



# Moderate Aortic Stenosis and Heart Failure

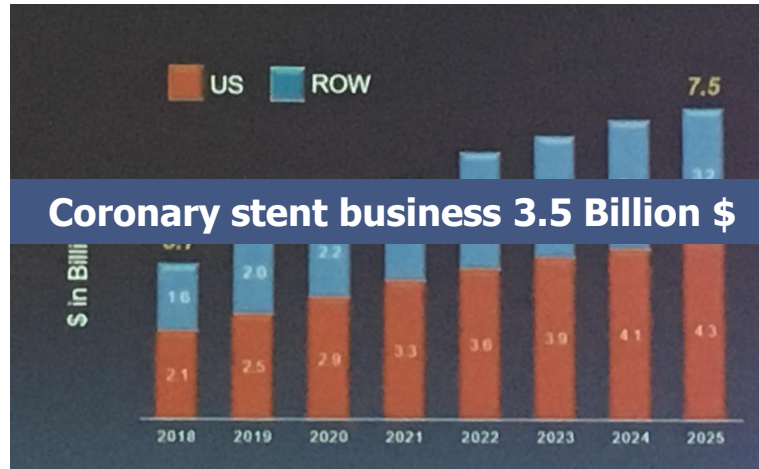
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**Director of Interventional Cardiology**  
**Thoraxcenter, Erasmus MC**  
**Rotterdam**

# TAVI Market Projections for 2025

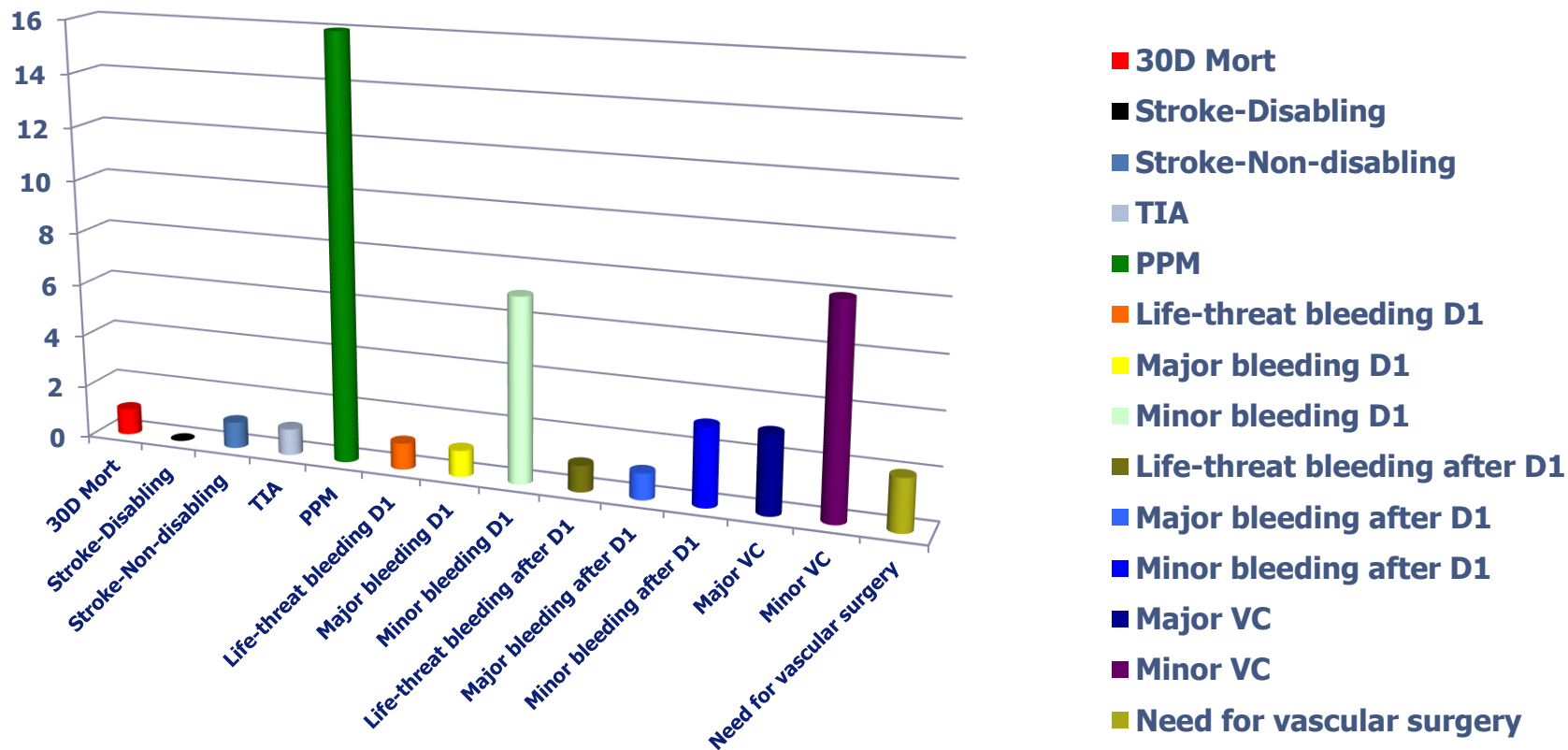
## Expected TAVI Market Share



## Expected TAVI Revenue in \$



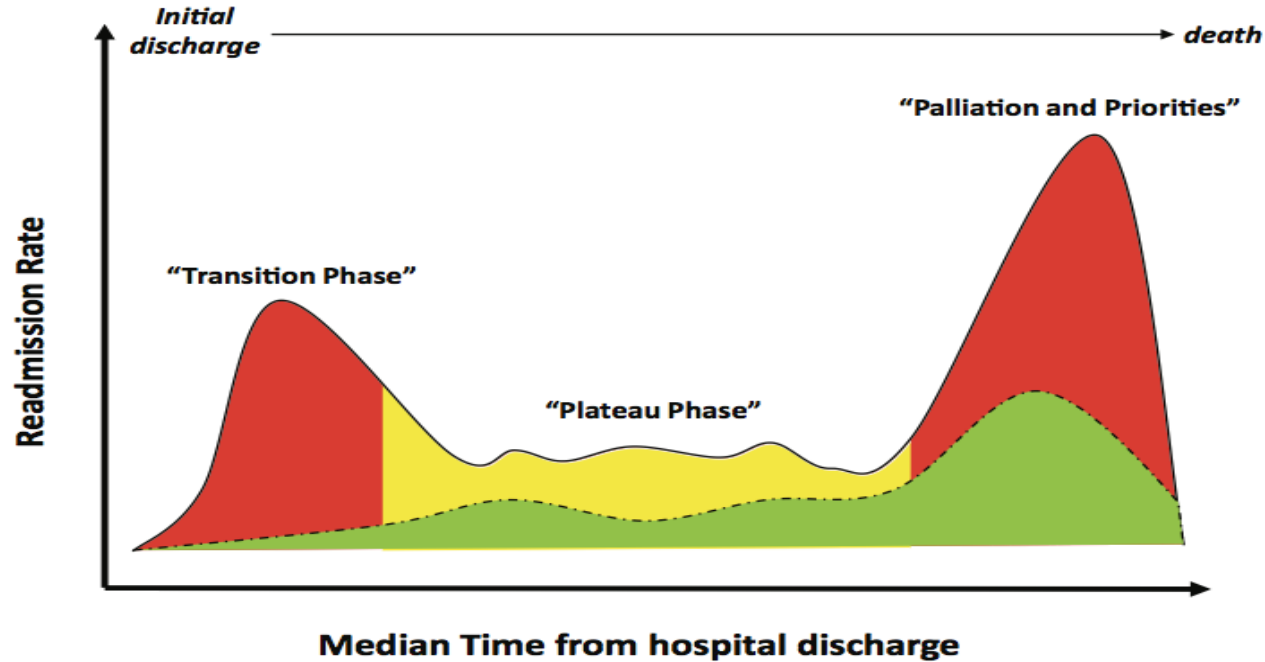
# Erasmus MC TAVI Outcome 2017



# AS – HF Facts

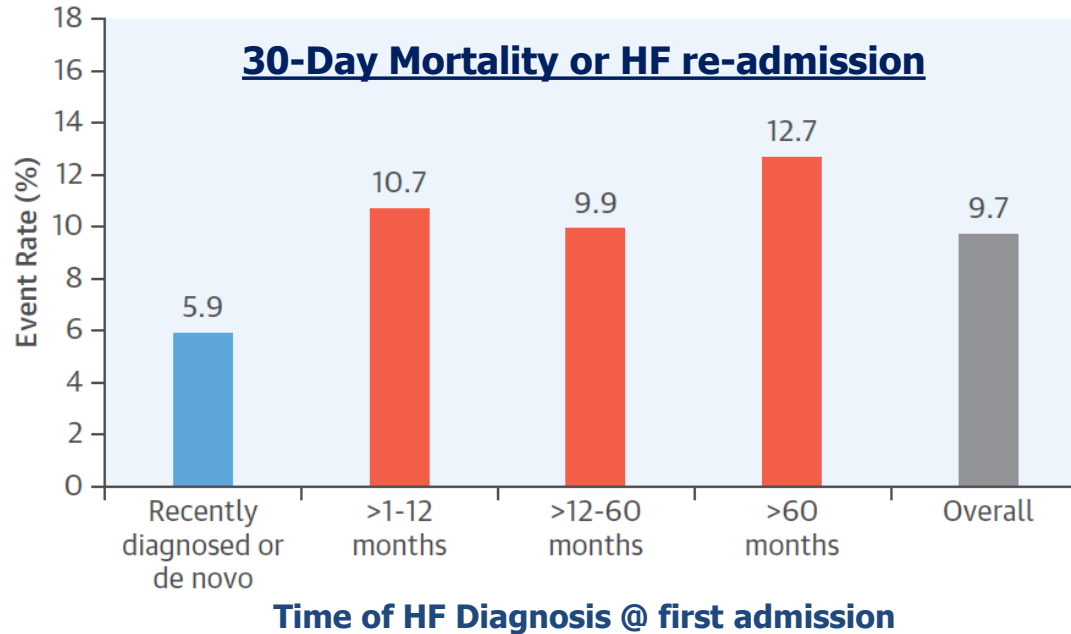
- In Western World prevalence of **Aortic sclerosis** > 65 y/o = 25%
  - ✧ 16% will progress to AS within 8 years
- **AS prevalence** in Elderly  $\cong$  4%, LV dysfunction in 25%
- **HF affects 4%** of the population, gradually increasing with age to  $\cong$  15% in 70 – 80 y/o
- After HF admission: rate for death or readmission @ 1 year = 40%

# HF Re-admission

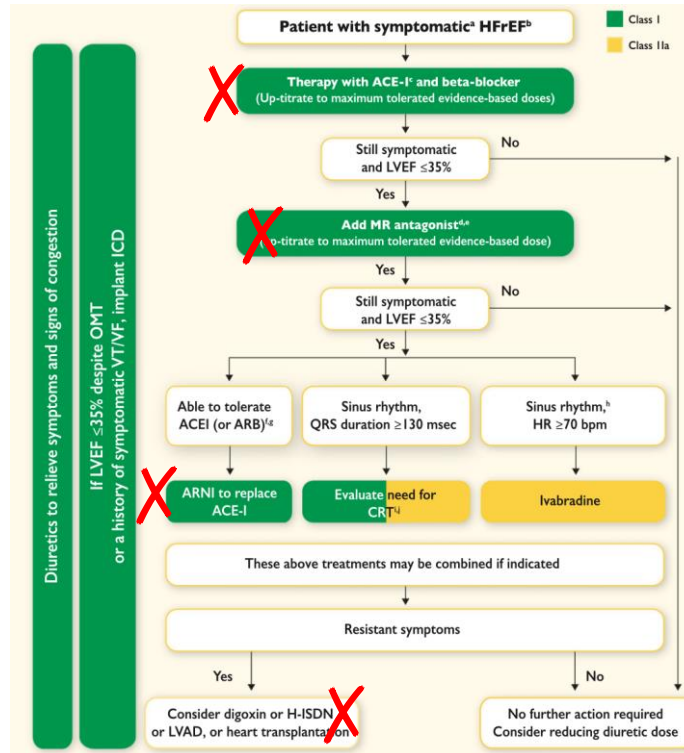


# Impact of HF Admission

*ASCEND-HF Trial Sub-study*



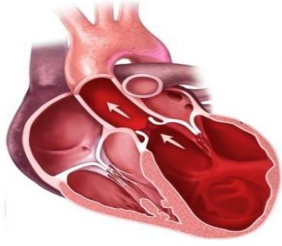
# ESC Guidelines 2016



**Afterload Reducers**

## Heart Failure

Leading cause of hospitalizations



**Increased AFTERLOAD**

(*sympathetic activity*)

Impaired LV systolic function

Diastolic dysfunction



**Beta-blockers**

**ACEi/ ARBs**

MRAs

Diuretics

**Coexistence of Heart  
Failure and Moderate  
Aortic Stenosis**



**High risk population**



**Early AVR may be  
beneficial**

## Aortic Stenosis

Most frequent valvulopathy



**Increased AFTERLOAD**

(*trans-valvular gradient*)

Impaired LV systolic function

Diastolic dysfunction



**Moderate AS**

**Watchful**

**Waiting**

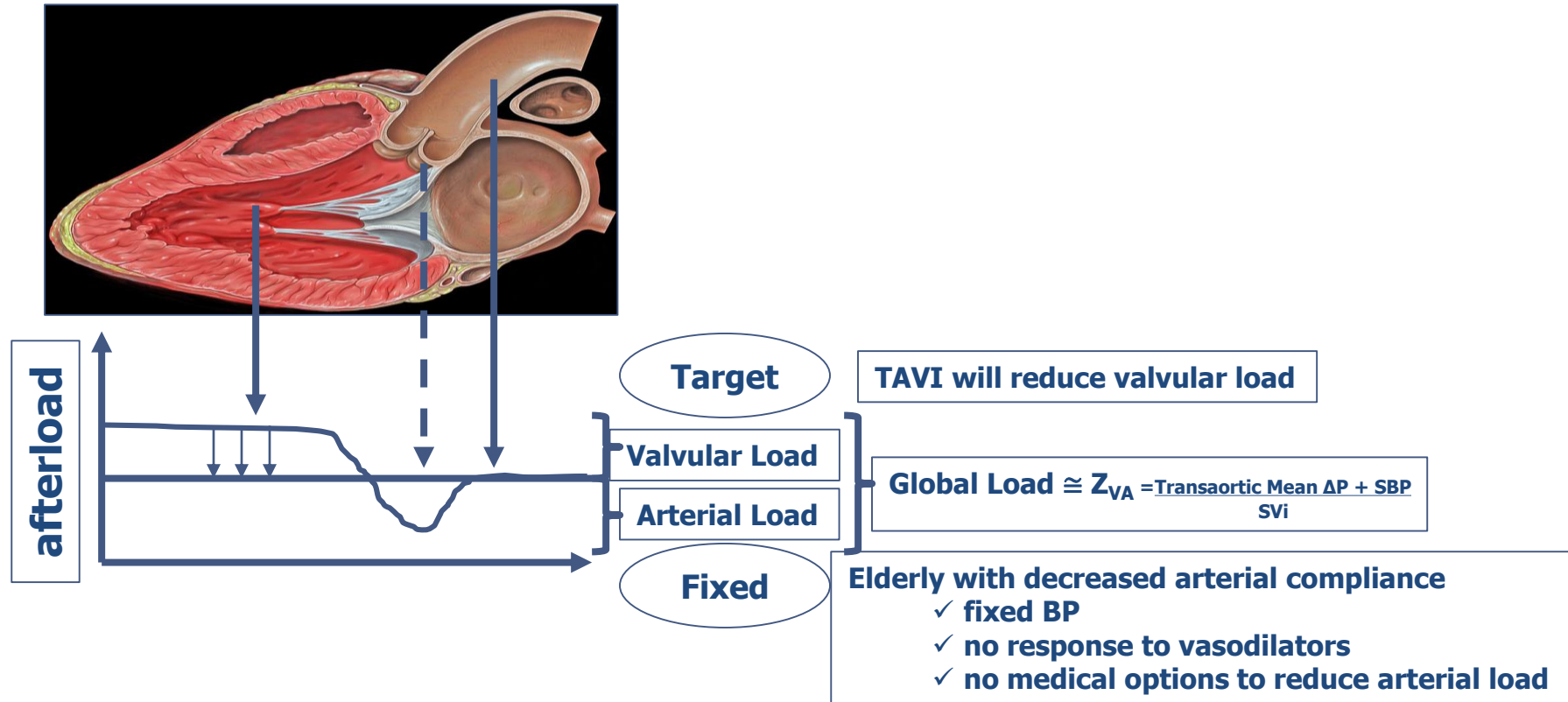
**Severe AS**

**Aortic Valve**

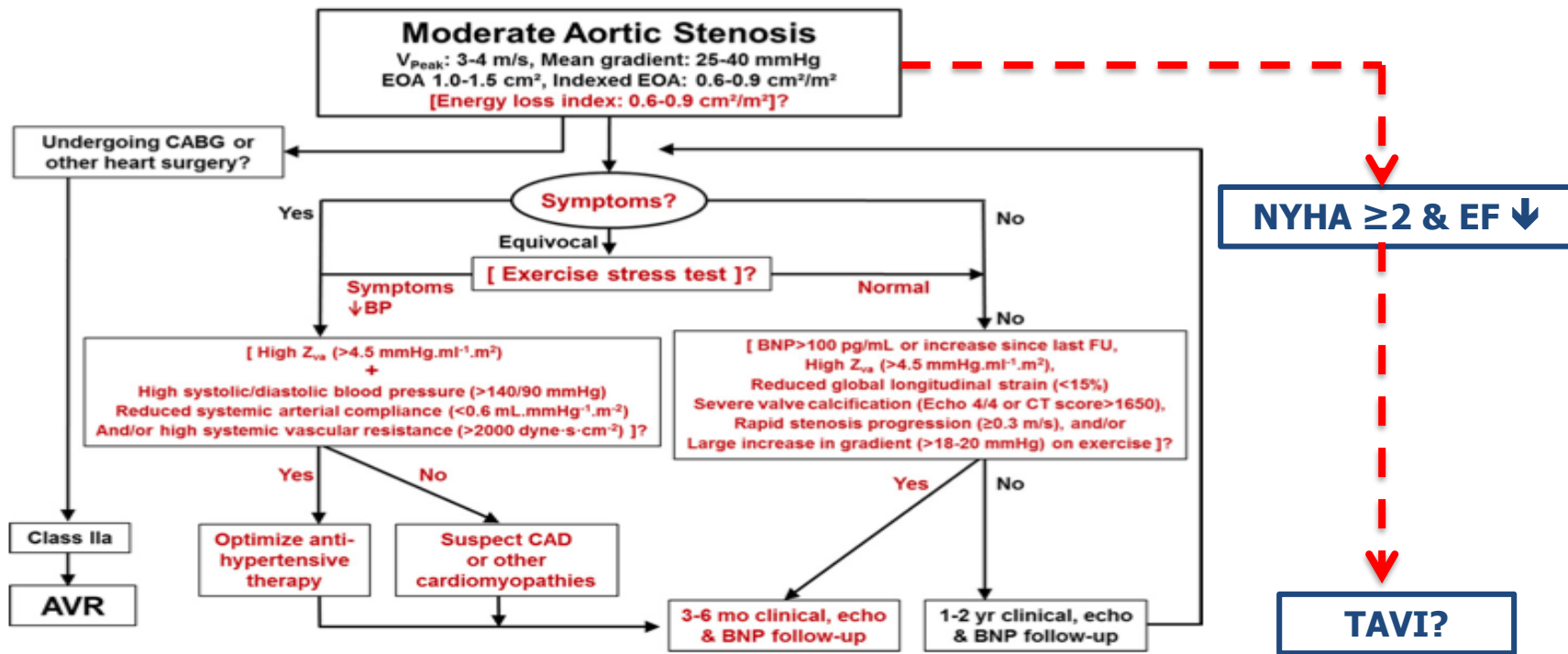
**Replacement**



# Hemodynamic Fundamentals



# Guidelines on Moderate AS



# AVR for Moderate AS

## Duke Echocardiographic Database

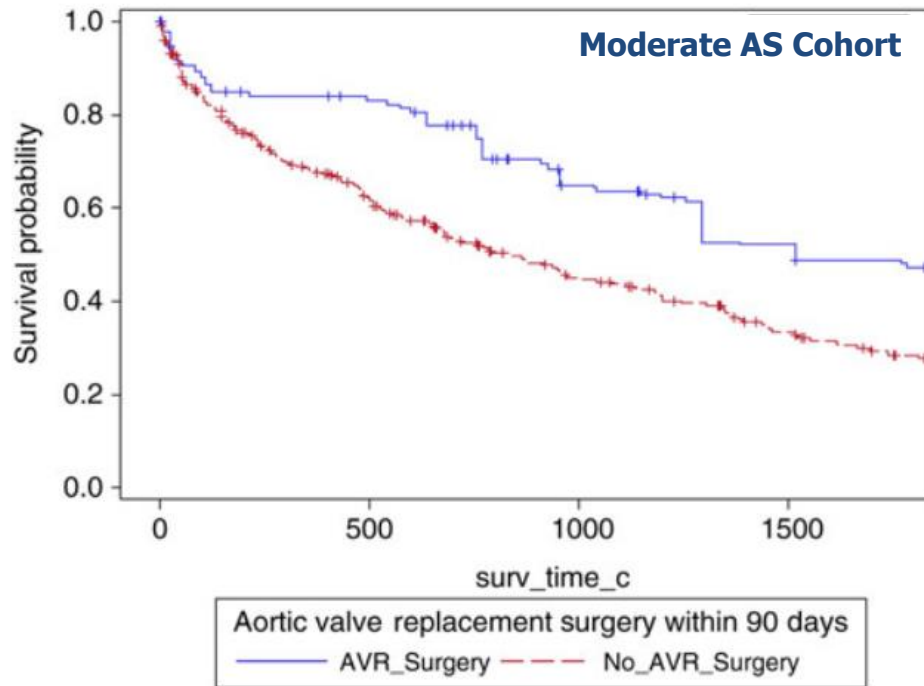
**N = 132804**

**AS defined as MG > 25 mmHg or  $v_{\max}$  3 m/s**

**N = 1634 patients with AS**

**N = 1090 with moderate AS, 26% SAVR**

**N = 544 with severe AS, 48% SAVR**



# Moderate Prosthesis-Patient Mismatch Clinical Impact

## Laval Hospital

N = 2567 patients after SAVR

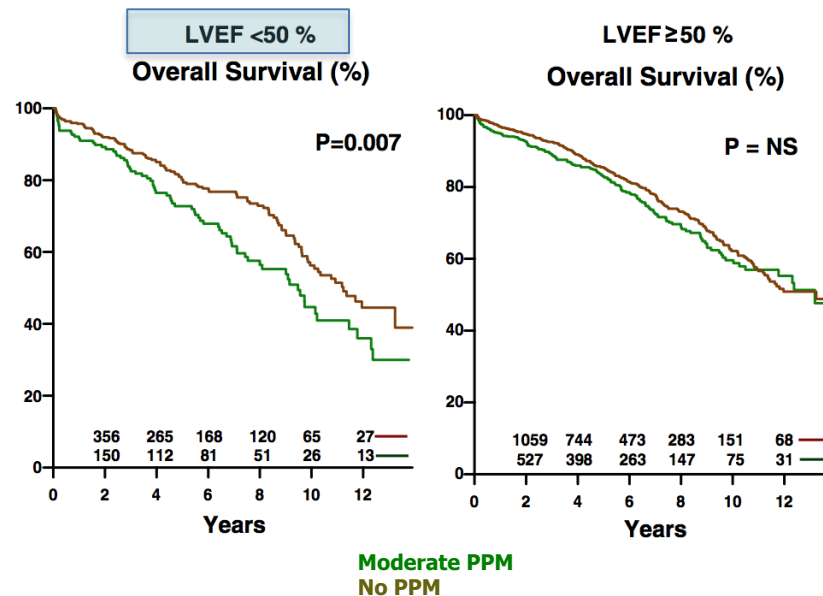
N = 1739 non-significant Patient-Prosthesis mismatch

N = 797 with Moderate Patient-Prosthesis mismatch

$$0.65 > AVA_i \leq 0.85 \text{ cm}^2/\text{m}^2$$

N = 40 Severe Patient-Prosthesis mismatch

**Moderate PPM increases mortality when EF < 50%**



# Prognostic Implications of Moderate Aortic Stenosis in Patients With Left Ventricular Systolic Dysfunction



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# Moderate AS & LV Dysfunction

	N=310
Age (mean $\pm$ SD)	72 $\pm$ 11
Male (n,%)	75%
Coronary artery disease (n,%)	72%
Prior myocardial infarction (n,%)	52%
Prior PCI (n,%)	35%
Prior CABG (n,%)	28%
COPD (n,%)	25%
eGFR in ml/min (mean $\pm$ SD)	61 $\pm$ 20
Peripheral arterial disease (n,%)	19%
Prior stroke (n,%)	43, 14%
NYHA-class (n,%)	
III	29%
IV	4%
Cardiac resynchronization therapy (n,%)	12%

Erasmus Medical Center Rotterdam



Leiden University Medical Center



Quebec Heart and Lung institute

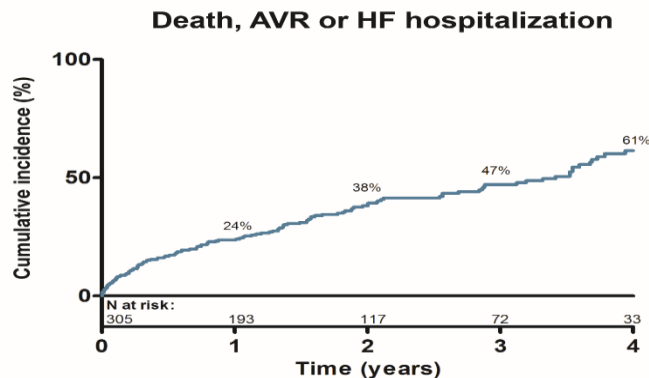


Columbia Medical University New York

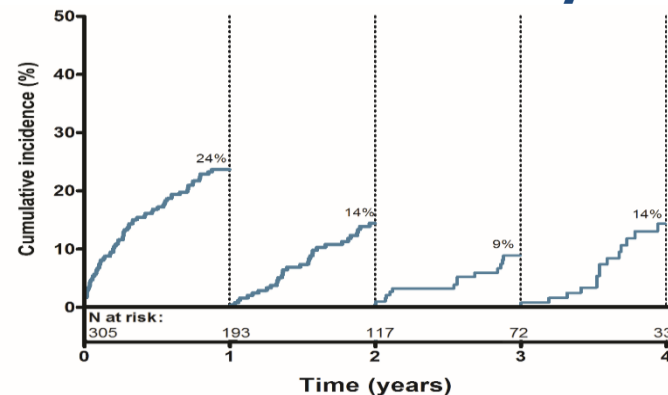


# Primary Composite Endpoint

## Overall

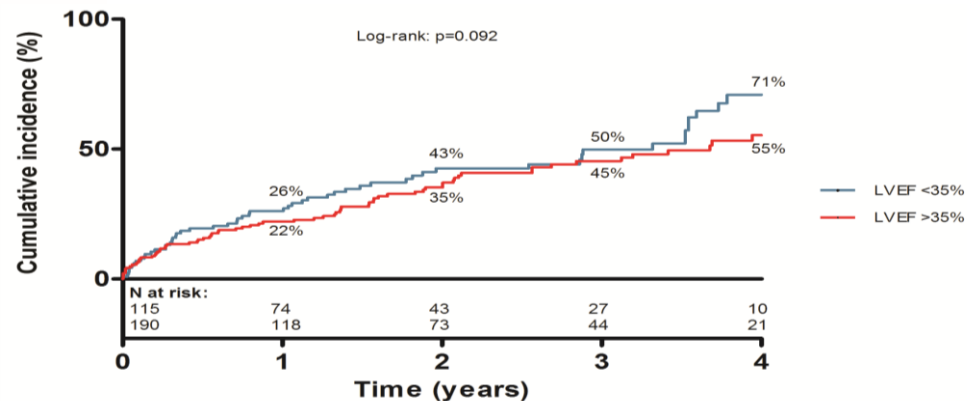
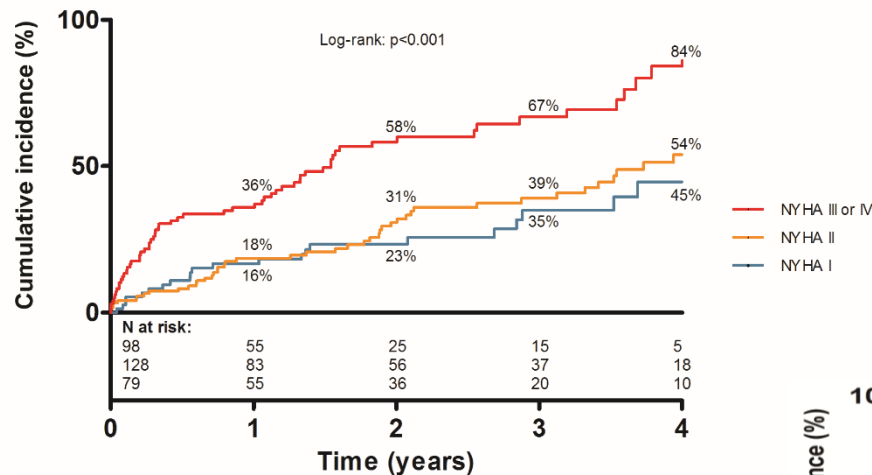


## Landmark Analysis



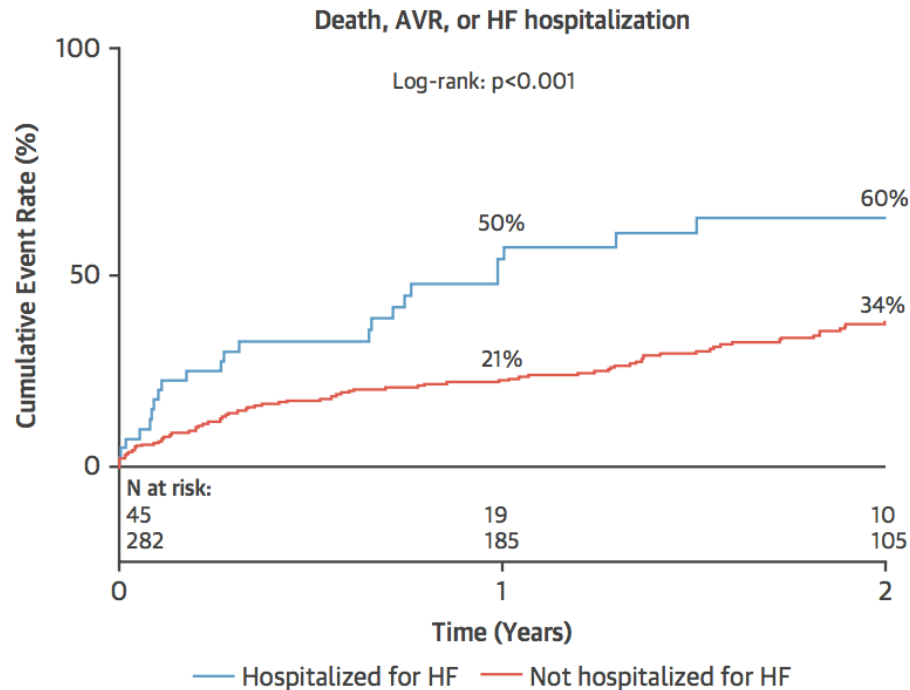
- ✓ Clinical events are common (61% @ 4 yrs FU)
- ✓ Most events occur within the first year
- ✓ 1 in 4 were NYHA 1, 42% NYHA 2!

# Impact of NYHA Class & EF

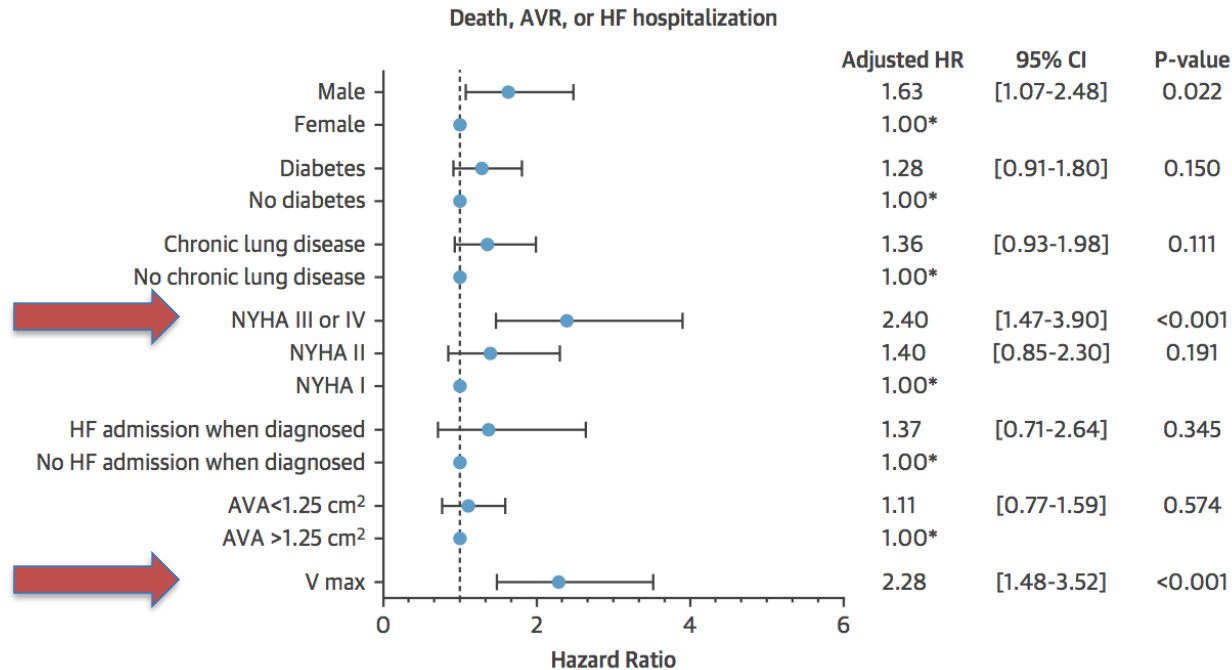




# Impact of HF Admission

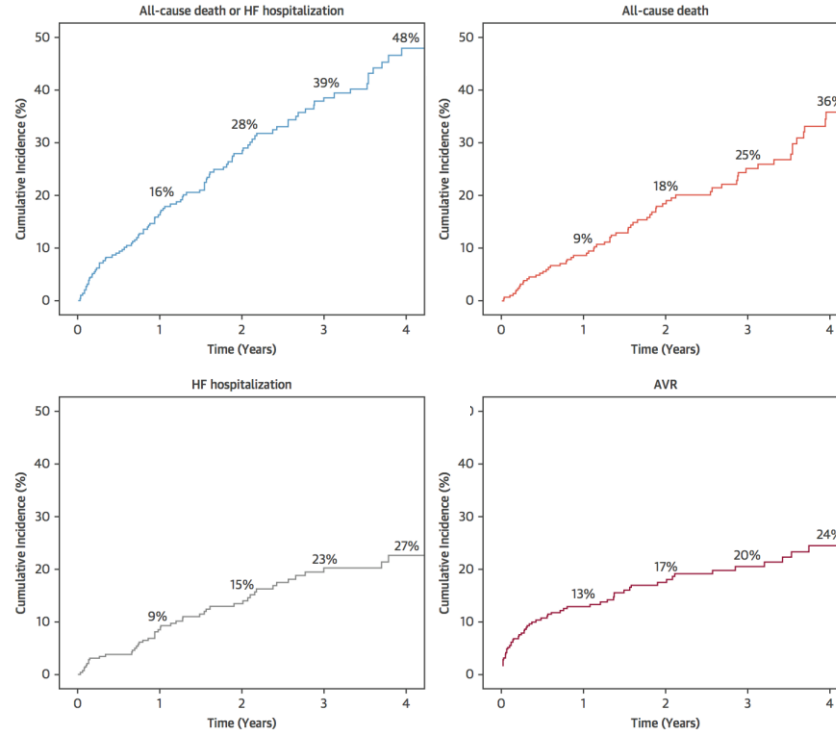


# Predictors for Composite Endpoint

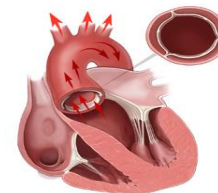
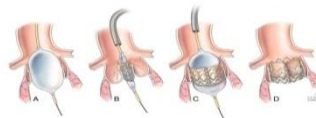
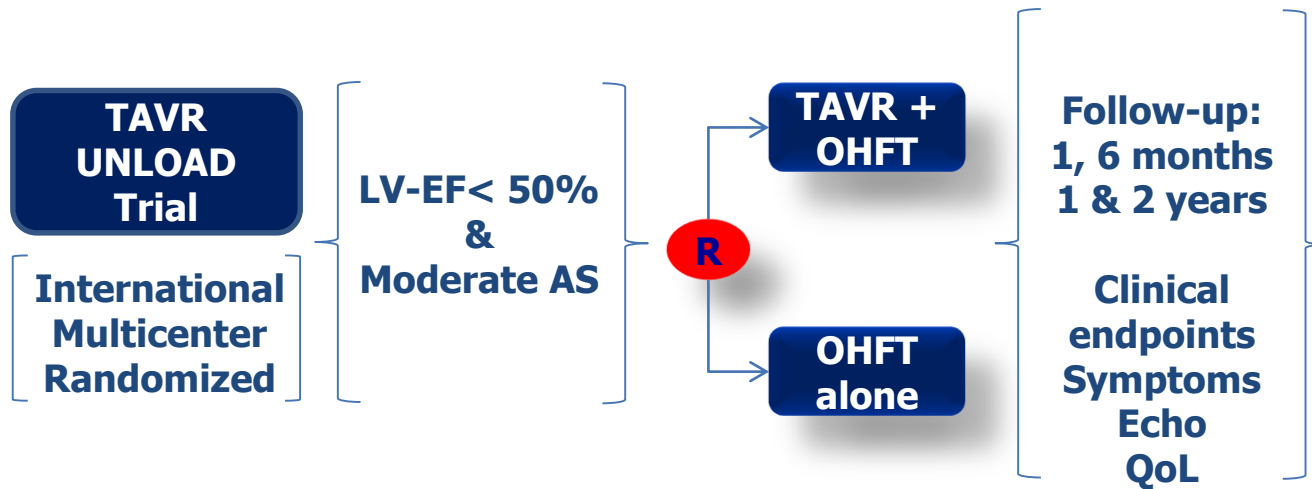


2-step hierarchical multivariate Cox regression model

# Individual Endpoints



# TAVR UNLOAD Concept



## International, multi-center, randomized trial

**n = 600 Patients**



**30 sites**



**5 sites**



**3 sites**



# Key Inclusion Criteria

- **NYHA class  $\geq 2$**
- **NT-proBNP  $> 1500$  pg/mL or hospitalization for HF within the last year**
- **Under appropriate guideline based heart failure therapy**
  - ✧ CRT first when indicated
  - ✧ Not necessarily maximal doses of HF medications
  - ✧ To be confirmed by local HF specialist on an individual basis
- **LVEF  $< 50\%$  , but  $> 20\%$**
- **Anatomically suitable for TF SAPIEN 3 THV**

# Key Inclusion Criteria (2)

## ✓ **Moderate AS =**

✧ **Aortic valve area (AVA)  $> 1.0 \text{ cm}^2$  and  $\leq 1.5 \text{ cm}^2$  on rest echo**

**OR**

✧ **AVA  $\leq 1 \text{ cm}^2$  with low flow at rest but  $> 1.0 \text{ cm}^2$  with low dose DSE**

**OR**

✧ **AVA  $\leq 1 \text{ cm}^2$  and indexed AVA  $> 0.6 \text{ cm}^2/\text{m}^2$  @ rest echo or DSE**

✓ **Note:** Independent Echo Corelab to determine eligibility

# Key Exclusion criteria

- LVEF < 20% or persistent need for intravenous **inotropic support**
- Hospitalization for acute decompensated HF within 2 weeks prior to randomization
- **Cardiac resynchronization therapy** device implantation within 3 months
- **Coronary artery revascularization** (PCI or CABG) within 3 months
- In need and suitable for revascularization per heart team consensus
- Severe aortic regurgitation
- Congenital unicuspid or congenital bicuspid aortic valve



## Key Exclusion criteria (2)

- Concomitant non-aortic valve disease with a formal indication for valve surgery
- Previous aortic valve replacement (mechanical or bioprosthetic)
- Severe mitral regurgitation due to **degenerative mitral** disease
- Severe chronic kidney disease: glomerular filtration rate  $< 30$  mL/min by MDRD or need for renal replacement therapy
- Absence of minimum amount of **aortic valve calcification** necessary for TAVR with the SAPIEN 3 THV
- **Life expectancy**  $< 2$  years due to cancer or other non-cardiac disease

# Primary endpoint @ 1 year

- Clinical efficacy of TAVR is assessed after 1 year of follow-up in all 600 patients. All patients are followed for minimum 2 years.
- Hierarchical occurrence of
  - ✓ All-cause death
  - ✓ Disabling stroke
  - ✓ Hospitalizations related to heart failure, aortic valve disease or non-disabling stroke
  - ✓ Change in KCCQ

*\*To be analyzed with the Finkelstein-Schoenfeld method, 99% Power*

*If FS endpoint is statistically significant, proceed with MACCE endpoint, with sufficient (2-sided  $\alpha = 0.05$ ) power if 40% endpoints are reached*

# TAVR UNLOAD - Team

**Heart Failure  
Specialist**

**Heart Team**

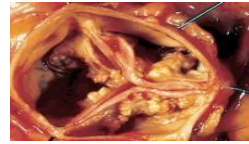
**Referring  
Cardiologist**

**Cardiac  
Surgeon**

**Imaging  
Specialist**

**Interventional  
Cardiologist**

**TAVR UNLOAD**



# PARADIGM SHIFT – PATIENT IDENTIFICATION

- ✧ **Query the Echo database**
- ✧ **“Negative” dobutamine stress echoes**
- ✧ **Heart failure clinic**
- ✧ **Valve clinic**
- ✧ **Referral hospitals**
- ✧ **Monthly screening log review**

- ✧ LV systolic dysfunction:
  - LVEF < 50%, OR
  - Systolic function: impaired, OR
  - LVEF ≠ normal, OR
  - LVEF dysfunction = Yes, OR
  - LV function = poor or moderate
- ✧ AND:
  - AVA >1.0 and ≤ 1.5 cm<sup>2</sup> on rest echo, OR
  - AVA < 1.0 cm<sup>2</sup> AND indexed AVA > 0.6 cm<sup>2</sup>, OR
  - AVA >1.0 and ≤ 1.5 cm<sup>2</sup> on dobutamine stress echo
- ✧ OR:
  - Mean trans-aortic gradient (MG) ≥ 20 mmHg and < 40 mmHg on rest echo
  - Mean trans-aortic gradient (MG) ≥ 20 mmHg and < 40 mmHg on dobutamine stress echo
- ✧ OR:
  - Peak aortic velocity >2.9 and <4 m/2

# Conclusion

- AS & HF increase with age
- HF patients face impaired QOL and premature death
- HF therapy primarily aims for afterload reduction
- In HF & moderate AS → TAVI may provide additional afterload reduction to improve QOL & outcome
- **TAVR UNLOAD** @ [ClinicalTrials.gov NCT02661451](https://clinicaltrials.gov/ct2/show/study/NCT02661451)