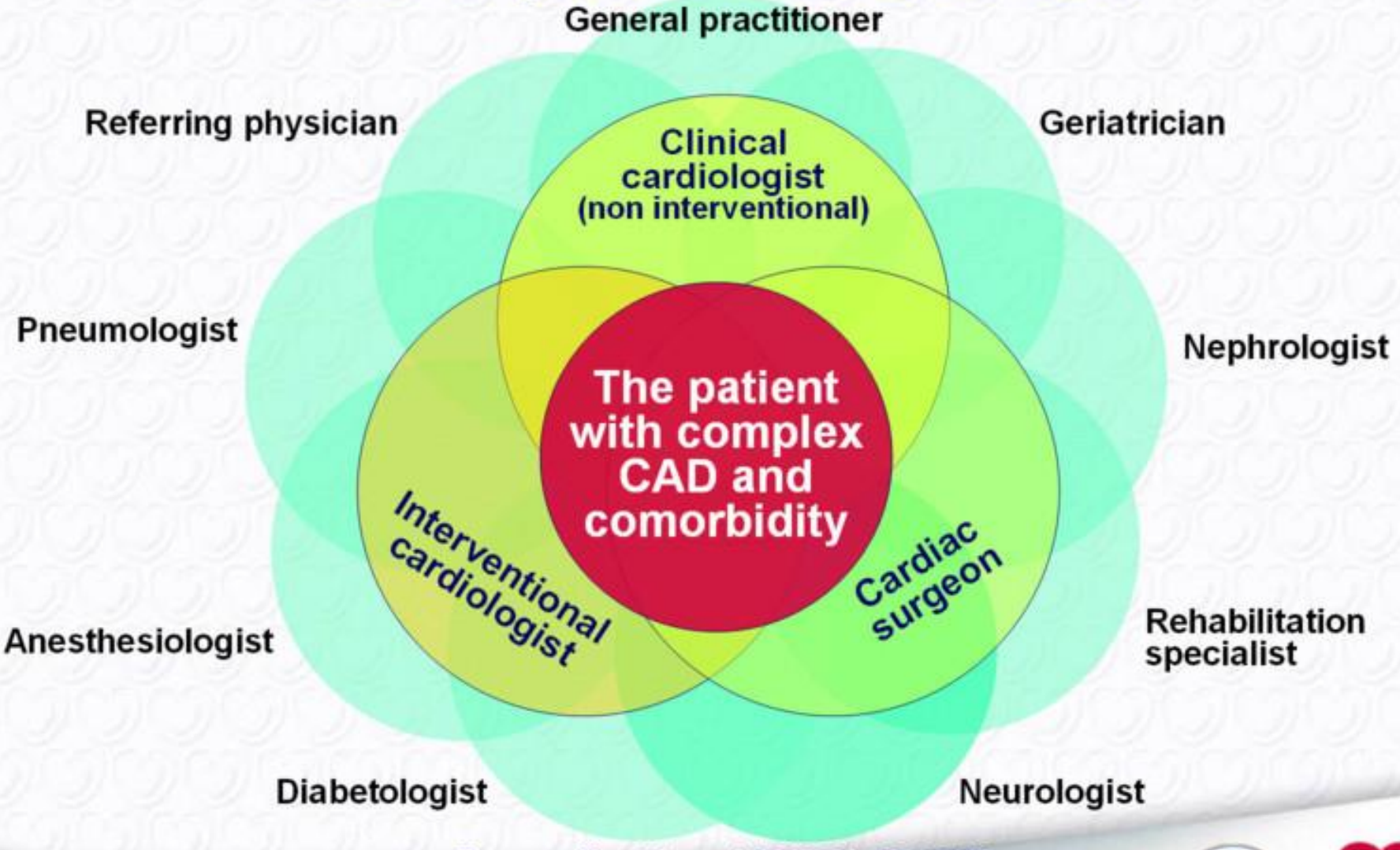
(Fried et al. J Gerontol A Biol Sci Med Sci 2001;56:M146-56)

Katz index of independence

A – Independent in feeding, continence, transferring, toileting, dressing, and bathing
B – Independent in all but one of these functions
C – Independent in all but bathing and one additional function
D – Independent in all but bathing, dressing, and one additional function
E – Independent in all but bathing, dressing, toileting, and one additional function
F – Independent in all but bathing, dressing, toileting, transferring, and one additional function
G – Dependent in all six functions

(Katz et al. JAMA 1963;185:914-919.)

The Expanded Heart Team



European Heart Journal (2010) 31, 2501-2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

www.escardio.org/guidelines

Joint 2010 ESC - EACTS Guidelines on Myocardial Revascularisation

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Refining clinical indications for TAVI

- **Patients who are not candidates to any intervention**
  - Poor expected life expectancy / QoL
  - Need for better identification

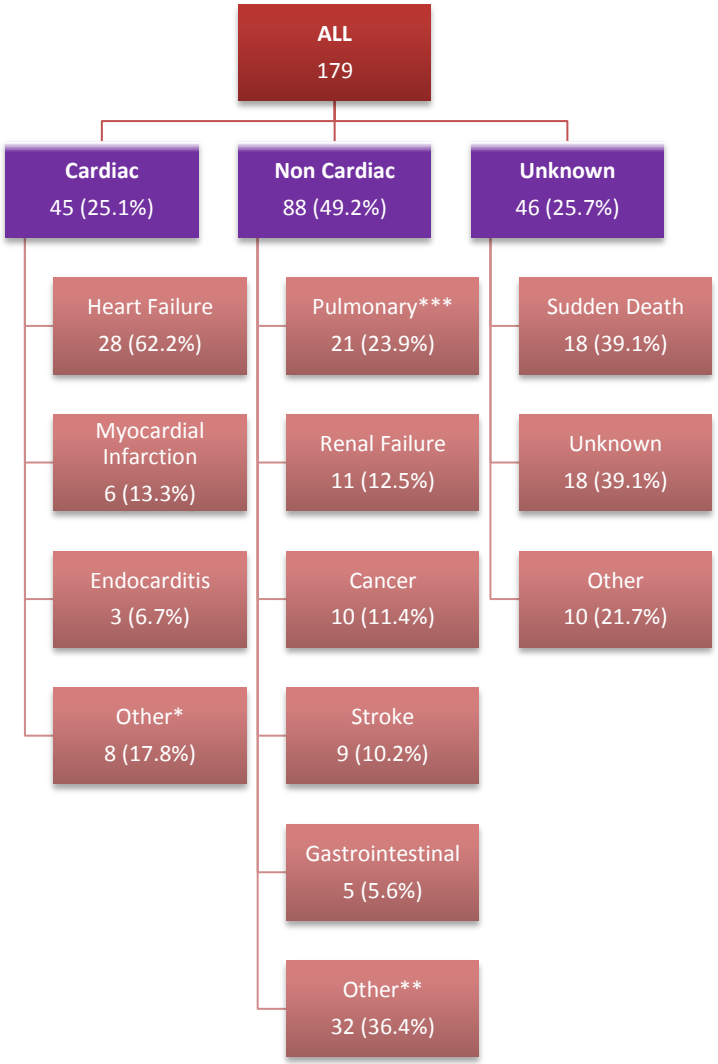
    (improved risk scores, assessment of comorbidities, functional and psychometric evaluation…)

- **TAVI in patients at low(er) risk for AVR**
  - Concerns on durability, residual AR
  - Comparative evaluation with the results of AVR (randomised trials)

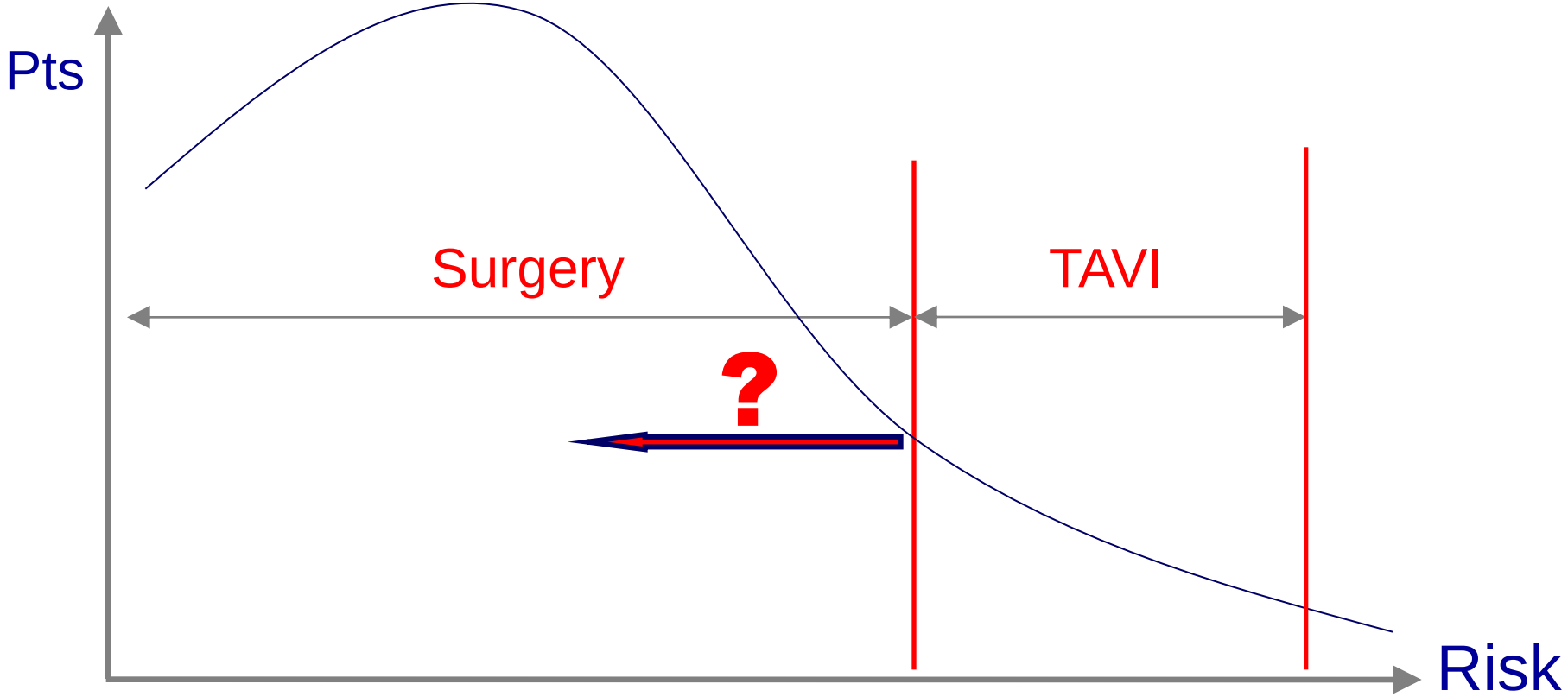
Impact of comorbidities on life expectancy

- Causes of death (30 days to 1 Year) in the Source Registry
- 1038 patients (TAVI using Sapien valve)
- Half of deaths were of non-cardiac cause

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



Intermediate- and low-risk patients

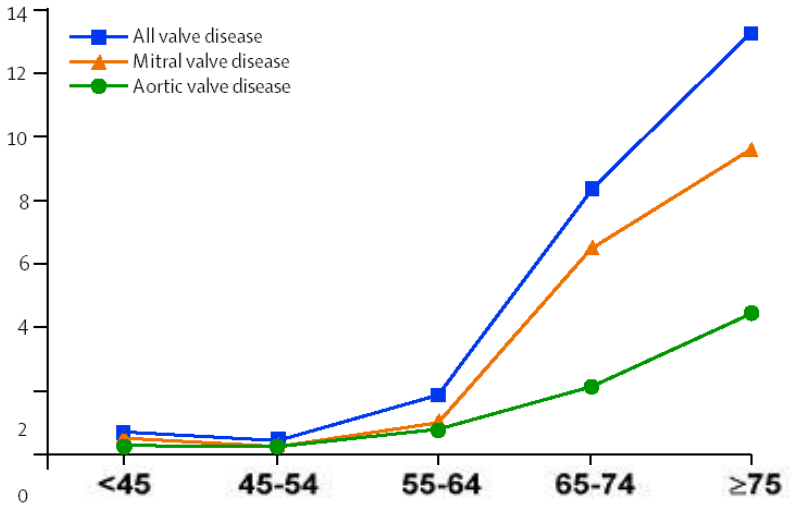


« At the present stage, TAVI should not be performed in patients at intermediate risk for surgery and trials are required in this population. »

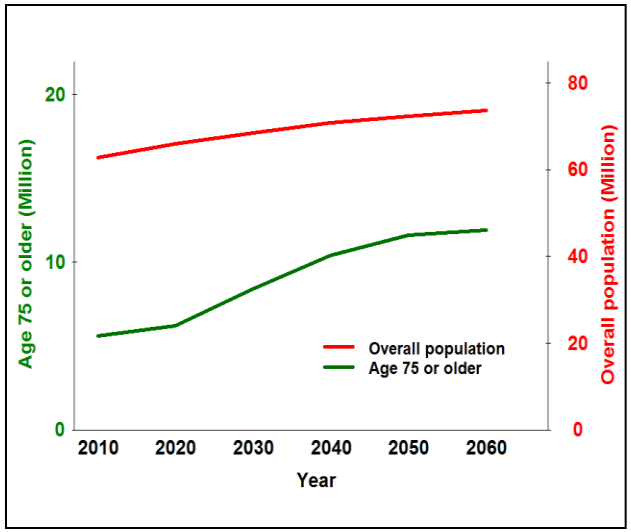
(ESC/EACTS Guidelines 2012)

Epidemiology of valvular disease

- High prevalence of valvular disease in the elderly
- Predicted increase
- Decision-making issues:
  - Risk of interventions
  - Life expectancy, QoL
  - Patient selection



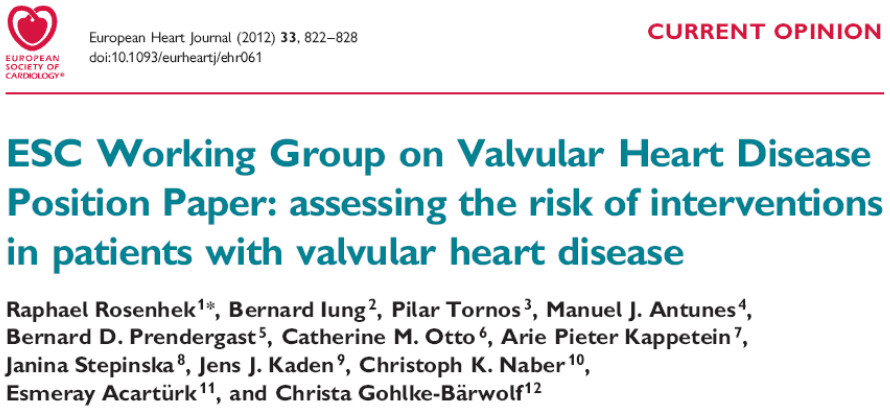
(Nkomo et al. Lancet 2006;368:1005-11)



(Iung and Vahanian Heart 2012;98:iv7–iv13)

Limitations of risk scores in high-risk patients

- Population characteristics
- Change in techniques
  (surgery, percutaneous techniques, anaesthesia)
- Choice and coding of variables
- Relative or absolute contraindications for surgery
  - Porcelain aorta
  - Chest radiation
  - Hepatic insufficiency
- Complex conditions requiring an individual approach
  - Active endocarditis
  - Cancer
  - Frailty


European Heart Journal (2012) 33, 822–828
doi:10.1093/eurheartj/ehr061

CURRENT OPINION

ESC Working Group on Valvular Heart Disease Position Paper: assessing the risk of interventions in patients with valvular heart disease

Raphael Rosenhek[1]*, Bernard Iung[2], Pilar Tornos[3], Manuel J. Antunes[4], Bernard D. Prendergast[5], Catherine M. Otto[6], Arie Pieter Kappetein[7], Janina Stepinska[8], Jens J. Kaden[9], Christoph K. Naber[10], Esmeray Acartürk[11], and Christa Gohlke-Bärwolf[12]

(Rosenhek et al. Eur Heart J 2012;33:822-8)

Frailty and management of AS

Pegaso study: 928 octogenarians with severe AS

Mean age 84±3 yrs, 59% female

49% were independent (Katz index A)

Planned management

	AVR (n=244 26%)	TAVI (n=261 28%)	Conservative (n=423 46%)	p
Age (yrs)	82±2	85±3	85±4	<0.001
Log. Euroscore I	21±13	31±18	33±17	<0.001
Katz index A (%)	70	48	39	<0.001

(Martínez-Sellés et al. ESC 2012)

Frailty and management of AS

Pegaso study: 928 octogenarians with severe AS

Predictive factors of the absence of surgery (TAVI or conservative management)

	OR [95% CI]	p
Age (yrs)	1.3 [1.2-1.4]	<0.001
Log. Euroscore I	1.02 [1.01-1.04]	<0.001
Katz index A (%)	1.5 [1.3-1.7]	<0.001
Max. gradient (mm Hg)	0.99 [0.98-0.99]	<0.001
Systolic PAP (mm Hg)	1.03 [1.01-1.05]	<0.001
LV EF < 40%	2.0 [1.1-3-7]	0.05

(Martínez-Sellés et al. ESC 2012)