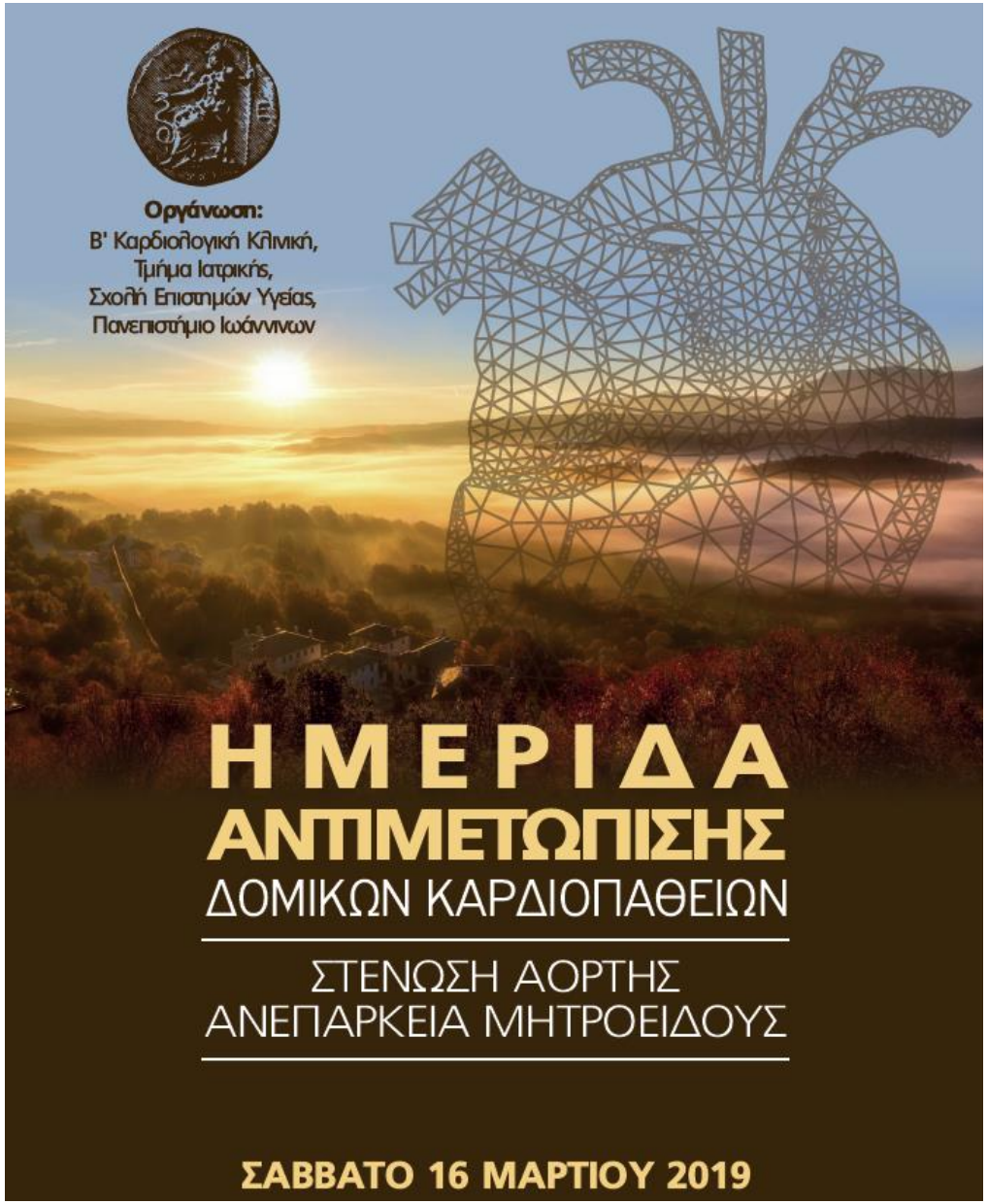


Στένωση Αορτικής Βαλβίδας

Αλγόριθμος αντιμετώπισης - Κατευθυντήριες Οδηγίες

Κατερίνα Κ. Νάκα MD, PhD(UK), FESC
Αναπληρώτρια Καθηγήτρια Καρδιολογίας
Ιατρική Σχολή, Πανεπιστήμιο Ιωαννίνων
Β΄ Καρδιολογική Κλινική ΠΓΝΙ

DISCLOSURES

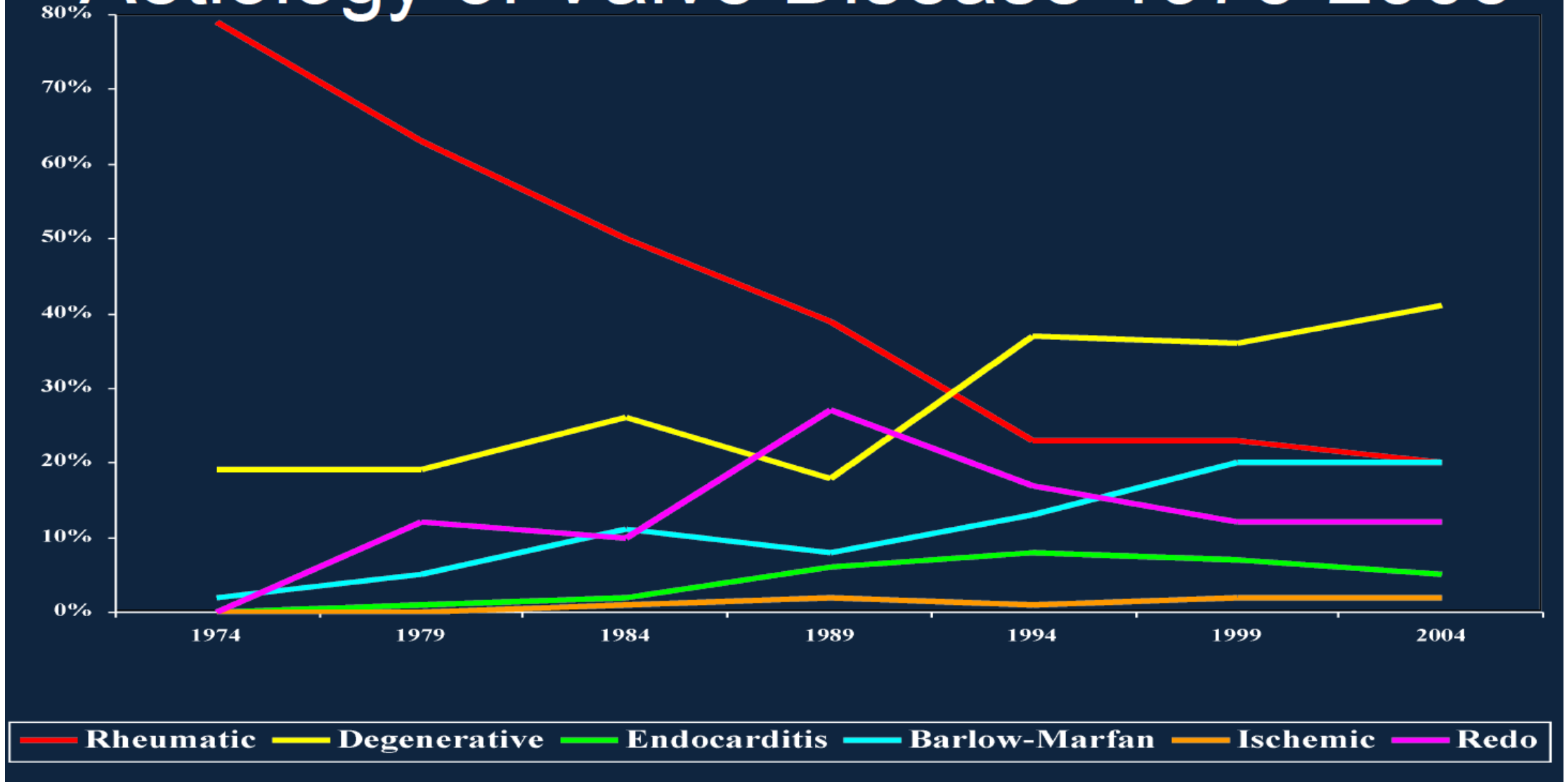
SPEAKER: KATERINA K. NAKA MD, PhD, FESC

RCTs, Registries - *Novartis, Merck, Amgen, Pfizer, Actelion, BMS, Boehringer*

Lectures – *Novartis, ΕΛΠΕΝ*

Horizon2020 funding – *KardiaTool, Insilc projects*

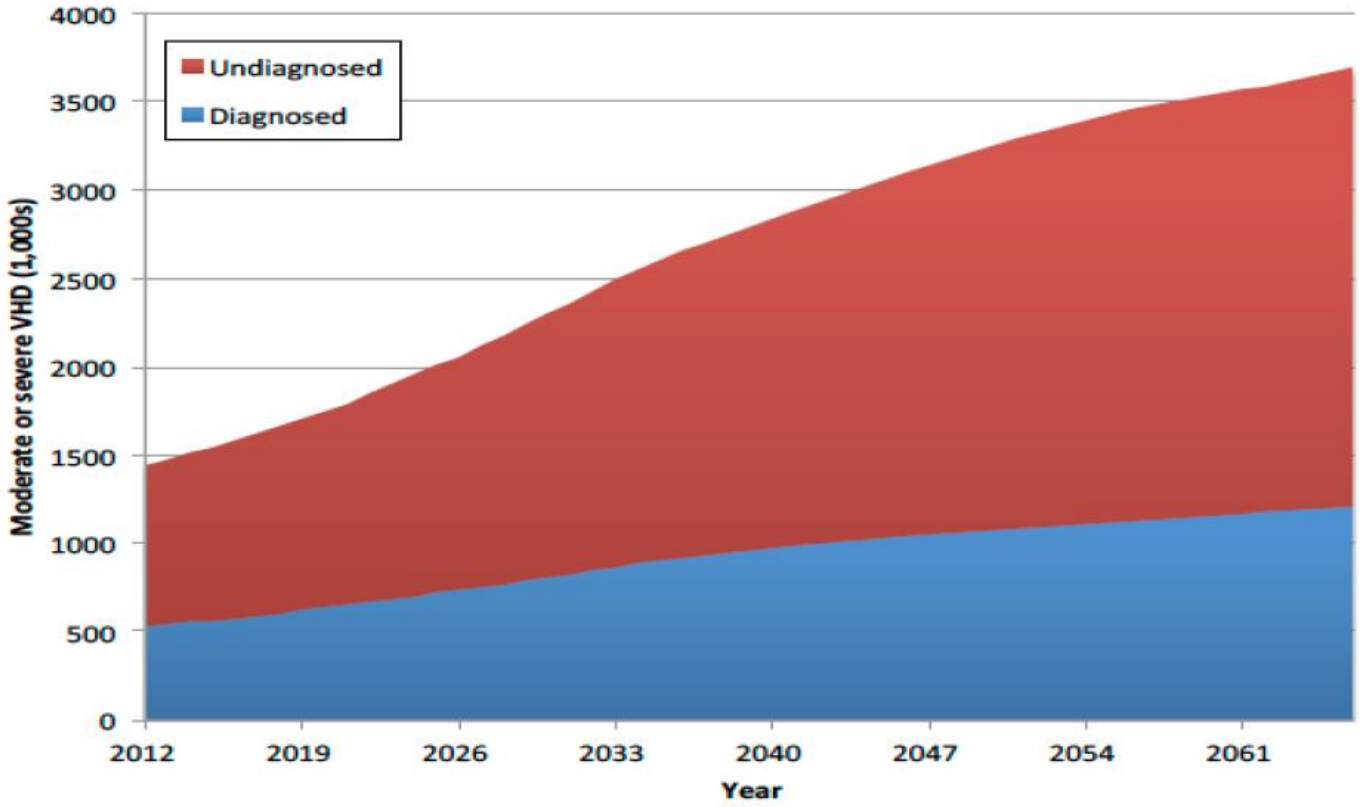
Aetiology of Valve Disease 1975-2005



Looking Ahead: What Does the Future Hold?

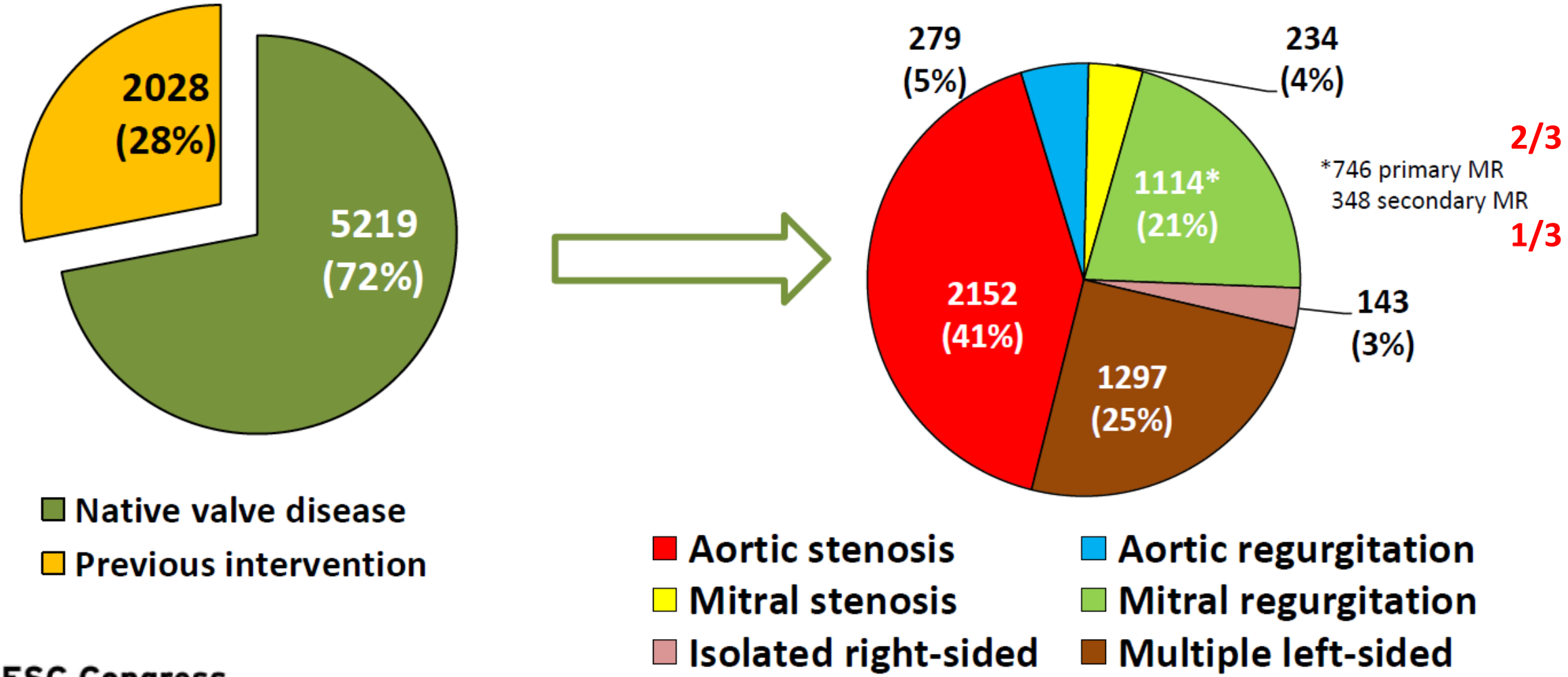
OxVALVE
VALVULAR HEART DISEASE
Population Cohort Study

65 years and older with moderate or severe VHD (in millions)



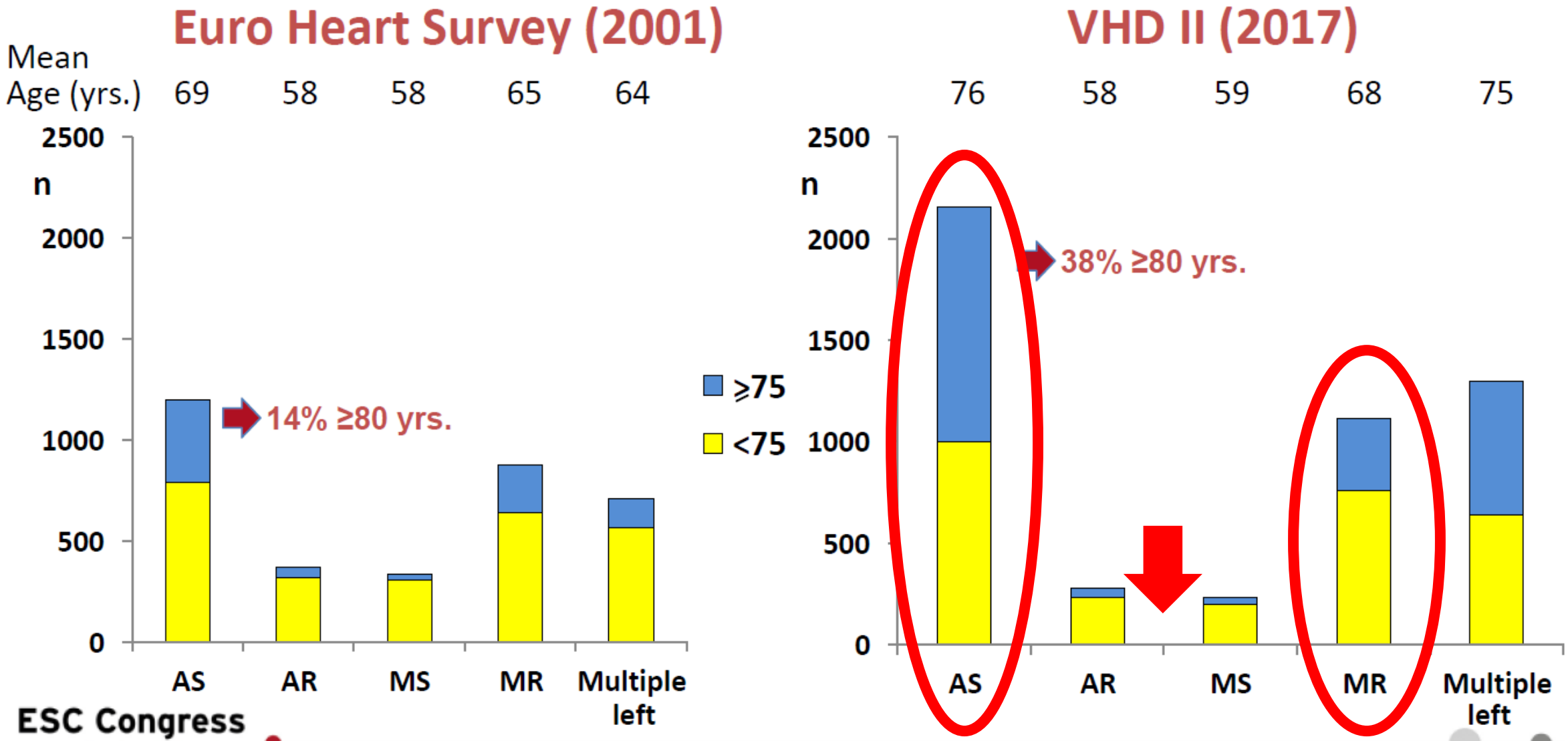
d'Arcy J *et al*. Eur Heart J 2016

EORP VHD II: Distribution of Valvular Disease



Iung B. Late Breaking Registries ESC Munich 2018.

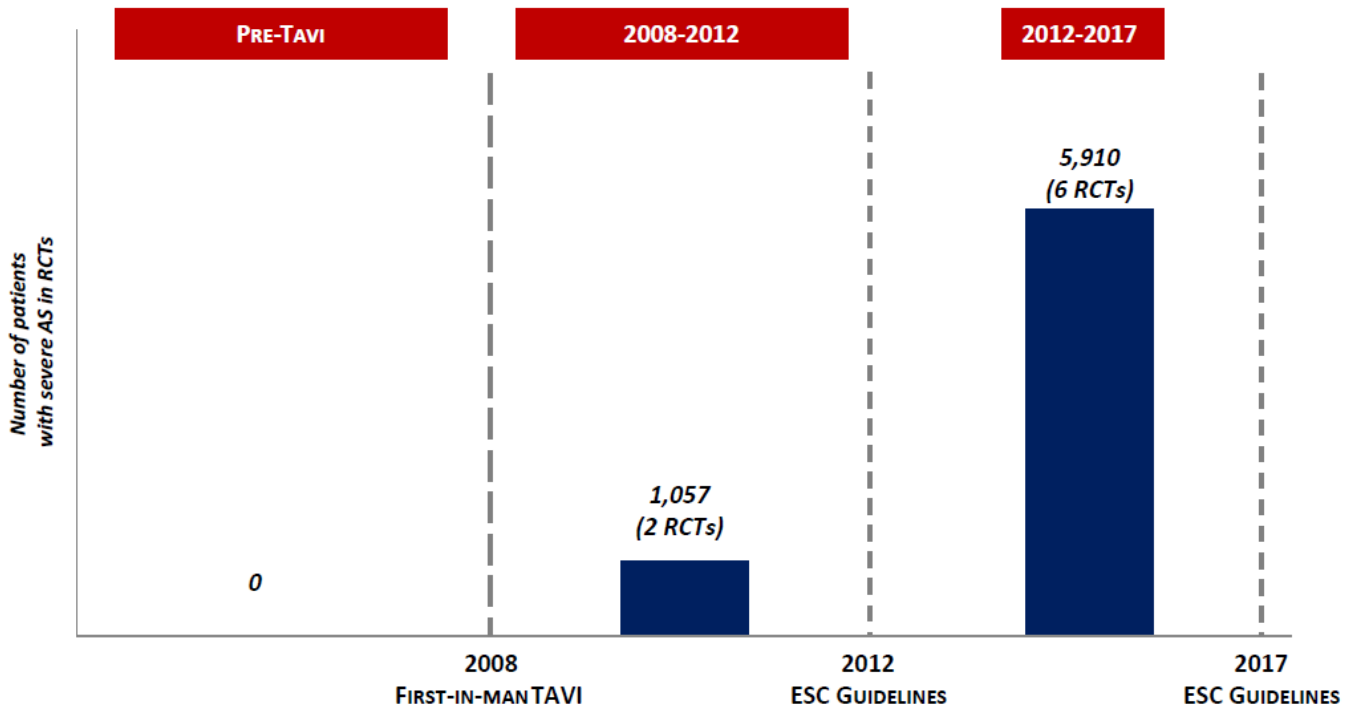
Patient Characteristics



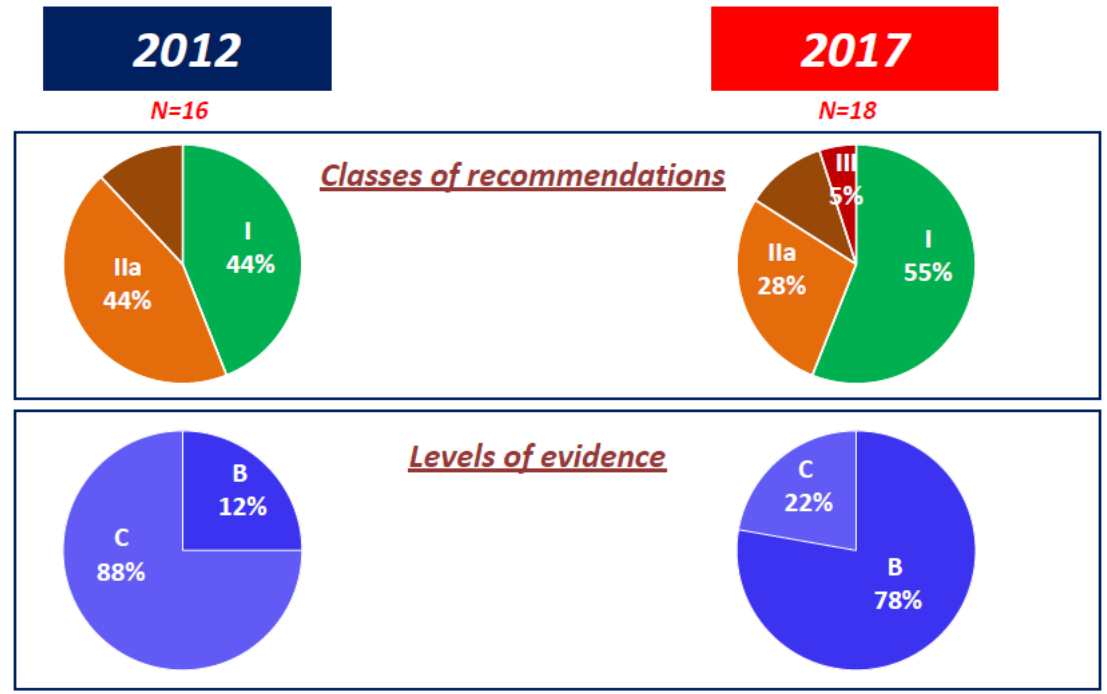
Latest ESC guidelines on AS (or any VHD) management

- Need for **Heart (Valve) Team**
- Put the **Patient** at the very Center of Care
- Keep up with the **Evidence that is Evolving**…

The Evolution of Evidence: RCTs in Patients with Severe Aortic Stenosis



2017 ESC/EACTS Guidelines: Management of Aortic Stenosis



Essential questions in the evaluation of patients for valvular intervention

10 questions

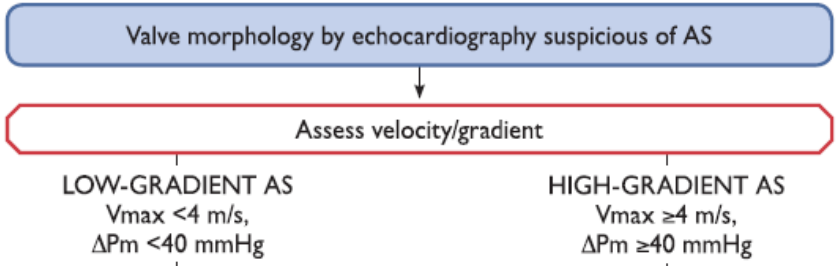
Questions
• How severe is VHD?
• What is the aetiology of VHD?
• Does the patient have symptoms?
• Are symptoms related to valvular disease?
• Are any signs present in asymptomatic patients that indicate a worse outcome if the intervention is delayed?
• What are the patient's life expectancy and expected quality of life?

Essential questions in the evaluation of patients for valvular intervention *(continued)*

10 questions

Questions *(continued)*
• Do the expected benefits of intervention (versus spontaneous outcome) outweigh its risks?
• What is the optimal treatment modality? Surgical valve replacement (mechanical or biological), surgical valve repair, or catheter intervention?
• Are local resources (local experience and outcome data for a given intervention) optimal for the planned intervention?
• What are the patient's wishes?

Stepwise integrated approach for the assessment of AS severity



High flow may be reversible in settings such as

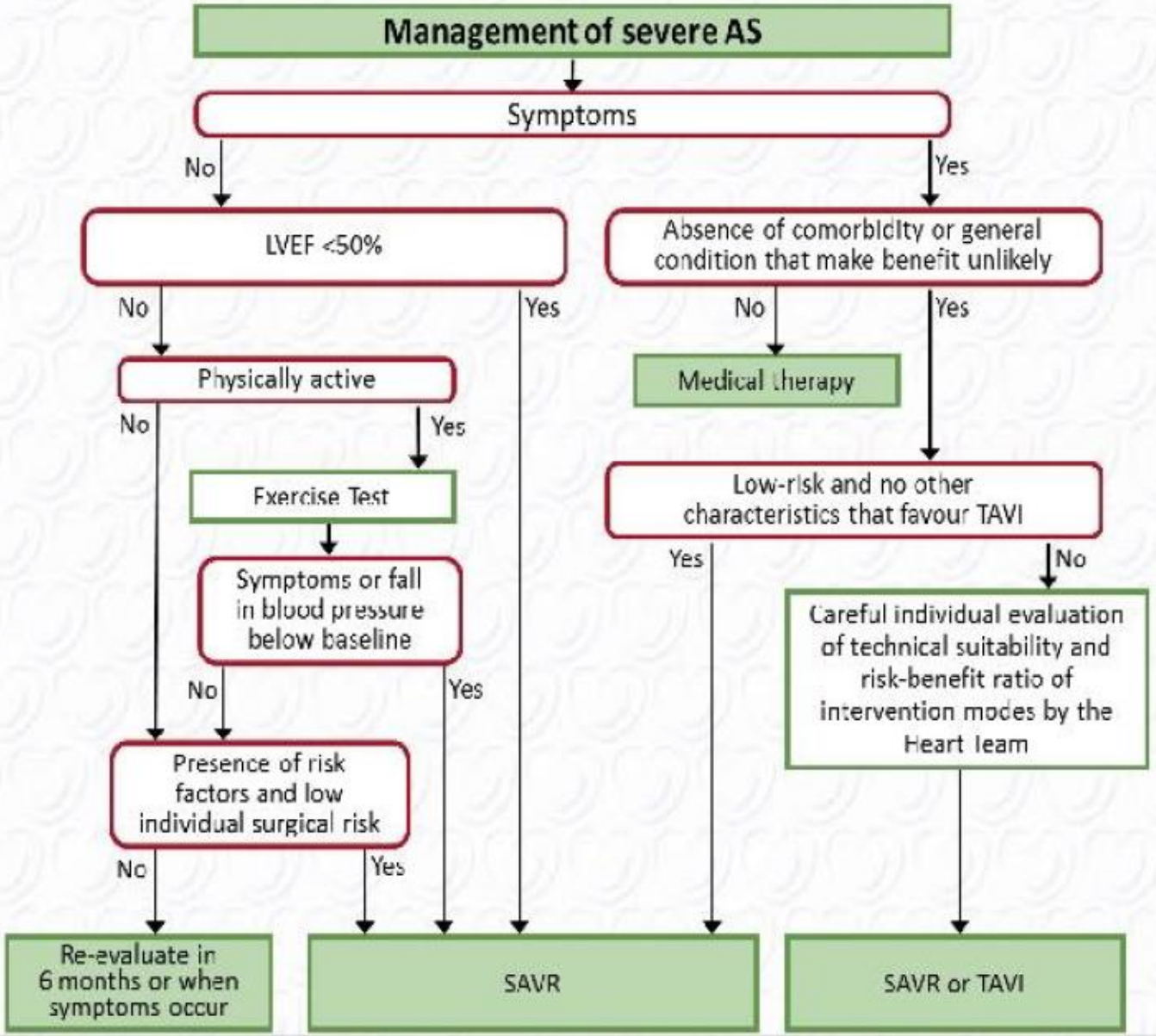
- anaemia
- hyperthyroidism,
- AV shunts

Pseudosevere AS:
an increase to an AVA >1.0 cm^2 with flow normalization

Paradoxical low-flow, low-gradient AS

Table 6 Criteria that increase the likelihood of severe aortic stenosis in patients with AVA <1.0 cm^2 and mean gradient <40 mmHg in the presence of preserved ejection fraction (modified from Baumgartner *et al.*[4])

Criteria	
Clinical criteria	• Typical symptoms without other explanation • Elderly patient (>70 years)
Qualitative imaging data	• LV hypertrophy (additional history of hypertension to be considered) • Reduced LV longitudinal function without other explanation
Quantitative imaging data	• Mean gradient 30–40 mmHg[a]
	• AVA ≤0.8 cm^2 **when patient is normotensive**
	• Low flow (SVi <35 mL/m^2) confirmed by techniques other than standard Doppler technique (LVOT measurement by 3D TOE or MSCT; CMR, invasive data)
	• Calcium score by MSCT[b] Severe aortic stenosis very likely: men ≥3000; women ≥1600 Severe aortic stenosis likely: men ≥2000; women ≥1200 Severe aortic stenosis unlikely: men <1600; women <800 **Agatston score**



If high-risk or other features that favor TAVI

- Technical suitability
- Risk-benefit discussion in Heart Team

2017 ESC/EACTS Guidelines for the Management of Valvular Heart Disease
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx391)

Indications for intervention in AS (I)

Recommendations	Class	Level
a) Symptomatic aortic stenosis		
Intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (mean gradient ≥40 mmHg or peak velocity ≥4.0 m/s).	I	B
Intervention is indicated in symptomatic patients with severe low-flow, low-gradient (<40 mmHg) aortic stenosis with reduced ejection fraction, and evidence of flow (contractile) reserve excluding pseudo-severe aortic stenosis.	I	C
Intervention should be considered in symptomatic patients with low flow, low-gradient (<40 mmHg) aortic stenosis with normal ejection fraction after careful confirmation of severe aortic stenosis.	IIa	C
Intervention should be considered in symptomatic patients with low-flow, low-gradient aortic stenosis and reduced ejection fraction without flow (contractile) reserve, particularly when CT calcium scoring confirms severe aortic stenosis.	IIa	C
Intervention should not be performed in patients with severe comorbidities when the intervention is unlikely to improve quality of life or survival.	III	C

EACTS European Association for Cardio-Thoracic Surgery

ESC European Society of Cardiology

Recommendations for choice of intervention in symptomatic severe AS (I)

b) Choice of intervention in symptomatic aortic stenosis		
Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on-site, and with structured collaboration between the two, including a Heart Team (heart valve centres).	I	C
The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality (aspects to be considered are listed in the according table). In addition, the local expertise and outcomes data for the given intervention must be taken into account.	I	C
SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II <4% or logistic EuroSCORE I <10% and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation).	I	B
TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team.	I	B

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ESC European Society of Cardiology

Recommendations for choice of intervention in symptomatic severe AS (II)

BAV

b) Choice of intervention in symptomatic aortic stenosis			
	Recommendations	**Class**	**Level**
1	Balloon aortic valvotomy may be considered as a diagnostic means in patients with severe aortic stenosis and other potential cause for symptoms (i.e. lung disease) and in patients with severe myocardial dysfunction, pre-renal insufficiency or other organ dysfunction that maybe reversible with balloon aortic valvotomy when performed in centres that can escalate to TAVI.	IIb	C
2			

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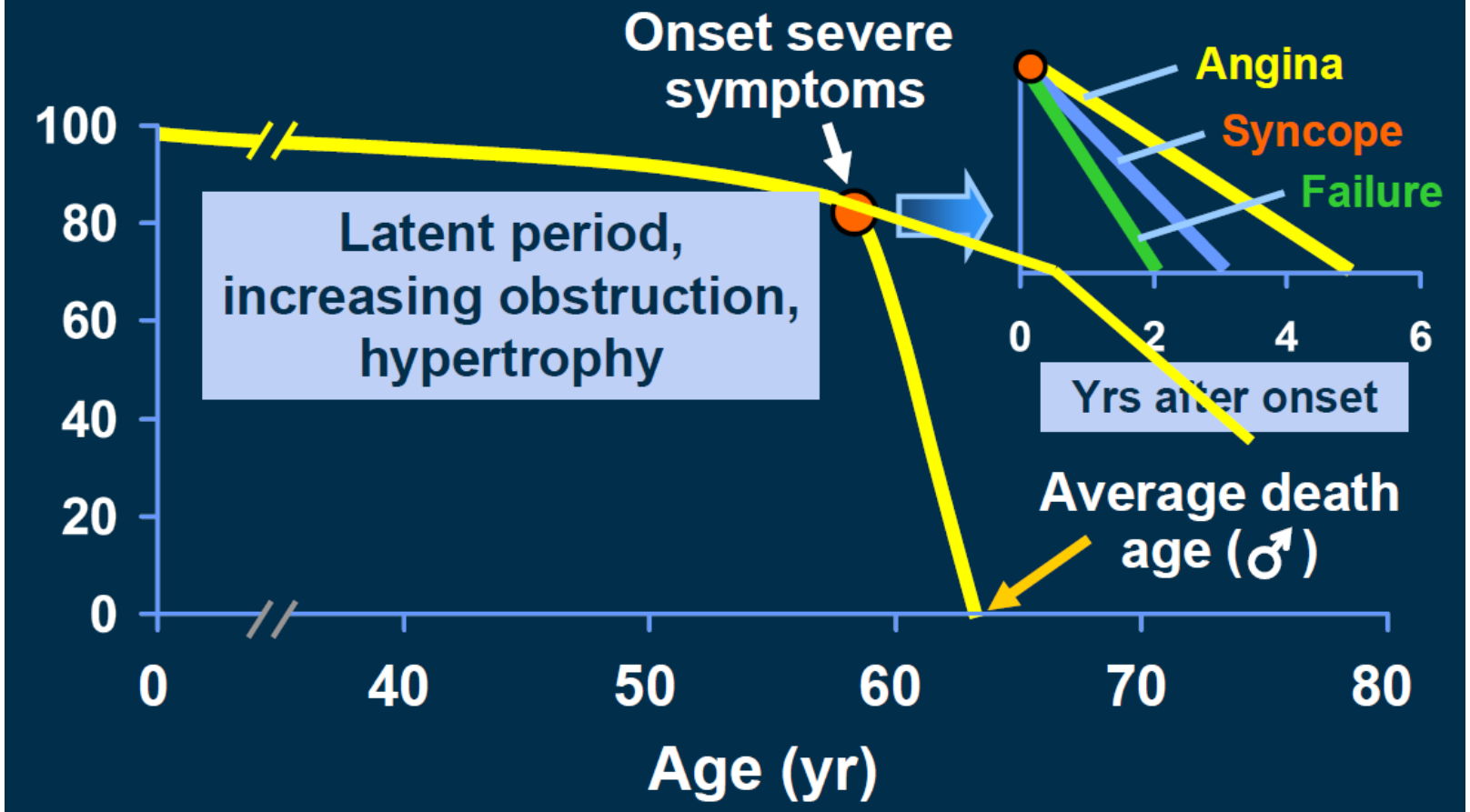
Asymptomatic Severe AS

2 Questions

1. **When: Can intervention (i.e., AVR) be justified prior to symptom onset or the development of LV systolic dysfunction?**

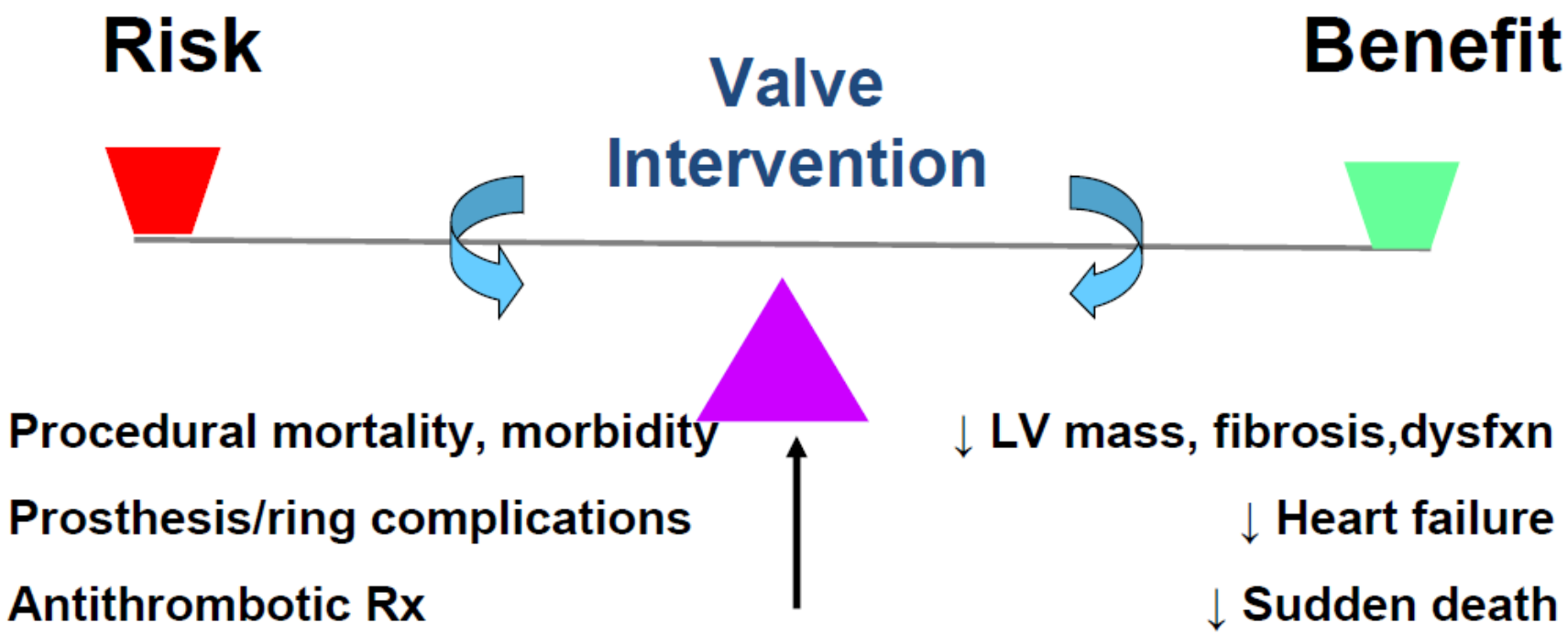
2. **How: What is the evidence base for AVR?**

Natural History of Aortic Stenosis



Ross J Jr. and Braunwald E: *Circ* 38 (Suppl 5):61, 1968

Considerations in the Asymptomatic Patient

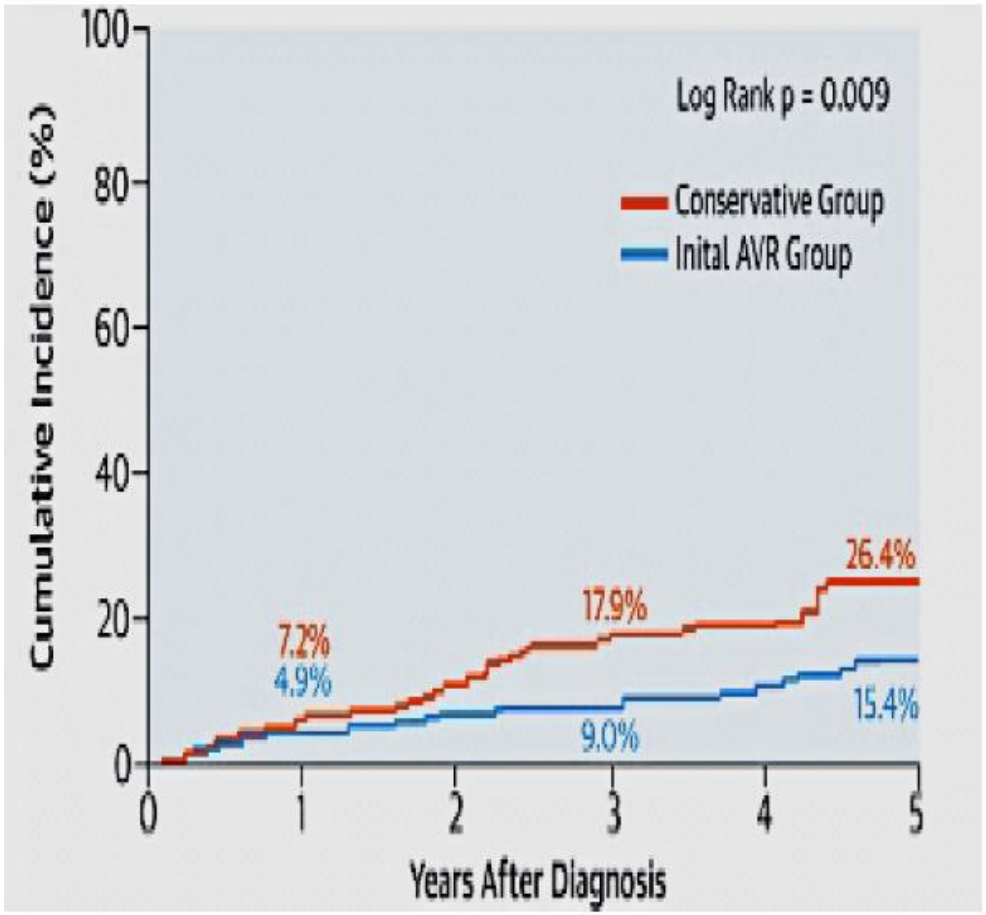


Advances in VHD allow earlier interventions

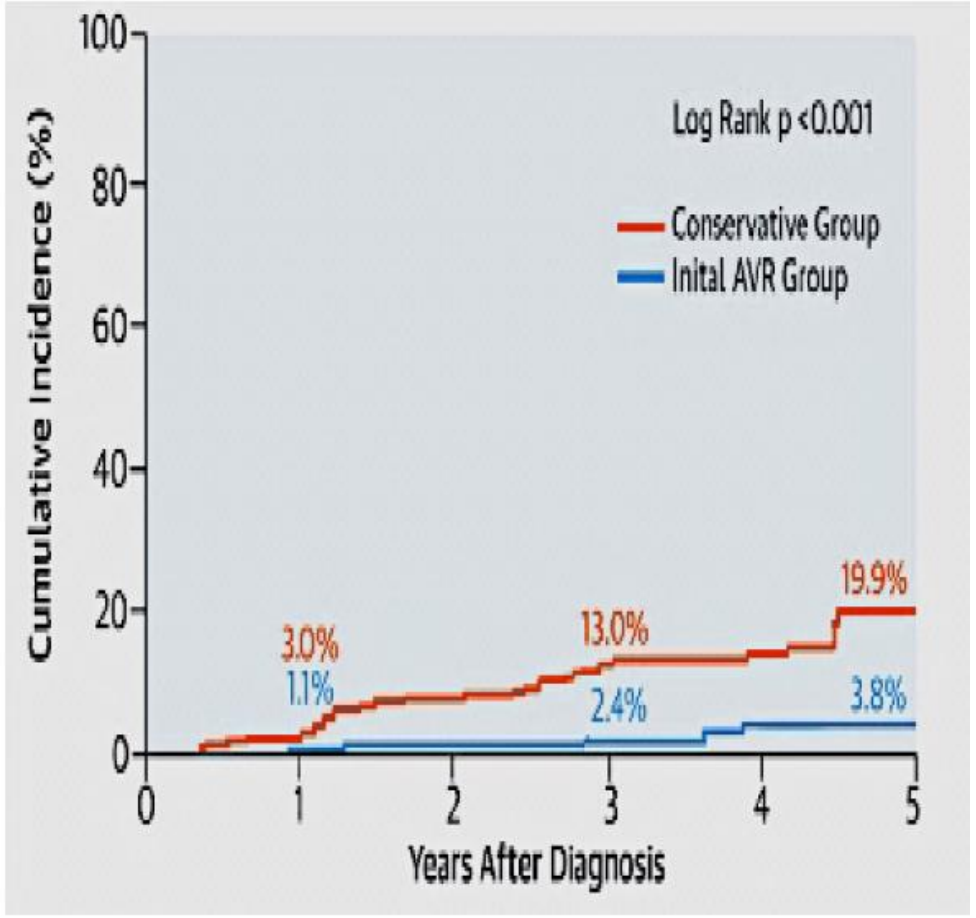
- Improved knowledge of natural hx
- Better patient selection & earlier timing of valve intervention
- Multi-modality imaging
- Surgical & transcatheter techniques
- Peri-procedural management
- Long-term follow-up

A-symptomatic AS: better with SAVR

Death

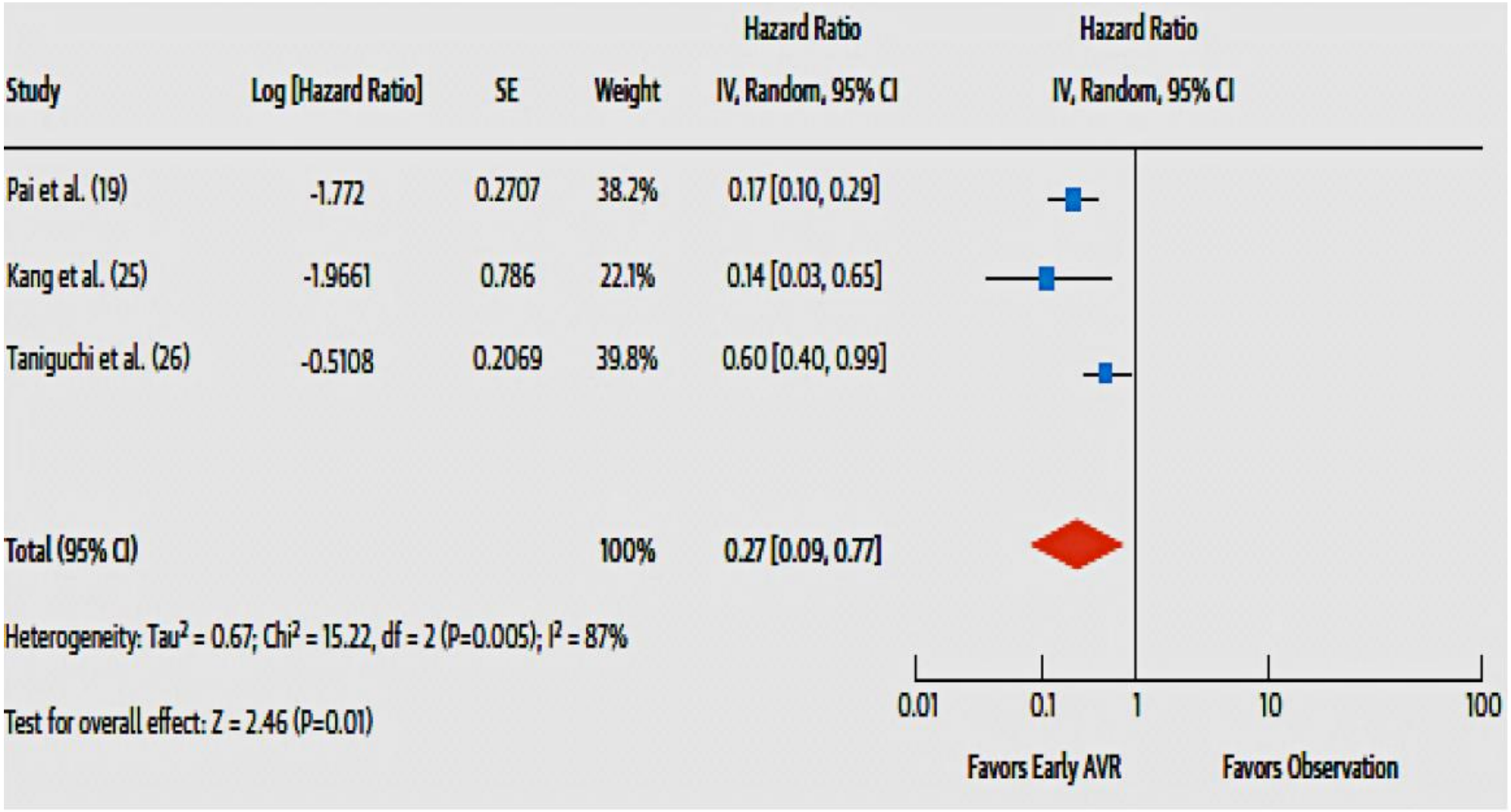


HF Hospitalization



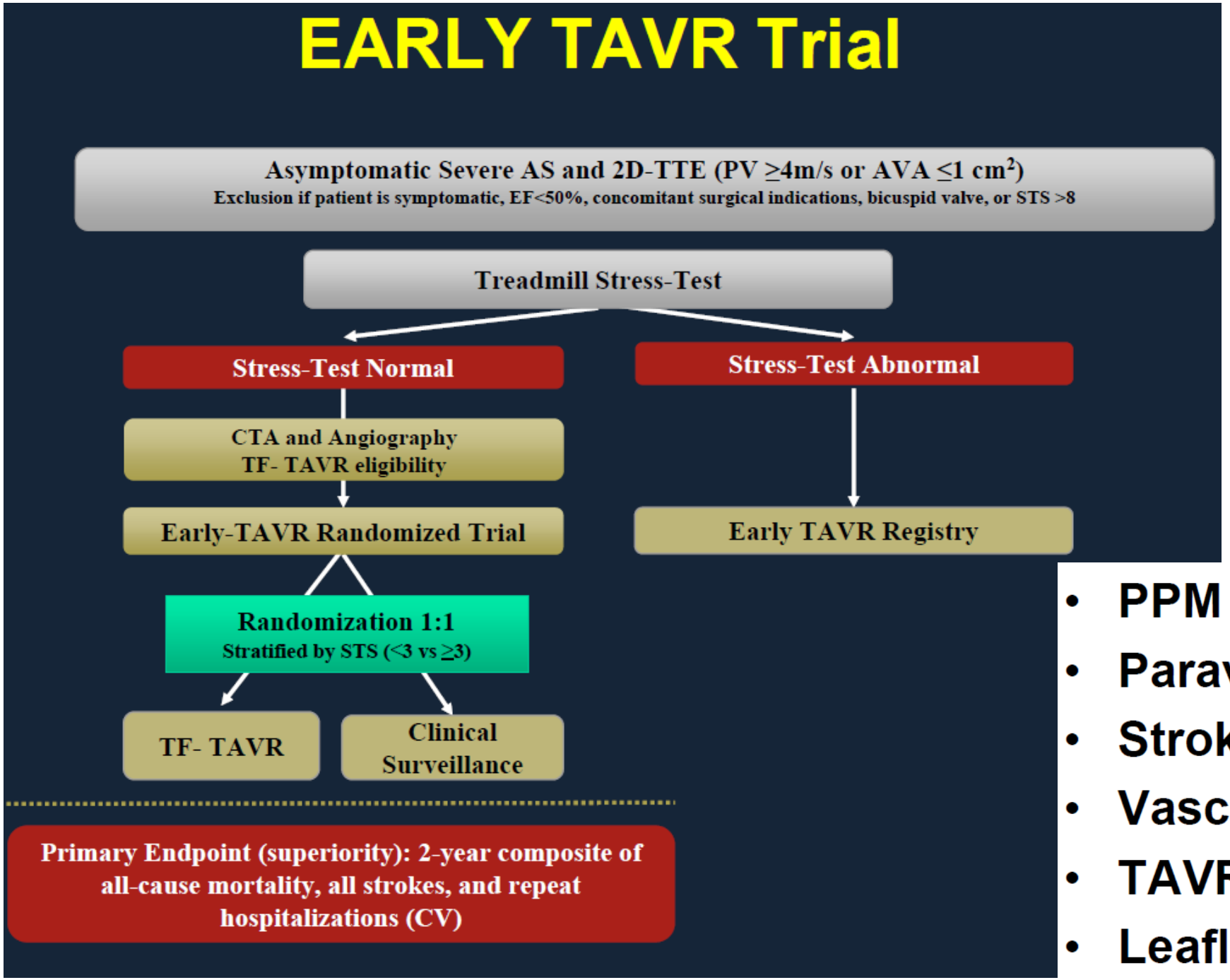
Taniguchi T et al. JACC 2015; 66:2827-38

A-symptomatic AS: better with SAVR



Genereux P et al. JACC 2016; 67:2263-88

EARLY TAVR Trial



TAVI limitations

- PPM requirement (~ 10%)
- Paravalvular leak (~1-2%)
- Stroke (~2%)
- Vascular complications
- TAVR valve durability
- Leaflet thrombosis

LRT: TAVR is safe in low-risk patients with severe symptomatic AS at 1 year

The Low-Risk TAVR (LRT)

- an investigator-initiated, prospective, multicenter study and the first FDA-approved Investigational Device Exemption trial to evaluate the feasibility of TAVR in low-risk patients
- late-breaking trial results presented at CRT 2019
- viewed as a possible signal of what's to come from larger, industry-funded trials of TAVR in low-risk patients that will be released at the ACC 2019

- 200 low-risk patients with symptomatic severe AS to undergo TAVR at 11 centers
- The initial results were released last year and showed: **at 30 days, there was 0 mortality and 0 disabling stroke, as well as low permanent pacemaker implantation rate (5.0%)**
- TAVR continued to be safe in patients at low risk of surgical mortality with symptomatic severe AS 1 year post-procedure
  - **At 1-year, mortality was 3.0%, stroke rate 2.1% and PPM implantation rate 7.3%**
  - Of the 14% of TAVR subjects who had evidence of subclinical leaflet thrombosis at 30 days, there was no impact on valve hemodynamics at 1 year

A-symptomatic AS
Predictors of reduced Survival

- "Very severe" AS (Vmax ≥ 5.0-5.5 m/s)
- Severe Ca^{++}, ↑rate progression, severe LVH
- Abnl response to exercise, ↑▼, ↑PA pressure
- ↓ strain, strain rate, twist; ↑ E/E' ratio
- LGE on cardiac MRI
- ↑ BNP

A-symptomatic patients with severe AS - indications for SAVR only

	Recommendations	Class	Level
1	d) Concomitant aortic valve surgery at the time of other cardiac/ascending aorta surgery		
1a	SAVR is indicated in patients with severe aortic stenosis undergoing CABG, or surgery of the ascending aorta or of another valve.	I	C
1b	SAVR should be considered in patients with moderate aortic stenosis* undergoing CABG, or surgery of the ascending aorta or of another valve after Heart Team decision.	IIa	C

EACTS
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European Society of Cardiology

A-symptomatic patients with severe AS - indications for SAVR only

	c) Asymptomatic patients with severe aortic stenosis (refers only to patients eligible for surgical valve replacement)		
2	SAVR is indicated in asymptomatic patients with severe aortic stenosis and systolic LV dysfunction (LVEF <50%) not due to another cause.	I	C
3a	SAVR is indicated in asymptomatic patients with severe aortic stenosis and abnormal exercise test showing symptoms on exercise clearly related to aortic stenosis.	I	C
3b	SAVR should be considered in asymptomatic patients with severe aortic stenosis and abnormal exercise test showing fall in blood pressure below baseline.	IIa	C
4	SAVR should be considered in asymptomatic patients with normal ejection fraction and none of the above-mentioned exercise test abnormalities if the surgical risk is low and one of the following findings is present: a – very severe aortic stenosis defined by a V_{max}>5.5 m/s, b – severe valve calcification and a rate of V_{max} progression ≥0.3m/s/year, c – markedly elevated BNP levels (>threefold age- and sex-corrected normalrange) confirmed by repeated measurements without other explanations, d – severe pulmonary hypertension (systolic pulmonary artery pressure at rest >60 mmHg confirmed by invasive measurement) without other explanation.	IIa	C

EACTS European Association for Cardio-Thoracic Surgery

ESC European Society of Cardiology

Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk (I)

	Favours TAVI	Favours SAVR
Clinical characteristics		
STS/EuroSCORE II <4% (logistic EuroSCORE I <10%)[a]		+
STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)[a]	+	
Presence of severe comorbidity (not adequately reflected by scores)	+	
Age <75 years		+
Age ≥75 years	+	
Previous cardiac surgery	+	
Frailty[b]	+	
Restricted mobility and conditions that may affect the rehabilitation process after the procedure	+	
Suspicion of endocarditis		+

TAVI

STS <10%

EuroScore II <5%

EuroScore I <20%

Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk (II)

TAVI

Anatomical and technical aspects		
Favourable access for transfemoral TAVI	+	
Unfavourable access (any) for TAVI		+
Sequelae of chest radiation	+	
Porcelain aorta	+	
Presence of intact coronary bypass grafts at risk when sternotomy is performed	+	
Expected patient–prosthesis mismatch	+	
Severe chest deformation or scoliosis	+	
Short distance between coronary ostia and aortic valve annulus		+
Size of aortic valve annulus out of range for TAVI <18 or >30mm		+
Aortic root morphology unfavourable for TAVI		+
Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI		+
Presence of thrombi in aorta or LV		+

SAVR

Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk (III)

Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention		
Severe CAD requiring revascularization by CABG		+
Severe primary mitral valve disease, which could be treated surgically		+
Severe tricuspid valve disease		+
Aneurysm of the ascending aorta		+
Septal hypertrophy requiring myectomy		+

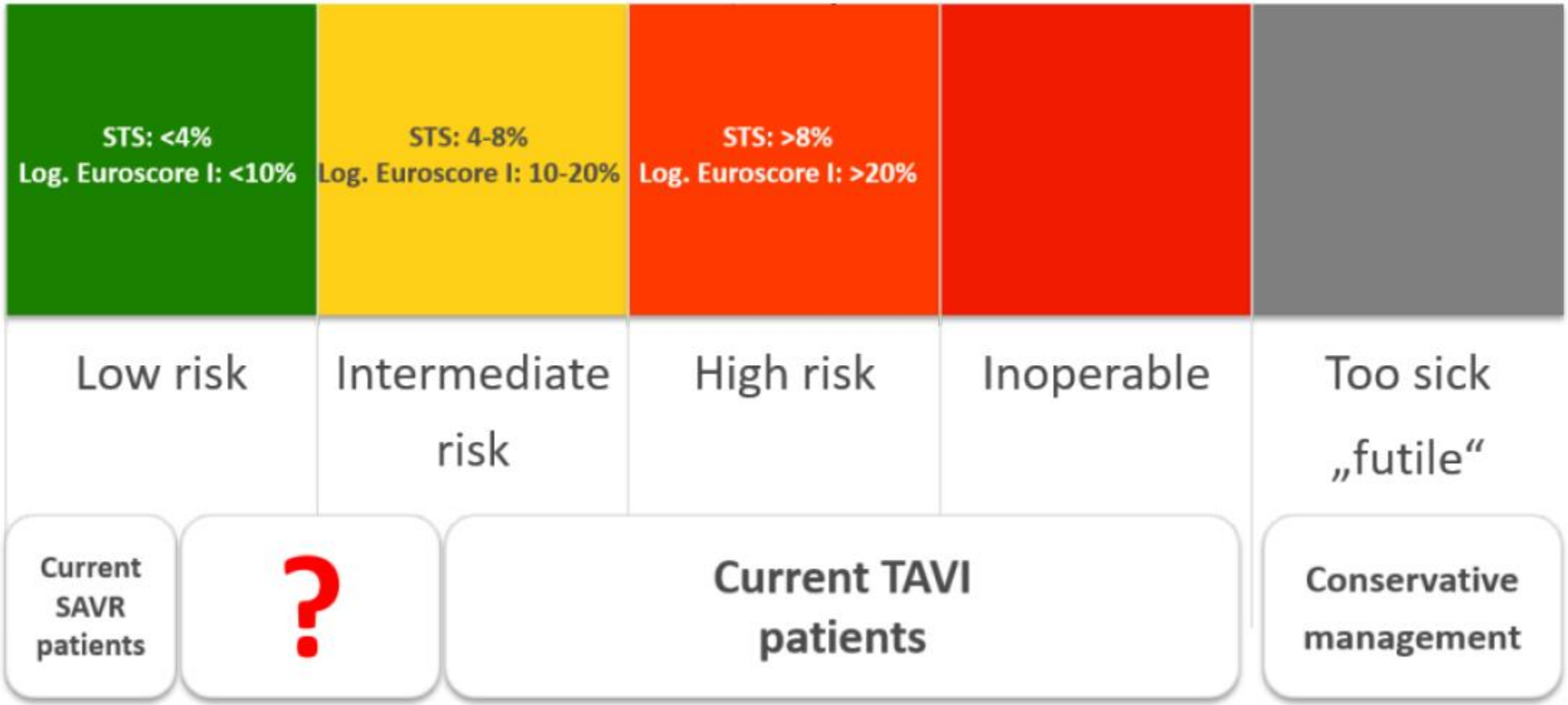
SAVR

Latest ESC guidelines on AS (or any VHD) management

- Need for **Heart (Valve) Team**
- Put the **Patient** at the very Center of Care
- Keep up with the **Evidence that is Evolving**…

Surgery in severe AS - Evolution of the Guidelines

		ACC/AHA 1998	ESC 2002	ACC/AHA 2006	ESC 2007	ACC/AHA 2008	ESC/EACTS 2012	ACC/AHA 2014	ESC/EACTS 2017
Asymptomatic / SAVR	Symptoms	I	I	I	I	I	I	I	I
	Symptoms during exercise testing		IIa	IIb	I	IIb	I	I	I
	LVEF < 50%	IIa	IIa	I	I	I	I	I	I
	Undergoing other cardiac surgery	I	I	I	I	I	I	I	I
	Very severe AS (ESC 5.5 m/s, ACC 5.0 m/s)			IIb		IIb	IIa	IIa	IIa
	Exercise test: Blood pressure drop	IIa	IIa	IIb	IIa	IIb	IIa	IIa	IIa
	Calcified valve + rapid progression (≥ 0.3 m/s/yr)		IIa	IIb	IIa	IIb	IIa	IIb	IIa
	Elevated BNP (3x age/gender corrected)						IIb		IIa
	Severe pulmonary hypertension (sPAP > 60mmHg)								IIa
	Exercise echo: ↗mGrad ≥ 20 mmHg						IIb		
	Excessive LVH – no hypertension	IIb	IIb				IIb		
	Ventricular Arrhythmias	IIb	IIb						


STS: <4%
Log. Euroscore I: <10%
STS: 4-8%
Log. Euroscore I: 10-20%
STS: >8%
Log. Euroscore I: >20%
Low risk
Intermediate risk
High risk
Inoperable
Too sick „futile“
Current SAVR patients
?
Current TAVI patients
Conservative management

Transcatheter Aortic Valve Implantation Futility Risk Model

Please enter your patient information

- [x] Need for Diuretics
- [x] Previous oncological disease
- [x] Access

Pre-procedural AV gradient mean

10 | 55 | 80

10 17 24 31 38 45 52 59 66 73 80

Serum creatinine (mg/dl)

0.5 | 1 | 4

0.5 0.9 1.3 1.7 2.1 2.5 2.9 3.3 3.7 4

Hemoglobin (gr/dl)

5 | 7.6 | 18

5 6.3 7.6 8.9 10.2 11.5 12.8 14.1 15.4 16.7 18

Base NYHA

1 | 4

1 2 3 4

The raw probability of a futile TAVI by the model is 79%

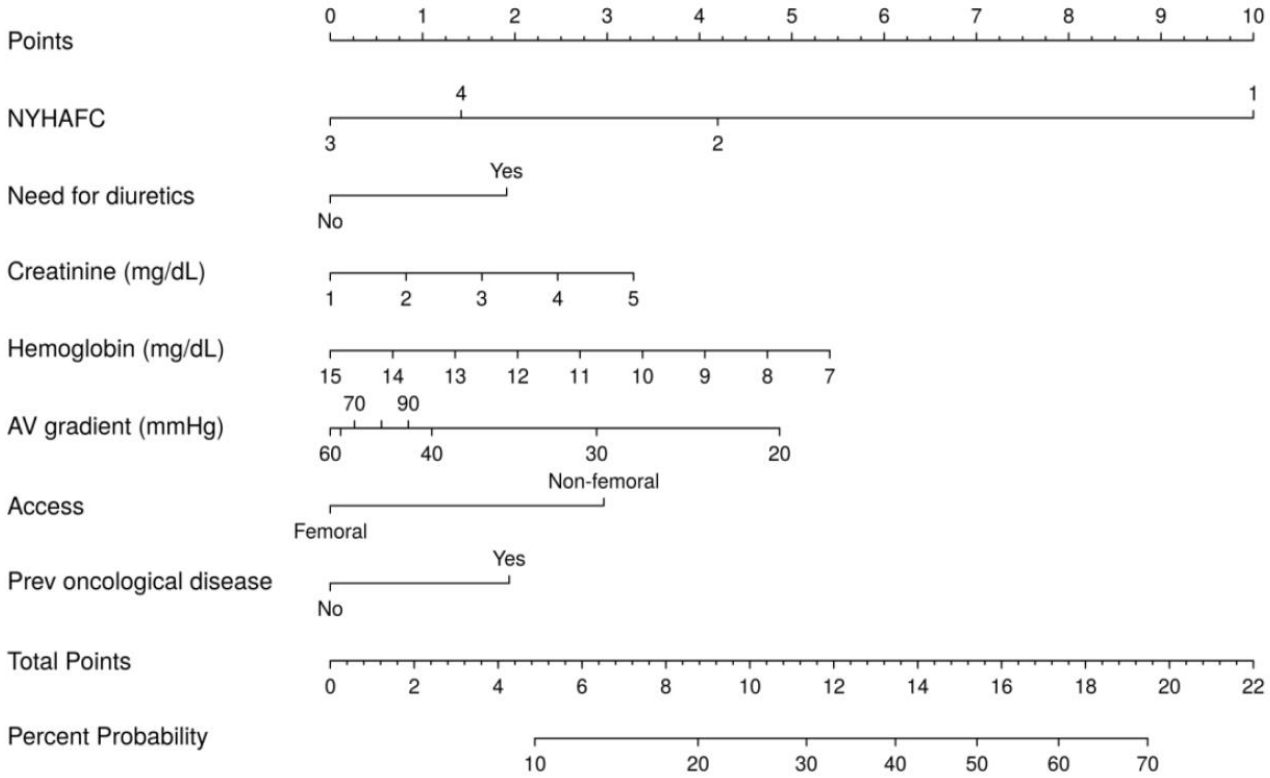
The prediction category is **High risk**

Based on the category, the predicted chance of a futile TAVI is 50%

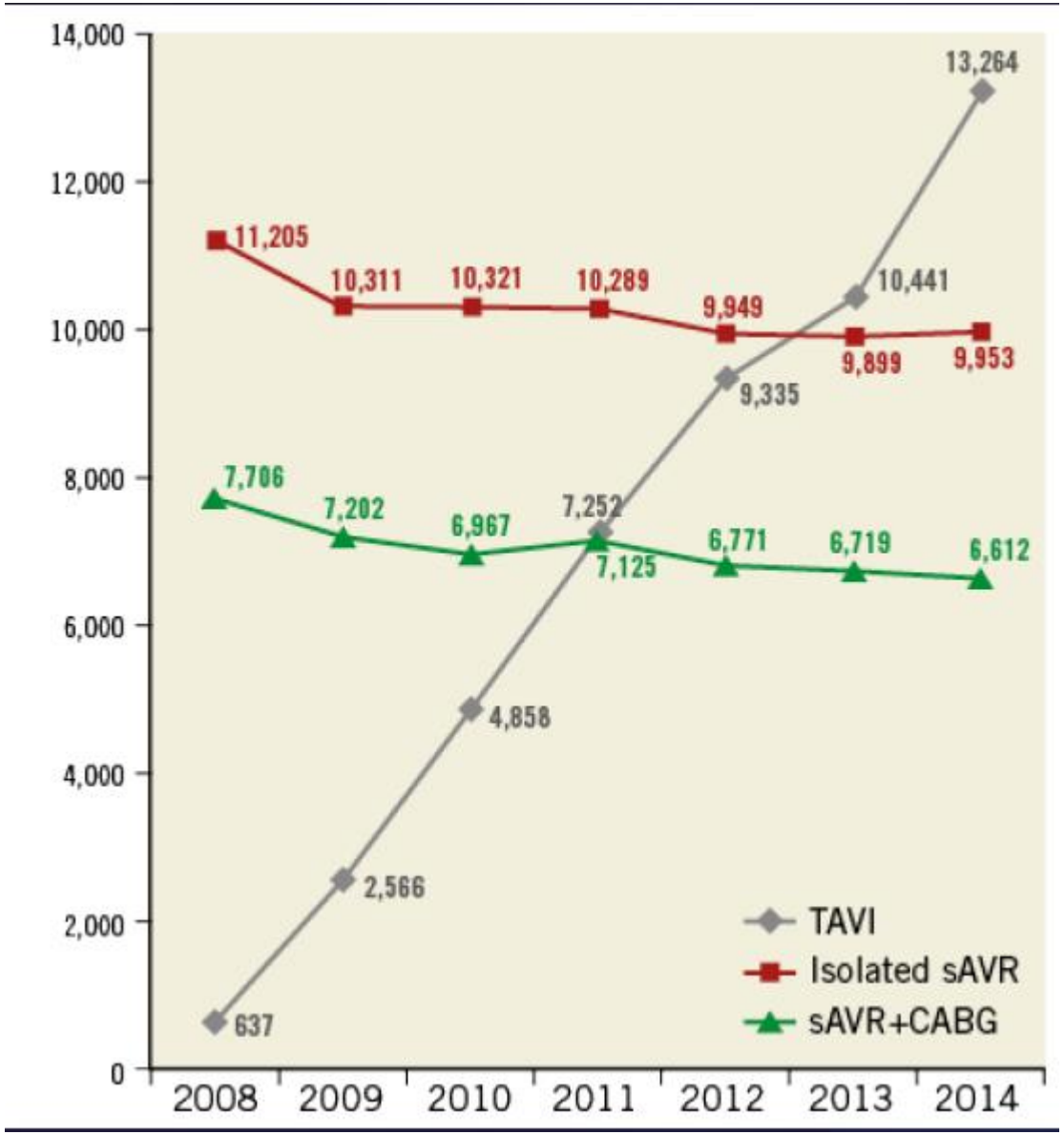
Up to **5** points = 6% overall risk of futility.
"Low" category

6 - 11 points = 16% overall risk of futility.
"Medium" category

Above **11** points = 50% futility.



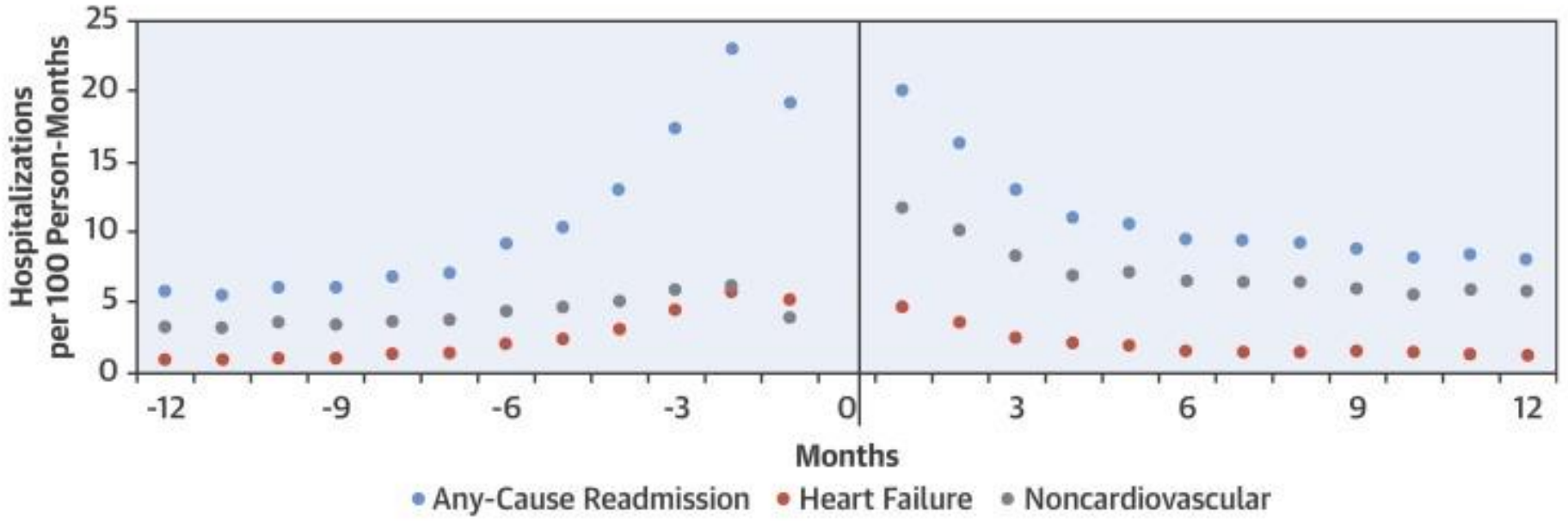
AV procedures
Germany 2008 - 2014



Eggebrecht et al, EuroIntervention 2015

Post TAVR: lower costs and fewer HF hospitalizations but more all-cause, non-CV and bleeding hospitalizations

CENTRAL ILLUSTRATION: 3-Month Moving Average and Hospitalization Cause-Specific Event Rates in the Year Pre-Transcatheter Aortic Valve Replacement and Post-Transcatheter Aortic Valve Replacement



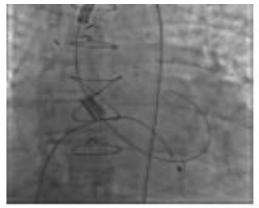
Vemulapalli, S. et al. J Am Coll Cardiol. 2019;73(10):1135-46.

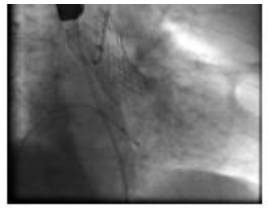
PCR London Valves Innovators Day 2017. Where will valve intervention be in 2025?

Prendergast B, ESC & EuroIntervention 2018

Sam Dawkins[1]*, MBBS, DPhil; Thomas Modine[2], MD, PhD; Stephan Windecker[3], MD; Nicolo Piazza[4], MD, PhD; Bernard D. Prendergast[5], DM

Aortic Valve



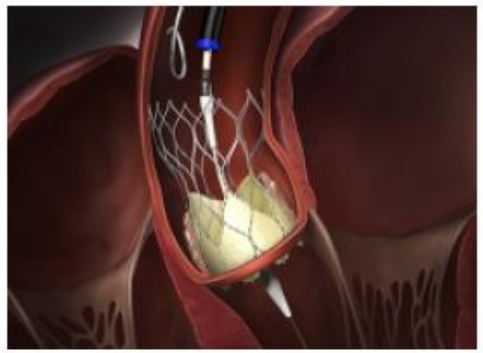
Implementation	TAVI will account for 90-100% of all aortic valve replacement procedures
	Surgery will remain the treatment of choice for some patient groups (infective endocarditis, diffuse complex coronary artery disease, and diseases of the ascending aorta)
	Ad hoc TAVI will be a reality
Engineering	12 Fr delivery systems will be the standard
	Tissue engineered heart valves
	Resorbable stent frame
	Advanced leaflet technologies such as polymers, printed leaflets customised to the patient
	Complications
	Pacemaker rates comparable to surgery
	No paravalvular leak
Research	No more randomised trials
	Big data studies with surrogate endpoints
	More durability data
	Enhanced TAV-in-TAV data
	New developments in medical therapies for aortic stenosis
Geopolitics	Earlier diagnosis
	Wider geographical spread
	Cheaper devices

Σας ευχαριστώ πολύ

για την προσοχή

TAVI-PM
Post-mortem observation study of TAVI

Karakas et al, Hamburg, Germany, ESC LBT 2018



- 451 TAVI patients (implanted 2007 – 2018) with informed consent for post-mortem, implanted or medically treated at our site
- 39 post mortem TAVIs examined so far

Postmortem CT

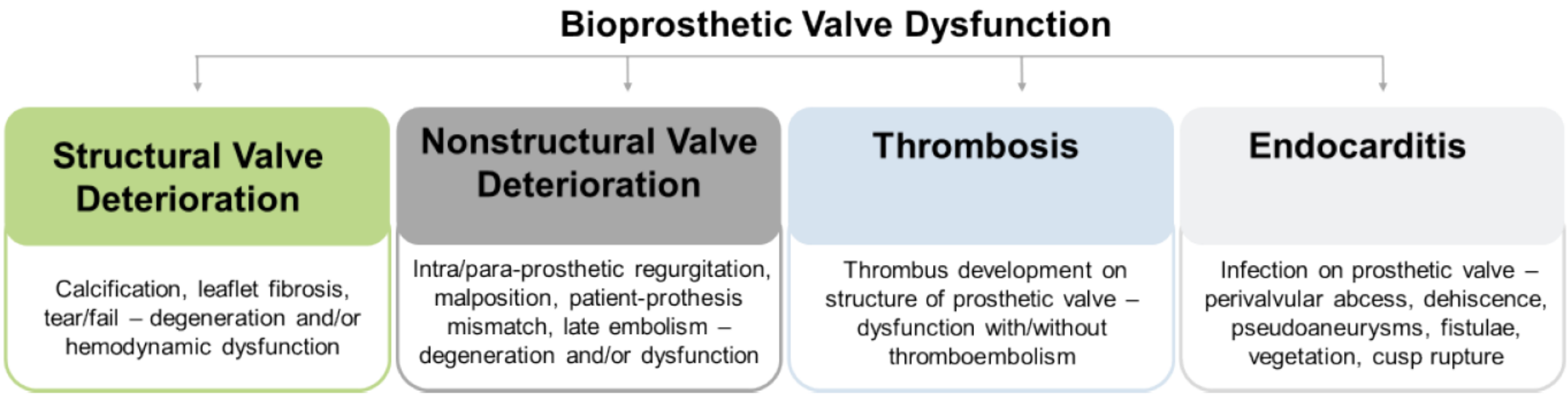
Macro-/Microscopic assessment

Corelab: Immunohistochemistry

Corelab: Electronmicroscopy

Assessing long-term durability of TAVI/ SAVR –

2017 Consensus statement of EAPCI, ESC, EACTS



adapted from Eur Heart J 2017;38:3382-90

Characteristics (n=39)	
Age (years)	81.1 ± 7.2
Gender (female)	44 %
Insulin-dependent diabetes mellitus	26 %
Hypertension	74 %
Renal insufficiency	35 %
Atrial fibrillation	48 %
Coronary artery disease	64 %
Log Euro-Score	23.1 %

Time from implantation to death & post mortem assessment	N
< 1 year	14
1-2 years	9
2-4 years	8
> 4 years	8
Valve Type	
Self-expandable	27
Balloon-expandable	12

Bioprosthetic Valve Dysfunction

Structural Valve Deterioration

Calcification, leaflet fibrosis, tear/fail – degeneration and/or hemodynamic dysfunction

- fragmentation and irregularity +

Nonstructural Valve Deterioration

Intra/para-prosthetic regurgitation, malposition, patient-prothesis mismatch, late embolism – degeneration and/or dysfunction

- Grade 3/4 regurgitation ⊘
- Prosthesis malposition: **1**
- Prosthesis mismatch: ⊘

Thrombosis

Thrombus development on structure of prosthetic valve – dysfunction with/without thromboembolism

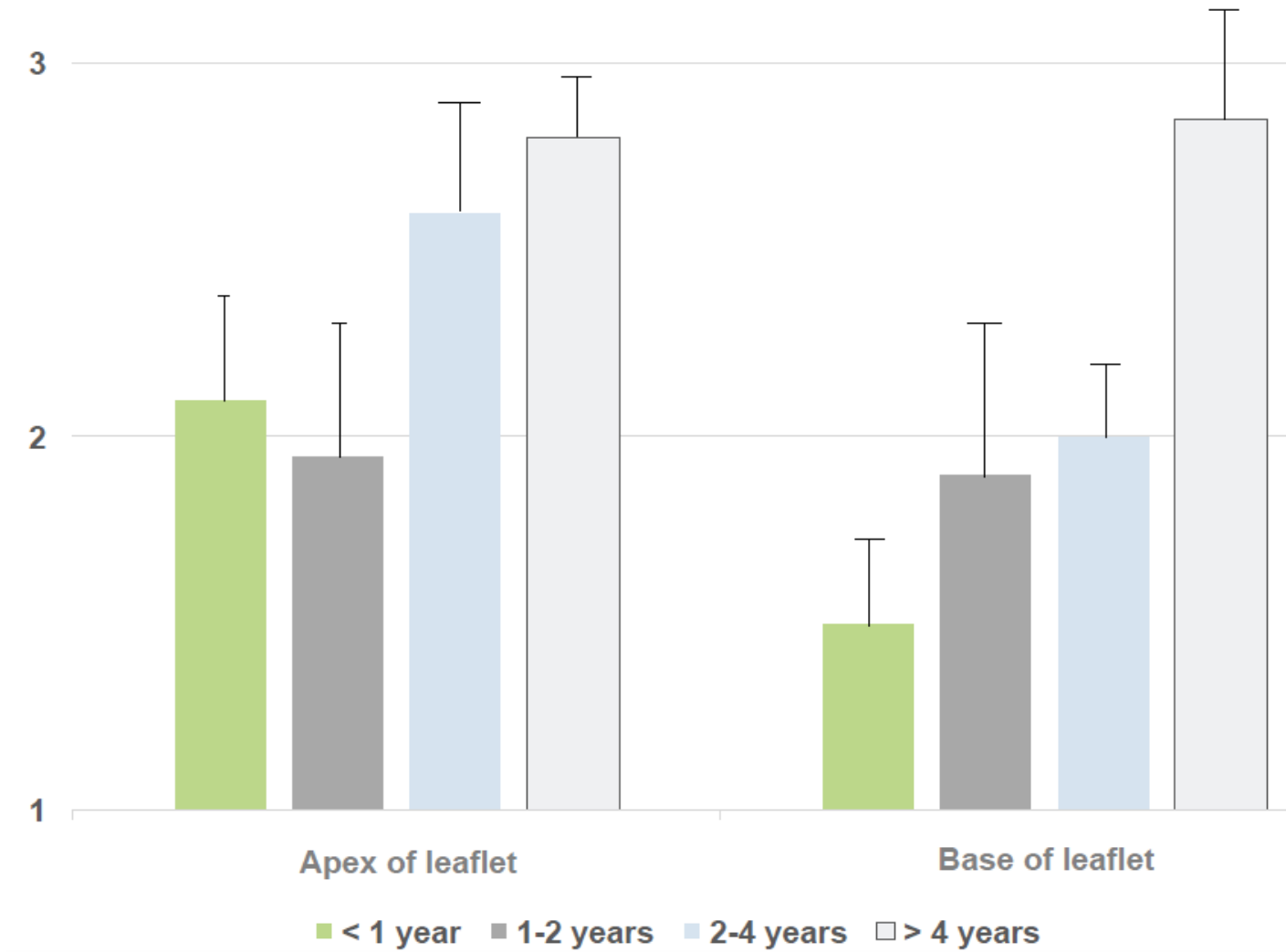
- Thrombus development: **1**
- Thromboembolism: ⊘

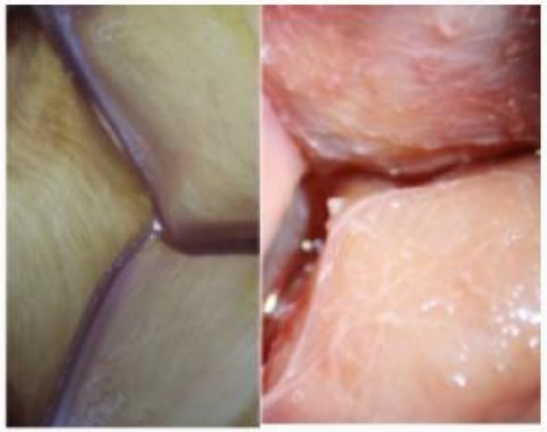
Endocarditis

Infection on prosthetic valve – perivalvular abcess, dehiscence, pseudoaneurysms, fistulae, vegetation, cusp rupture

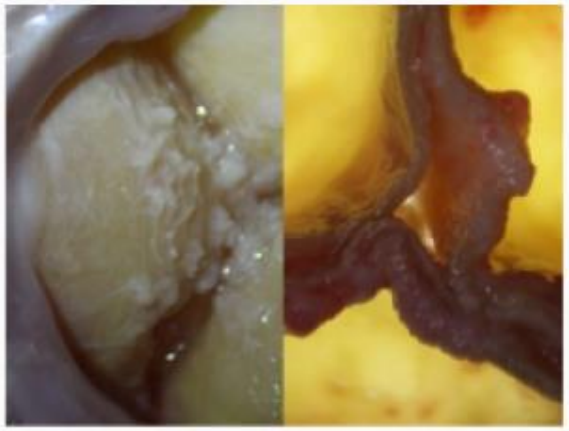
- Perivalvular abscess: ⊘
- Dehiscence: ⊘
- Vegetations: ⊘
- Perforation: **1**

Histological scoring (fragmentation/irregularity)

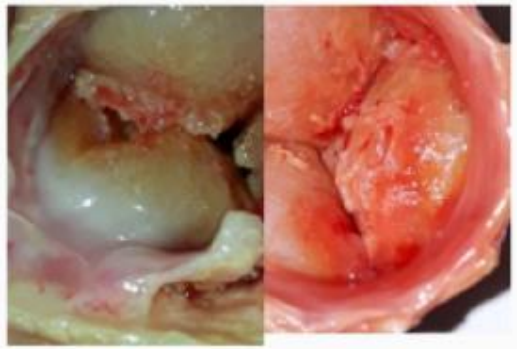




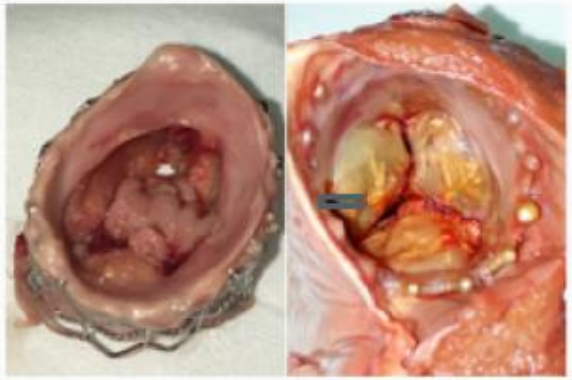
1- no/low deteriorations



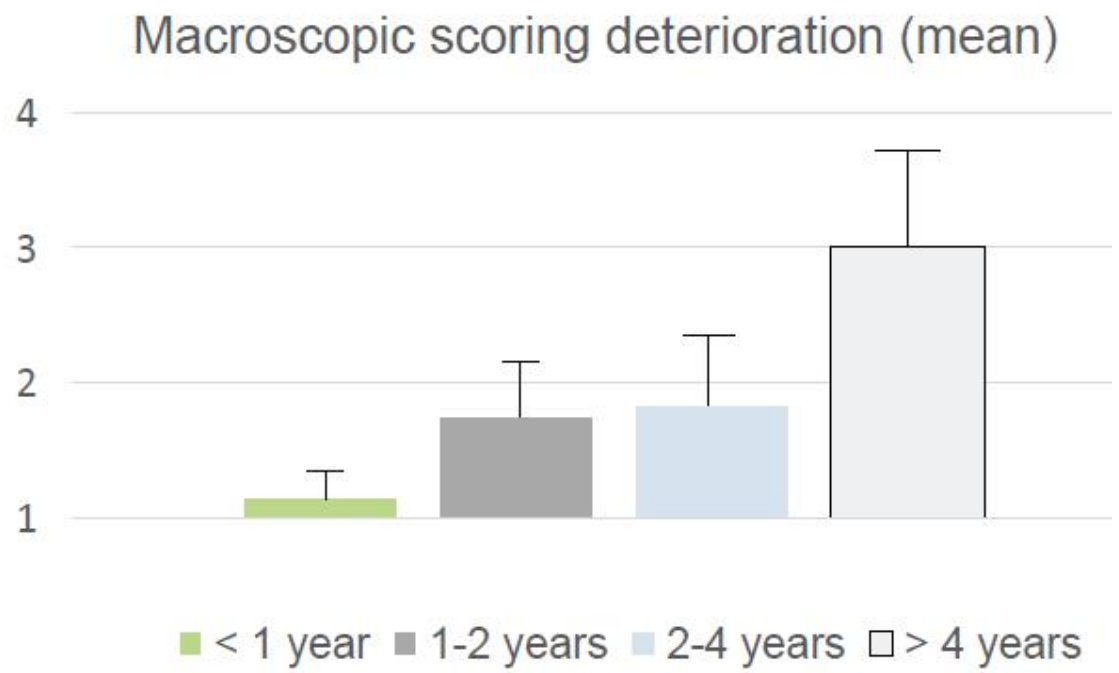
2- low/medium deteriorations



3- single leaflet deteriorated



4 – all leaflets deteriorated



3 questions to ask:

- Do they correlate with clinical outcomes ?
- Do they have haemodynamic consequences ?
- How do they compare with surgical bioprosthetic valves ?