TAVR Low Risk

Can It Be Standard?

Pr Alain Cribier
University of Rouen, France

24th CARDIOVASCULAR SUMMIT
TCTAP 2019
April 27-30, 2019
Coex, Seoul, Korea

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
► Consulting Fees/Honoraria	► Edwards Lifesciences

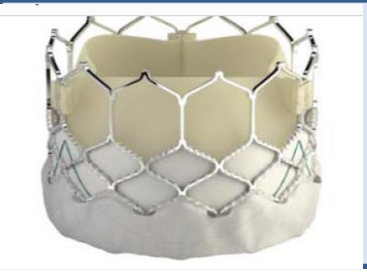
2019: Results of Randomized Trials in Low Risk Patients Were Eagerly Expected

Low risk p

trial

March 2019: PARTNER 3
The apotheosis of TAVI

M.Mack et al: NEJM March 17, 2019
M. Leon: ACC, March 18, 2019



PARTNER 3: Study design

Symptomatic Severe Aortic Stenosis

Low Risk/TF ASSESSMENT by Heart Team (STS < 4%)

1:1 Randomization
1000 Patients

As-treated
496 Pts

As-treated
454 Pts

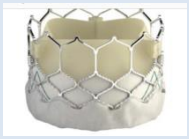
TF-TAVR
(SAPIEN 3 THV)

Surgery
(Surgical Bioprosthetic Valve)

Follow-up: 30 day, 6 mos, and annually through 10 years

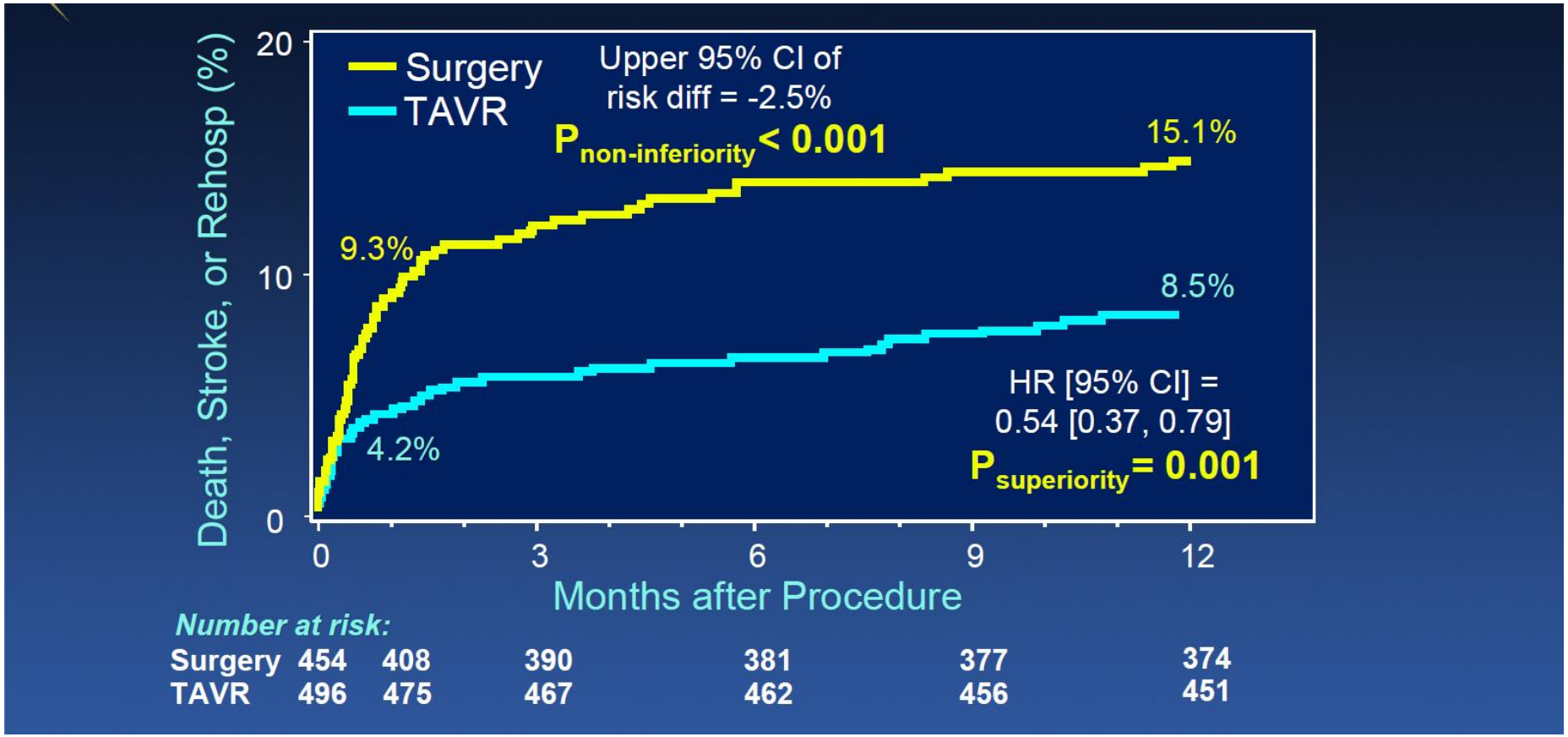
PRIMARY ENDPOINT

Composite of all-cause mortality, stroke or CV re-hospitalization at 1 year post-procedure



PARTNER 3: Results

Primary endpoint: Death, Stroke, or Rehospitalization at one year



SUPERIORITY OF TAVR vs SAVR

PARTNER 3: Results
Key Secondary Endpoints (30-Day)

Table 2. Key Secondary End Points.*

End Point	TAVR (N=496)	Surgery (N=454)	TAVR vs. Surgery (95% CI)†	P Value‡
New-onset atrial fibrillation at 30 days — no./total no. (%)§¶	21/417 (5.0)	145/369 (39.5)	0.10 (0.06 to 0.16)	<0.001
Length of index hospitalization — median no. of days (interquartile range)	3.0 (2.0 to 3.0)	7.0 (6.0 to 8.0)	−4.0 (−4.0 to −3.0)	<0.001
Death from any cause, stroke, or rehospitalization at 1 year — no. (%)§	42 (8.5)	68 (15.1)	0.54 (0.37 to 0.79)	0.001
Death, KCCQ score of <45, or decrease from baseline in KCCQ score of ≥10 points at 30 days — no./total no. (%)‖	19/492 (3.9)	133/435 (30.6)	−26.7 (−31.4 to −22.1)	<0.001

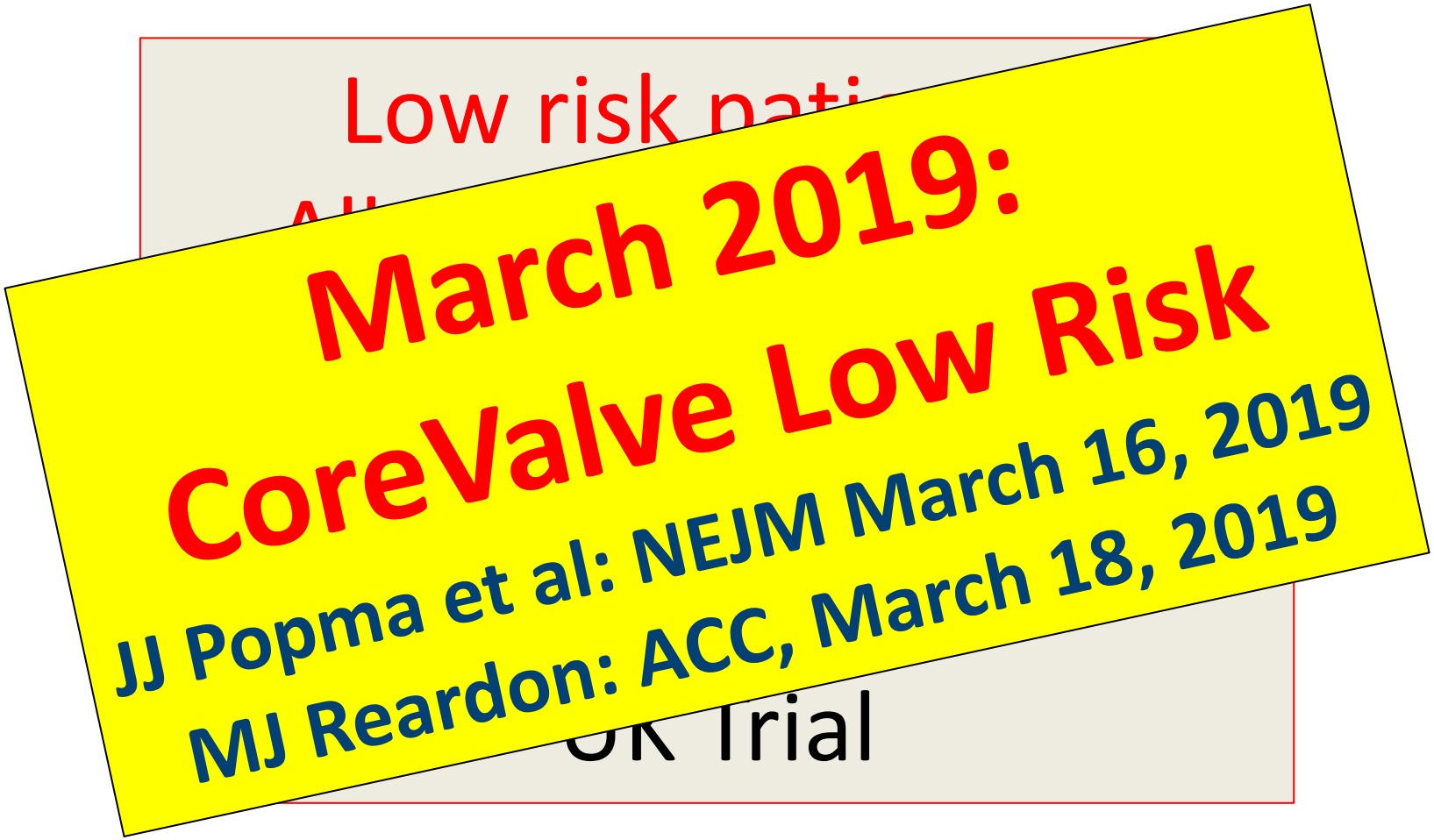
Main Lessons from PARTNER 3 Low Risk Trial:

Superiority of TAVR on death, stroke and rehospitalization at 1-Y

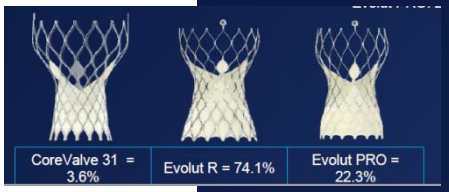
After TAVR:

- 1- Less AF, LOS, death, stroke, major bleeding, more rapid functional improvement
- 2- Simimilar rate of vascular complication, PPM, PVL

2019: Results of Randomized Trials in Low Risk Patients Were Eagerly Expected



Medtronic CoreValve Low Risk



Study Design

Evolut™ Low Risk Trial

Low Surgical Risk

Heart Team Evaluation — **Screening Committee** *Confirmed eligibility*

As-treated 725 Pts

As-treated 678 Pts

1:1 Randomization
Stratified by site and need for revascularization

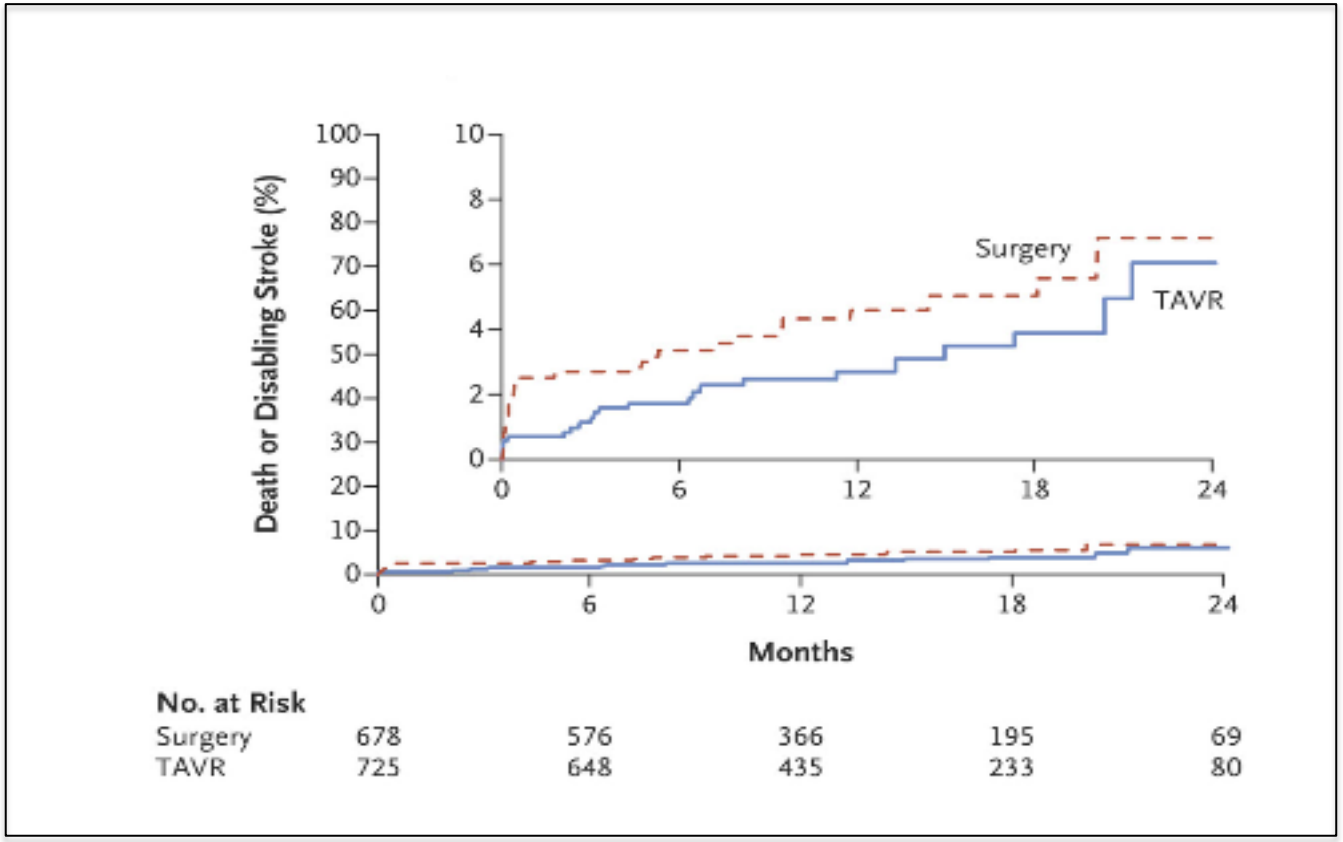
- **TAVR**
  - **TAVR only**
  - **TAVR + PCI**
  - **LTI Sub-Study**
- **SAVR**
  - **SAVR only**
  - **SAVR + CABG**
  - **LTI Sub-Study**

PRIMARY ENDPOINT

All-cause mortality or disabling stroke at 2 years

Medtronic CoreValve Low Risk

Primary endpoint: Death or Disabling Stroke at 2 years



NON-INFERIORITY OF TAVR vs SAVR at 2 years

Medtronic CoreValve Low Risk
Key Secondary endpoints (30-Day)

Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
30-Day composite safety endpoint*	5.3	10.7	(-8.3, -2.6)
All-cause mortality	0.5	1.3	(-1.9, 0.2)
Disabling stroke*	0.5	1.7	(-2.4, -0.2)
Life-threatening or disabling bleeding*	2.4	7.5	(-7.5, -2.9)
Acute kidney injury, stage 2-3*	0.9	2.8	(-3.4, -0.5)
Major vascular complication	3.8	3.2	(-1.4, 2.5)
Atrial fibrillation*	7.7	35.4	(-31.8, -23.6)
Permanent pacemaker implant*	17.4	6.1	(8.0, 14.7)
All-cause mortality or disabling stroke*	0.8	2.6	(-3.2, -0.5)
All stroke	3.4	3.4	(-1.9, 1.9)

Main Lessons from Medtronic CoreValve Low Risk Trial:

Non inferiority of TAVR vs SAVR on death or stroke at 2 Years

After TAVR:

- 1- At 30-D: Better safety / recovery, but more mod PVL and PPM
- 2- At 1-Y: Fewer strokes, CV rehosp. and better valvular function

Major consequences of these two trials: **A potential revolution in the therapeutic strategy for severe AS**

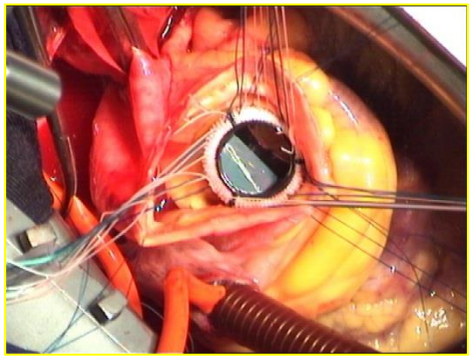
- **TAVR now appears as a possible and valuable alternative to SAVR in AS patients, *whatever the surgical risk!***

- **This greatly expands the potential indications of TAVR to low-risk / younger AS patients, those who were previously sent to surgery for AVR**

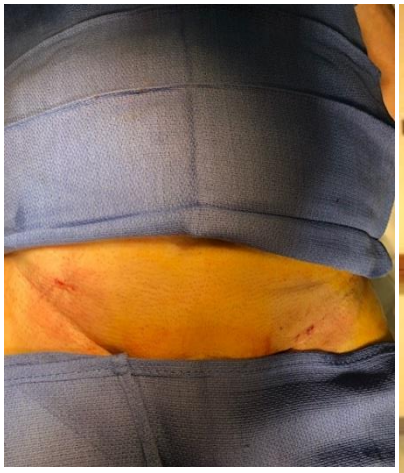
Should TAVR become the default strategy for all comers?

TAVR:
The standard strategy for Low-Risk patients ?

For the patient: definitely **YES**



- GA, ECC, scar, pain
- Longer LOS
- Need for rehabilitation



Femoral puncture
Local anesthesia
No pain, no scar

- Early Discharge
- Back home
- Faster functional improvement

50% of all AS patients are at Low-Risk for surgery

TAVR:
The standard strategy for Low-Risk patients ?

For the Heart Team: several concerns

- Feasibility and safety of TF approach
- Valve anatomy / calcification (ex: severely calcified BCV)
- Associated aortic, valvular or CAD (requiring CABG)
- Pacemaker (but same rate vs SAVR in PARTNER 3)
- Re-access to coronary arteries (if associated CAD)

Long Term Durability of TAVR valves ?

AGE will become a key factor in the decision

TAVR Valves Durability Beyond 5 years

6 studies (elderly high-risk pts), 1 randomized (low-risk pts:NOTION 2)

No alarm so far !....

ESC/EACTS Standardized definitions except for NOTION

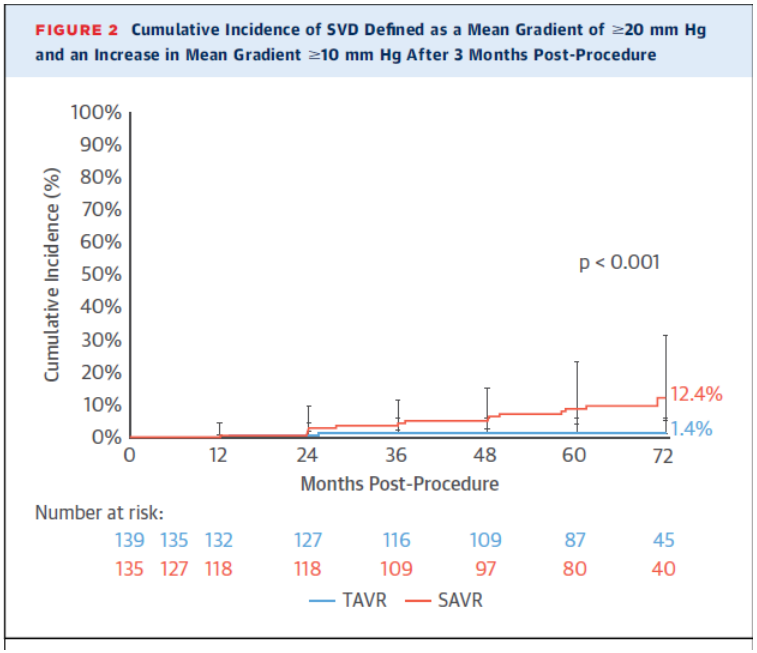
	7-y survival (KM)	7-y/8-y Total SVD	7/8-y Severe SVD	7-y/8-y Re-intervention
Eltchaninoff *Euro Interv 2018*	18%	3.2%	1%	0.6%
Deutch et al *Euro Interv 2018*	23.2%	14.9%		4 Pts (%?)
Holy et al *Euro Interv 2018*	35%		0%	3.3% (not for SVD)
Barbanti et al *AHA 2018*		8.2%	2.4%	0.7%
UK Registry* *JACC 2019*		8.7%	0.4%	0%
NOTION 2* *JACC 2019*	58%	4.3%	0.7%	2.2%
French Registry *Circulation Interv 2019*	18%	11.2%	4.2%	1%

Re-intervention: 0.7 – 1%

Is Surgery Doing Better?

Sandergaard et al: JACC 2018

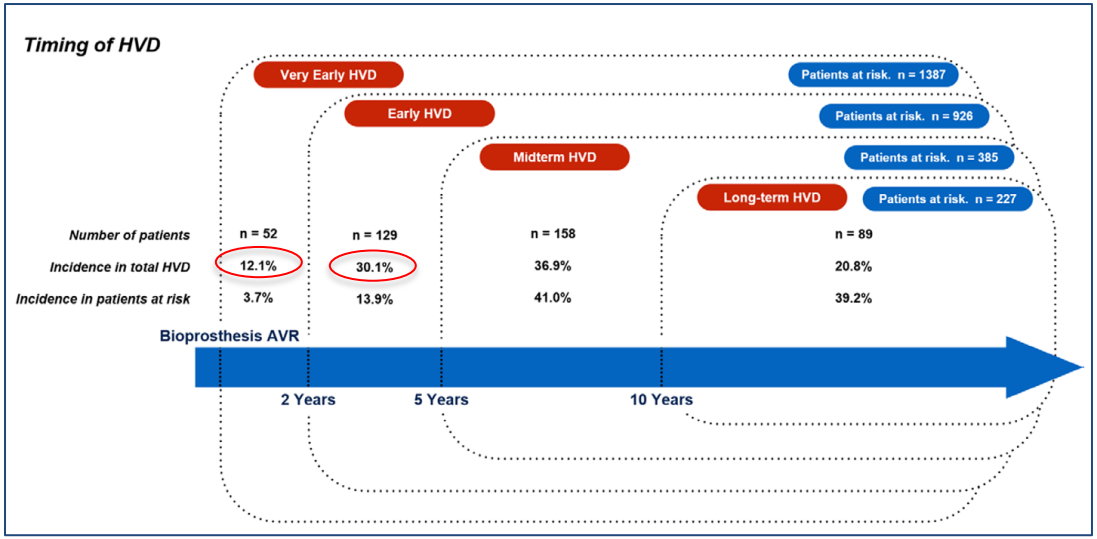
NOTION 2 Randomized
6-Year echo data



SVD at 6 years
TAVR: 1.4%
SAVR: 12.4%

Salaun et al: Circulation 2018

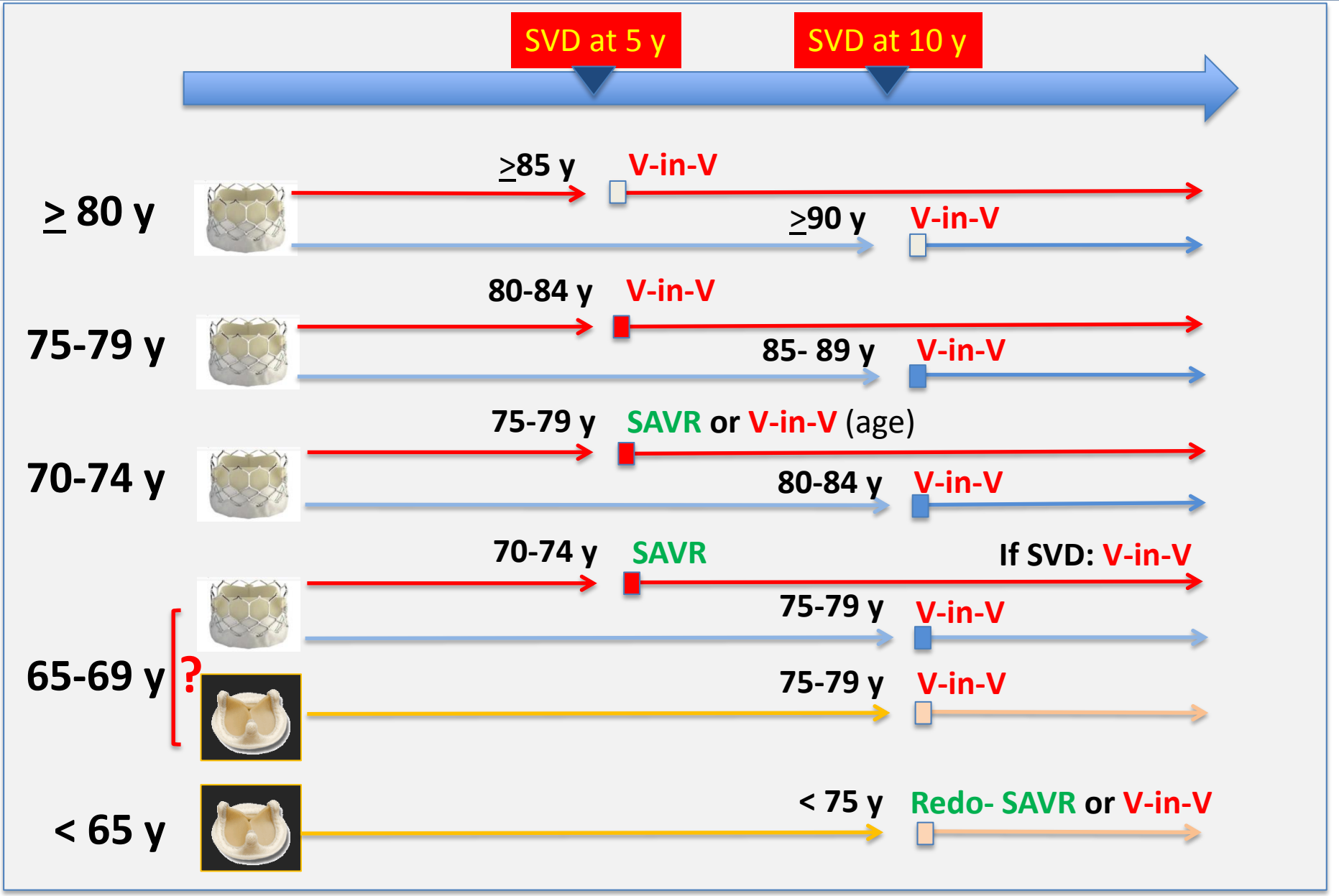
Rate, timing, correlates and outcomes of hemodynamic valve deterioration after bioprosthetic valve replacement *(echocardiographic follow-up)*



HVD during the total echo follow-up = 30.9% (428 Pts)
Very early HVD (< 2-y): 12%, Midterm HVD (2-5 y): 20.8%

HVD: ↑MG > 10mmHG, with ↓AVA or ↑AR by 1 grade

Possible Strategies According to Age



CONCLUSIONS

Following the impressive results of the randomized trials on low-risk AS patients

- TAVR should soon become the first option for a majority of patients at low-risk for surgery
- SAVR will remain the best option for patients who are not optimal candidates for TAVR, and for the youngest patients
- Age will become a key factor in the therapeutic decision
- In this low risk population, information of the patient and relatives about the two options will be essential in the Heart Team's decision.