Reflections on the Impact of TAVR on Aortic Valve Therapy: Now and Future

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Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria	• Edwards Lifesciences
• Proctoring-Training activities/Honoraria	• Edwards Lifesciences

TAVR: Where Are We Today?

An incredible expansion worldwide

> 300 000 TAVR procedures in 14 years

> 700 centers OUS, > 500 centers in USA

- **65 countries in the world**

Developing TAVR: A 25 years odyssey

US Pivotal: FDA 2014

> 2010: Registries

2010: CE Mark

04-10 Feasibility

2004: F.I.M.

SAPIEN XT

SAPIEN 3

Edwards SAPIEN

Cribier-Edw

PHV

Drawings

1985

1994

1999

2000

2002

2002-03

2004

2005-07

2007

Since 2007

2008-10

Since 2010

2016

Rouen, F.I.M., Balloon Aortic Valvuloplasty

Rouen, Autopsy study: concep

Start-up « Percutaneous

Animal experime

Rouen, F.I.M.

Rouen, Feasibility

Edwards Lifesciences TF & TA

Feasibility studies TF & TA

CE Mark,

Pos

Opinion of all experts: 1994-2002

- Technically impossible
- Clinically dangerous
- The most crazy project submitted

Just forget it !

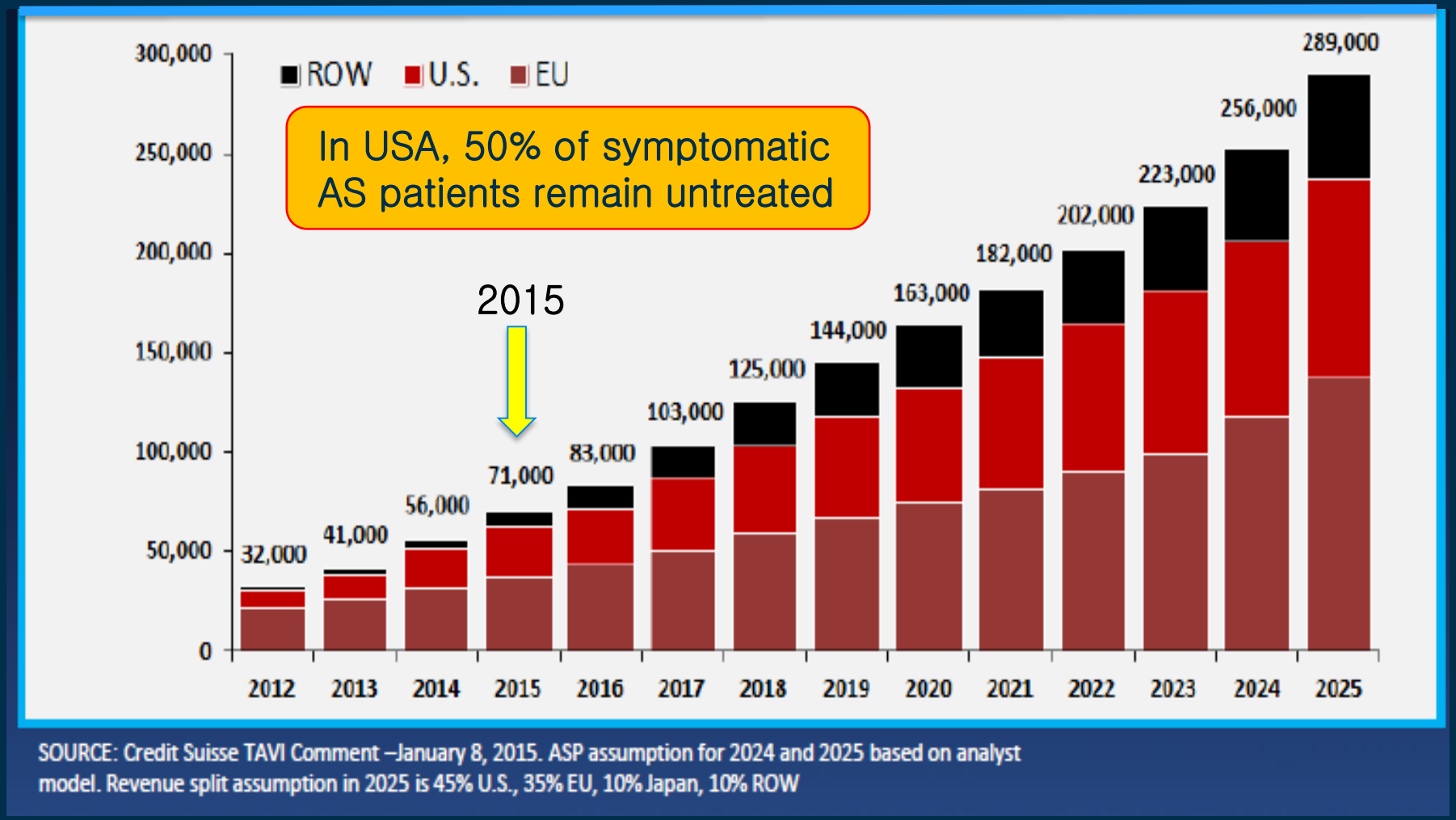
Oct 2011- FDA Approval :
Inoperable Patients (PARTNER B)

Oct 2012- FDA Approval:
High Risk Patients (PARTNER A)

Mars 2014- FDA Approval:
High Risk Patients (CoreValve)

In Guidelines
Europe 2012: ESC / EACTS
USA 2014: AHA / ACC

Estimated Global TAVR Growth



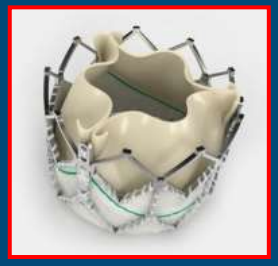
SOURCE: Credit Suisse TAVI Comment –January 8, 2015. ASP assumption for 2024 and 2025 based on analyst model. Revenue split assumption in 2025 is 45% U.S., 35% EU, 10% Japan, 10% ROW

In the next 10 years, TAVI growth will increase X 4

Advanced Valves and Delivery Systems, Have Changed the World of TAVI

Improved techniques, safety, and results

Edwards

	2005	2009	2012
	Edwards SAPIEN	SAPIEN XT	SAPIEN 3
			
Sheath size	24F	18-20F	14-16F
Valve size	23, 26mm	20, 23, 26, 29mm	20, 23, 26, 29mm

CoreValve

	2006		2012 Evolut ™ / 2015 Evolut R
			
Sheath	21F	18F	16F
Valve size	26, 29mm		23, 26, 29, 31mm

Impact of improved devices on the impressive growth of TAVR

1994

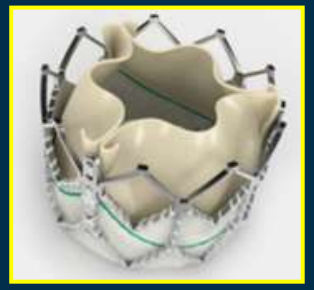
FIM
2002-04

PVT / Cribier-Edw

2005

Edw SAPIEN

2009



SAPIEN XT

2012

SAPIEN 3

SAVR ↘ 60%

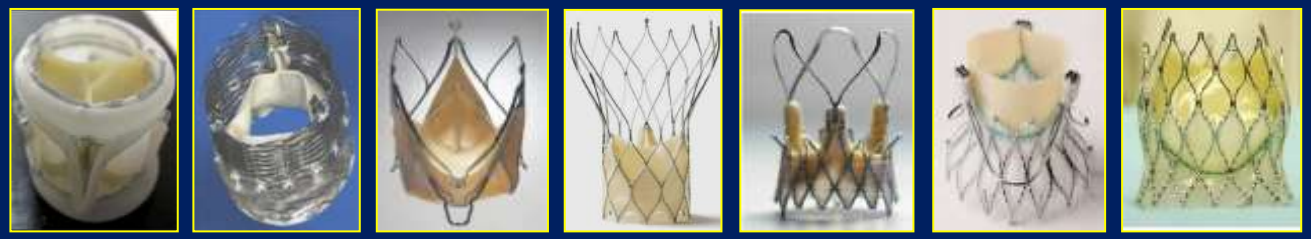
T A V R
~90% TF
Minimalist Strategy

Futile

2010-2015
Inoperable / High Risk / Intermediate

2004

COREVALVE

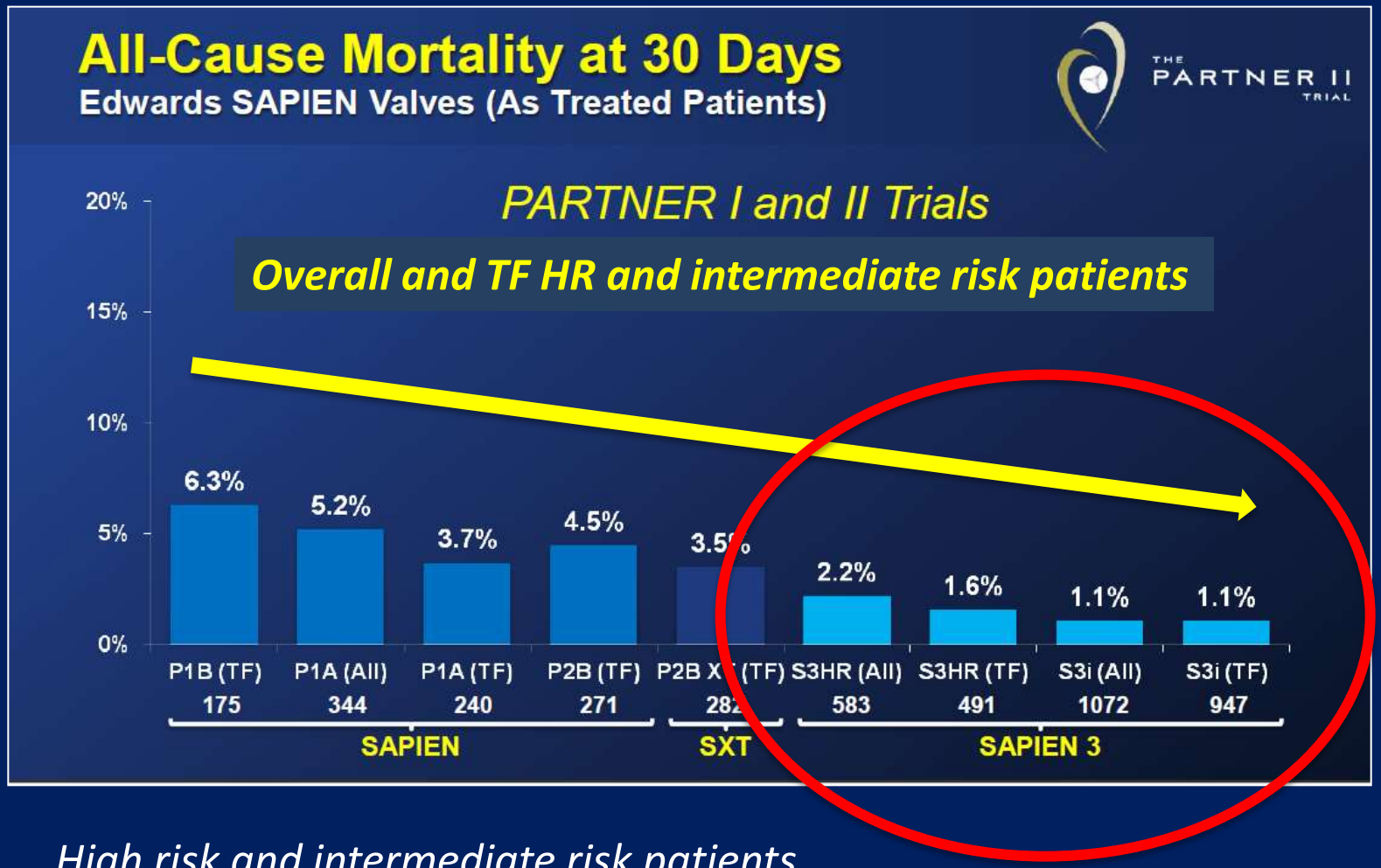


Other available THV systems

2012

EVOLUT R

Decreased mortality at 30-Day with new TAVR systems (from SAPIEN to SAPIEN 3)

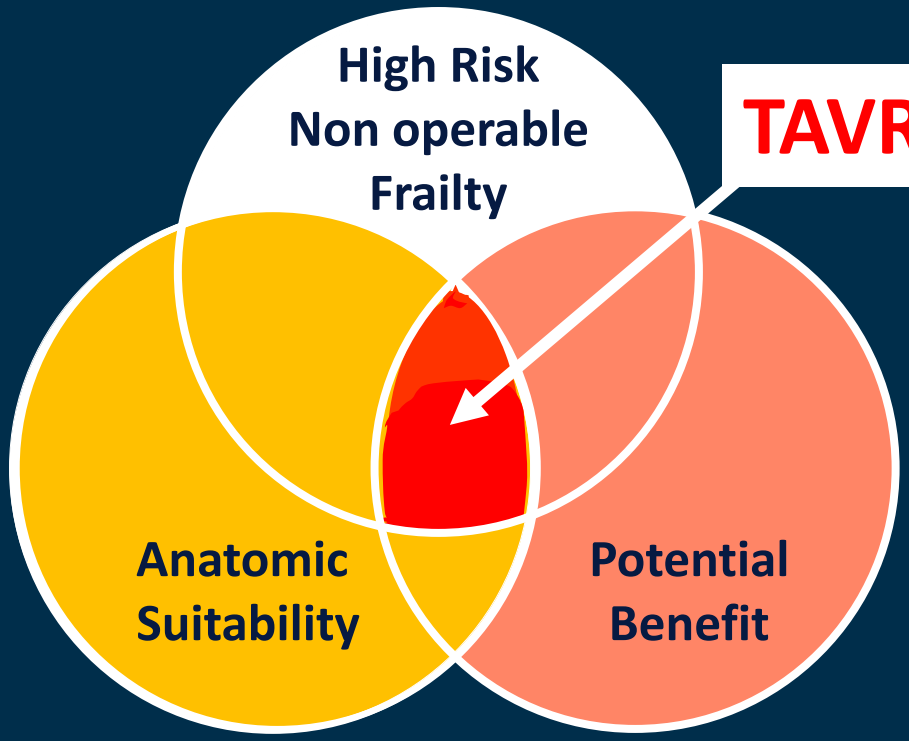


High risk and intermediate risk patients

Susheel Kodali, ACC 2015

In 2016: Current Recommendations Are Freezing TAVR in the Past

ESC Guidelines 2012 / US Guidellines 2014



Decison must be confirmed by a « Heart Team »

Cardiac Surgery On-site

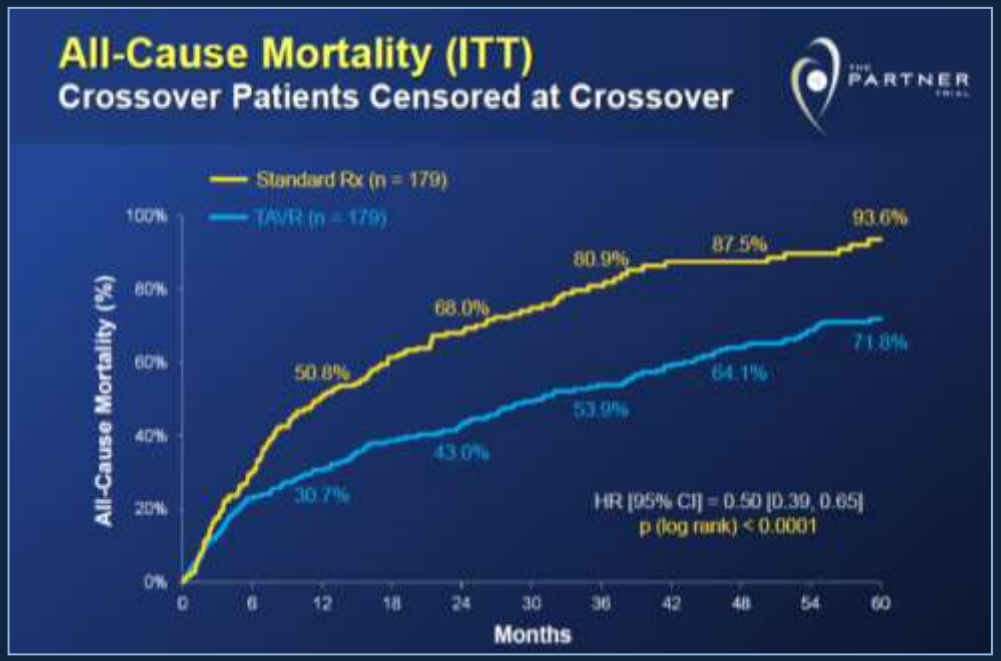
« Intermediate » risk patients (Log Euroscore < 10-20%, STS Score < 4-10%) are not candidates to TAVR

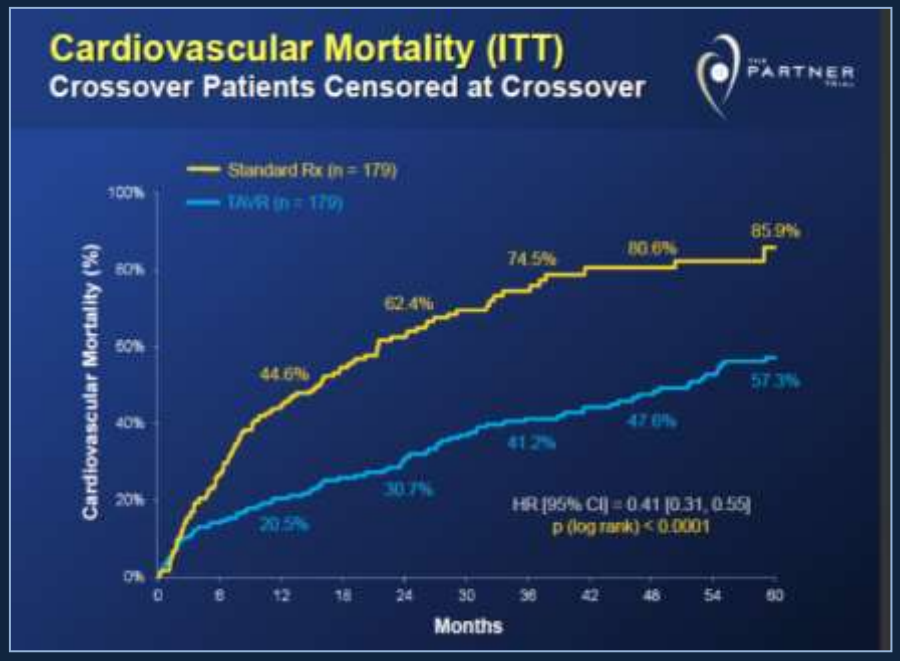
Current guidelines are based on randomized trials with old technologies

Edwards SAPIEN

PARTNER 1B: *Non-operable*
TAVR vs Med Tt

Results at 5 years





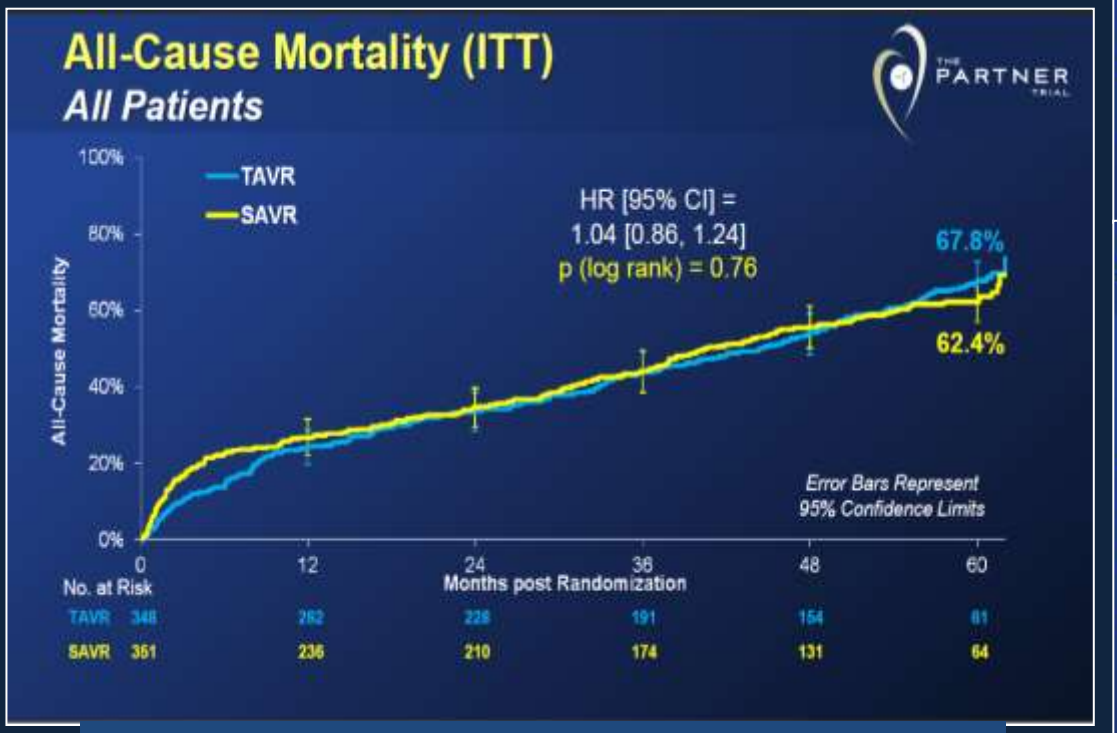
Samir R. Kapadia, TCT 2014

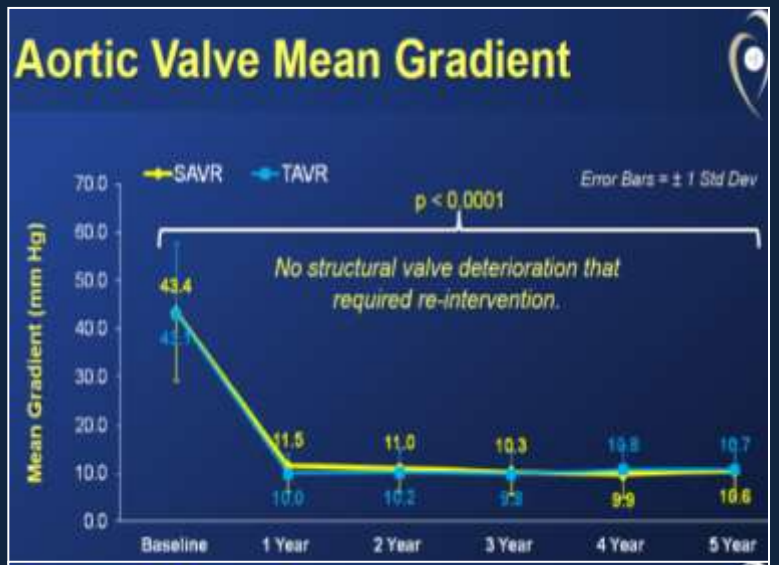
PARTNER U.S. Randomized Pivotal Trial

PARTNER 1A: *High-Risk* TAVR vs SAVR

No alarm on durability

Results at 5-y





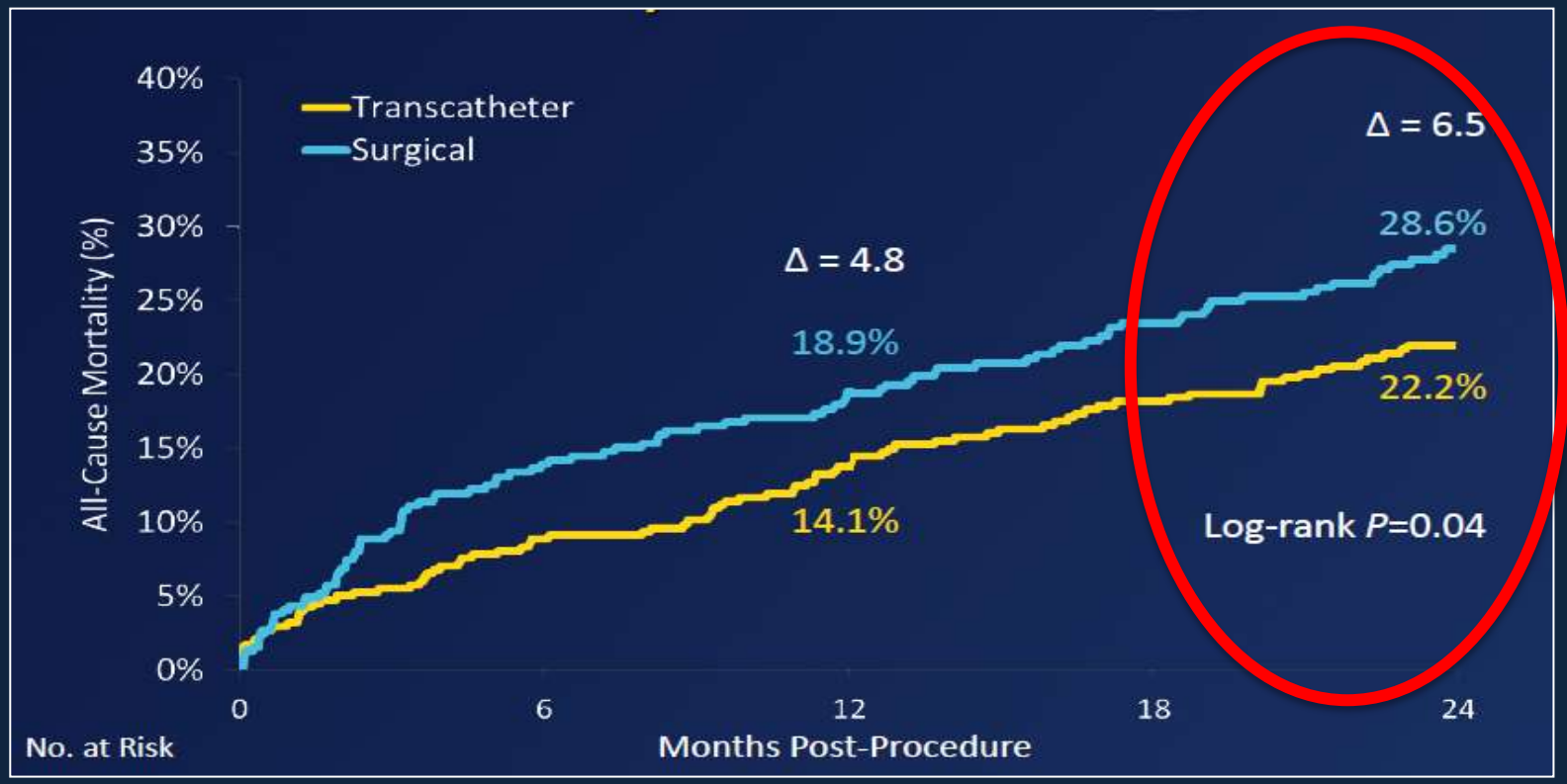
Similar striking functional improvement

Michael Mack, ACC 2015

COREVALVE U.S. Pivotal Trial

High Risk patients: Mortality at 2 years

Medtronic CoreValve



Michael, Reardon, ACC 2015

In 2016, do we have enough data allowing the expansion of TAVR to patients at lower risk?

Done

Propensity score analysis of TAVR vs SAVR in lower risk patients

2013: OBSERVANT Study
2016: PARTNER 2S3i

Evidence-based trials in lower risk patients

Done

2015: NOTION Study
2016: PARTNER 2A

Done

Improved devices and strategies making TAVI safer, simpler and cost effective

New TAVR Systems
Minimalist TF-TAVR

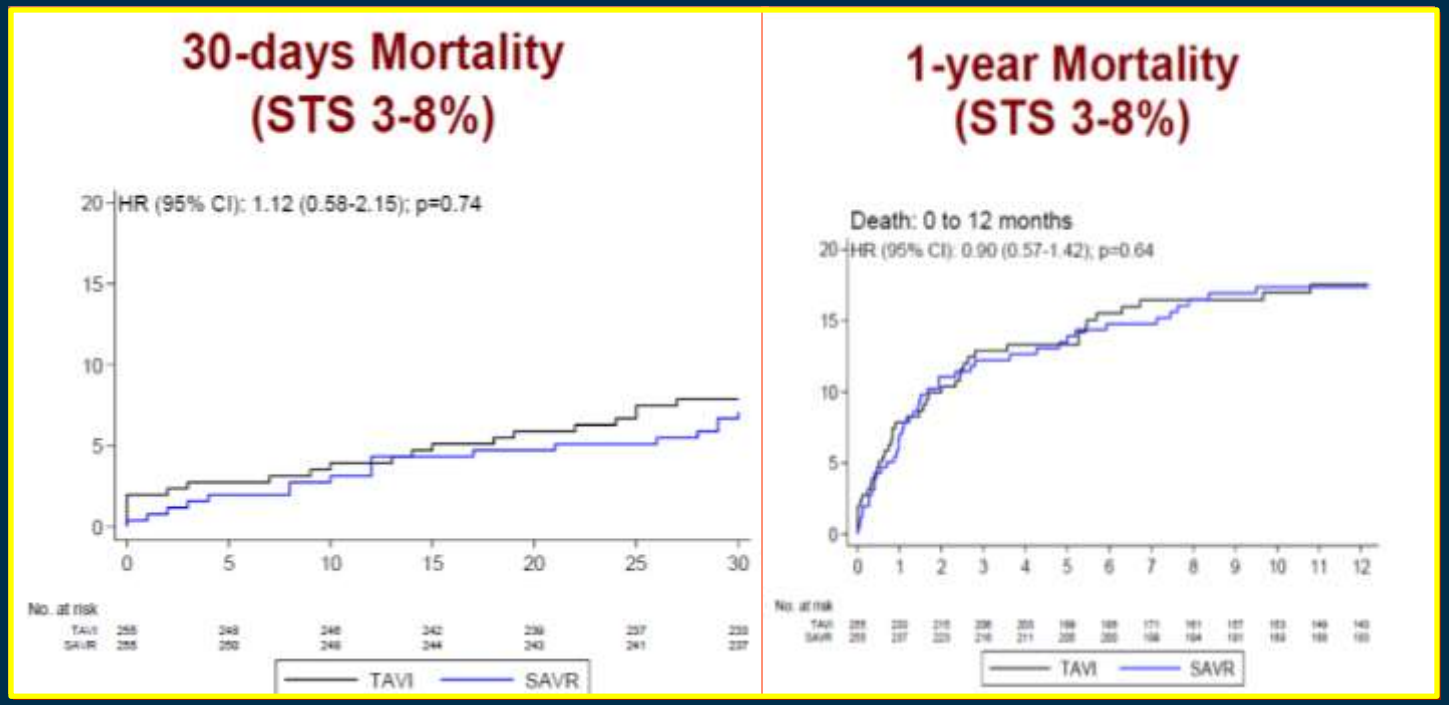
Assessment of Valve + Platform durability on long term

Ongoing

5 years
(PARNER 1A & B)

Propensity Score Analysis in Intermediate Risk Patients

784 Lower risk Patients
OBSERVANT Study(2013)

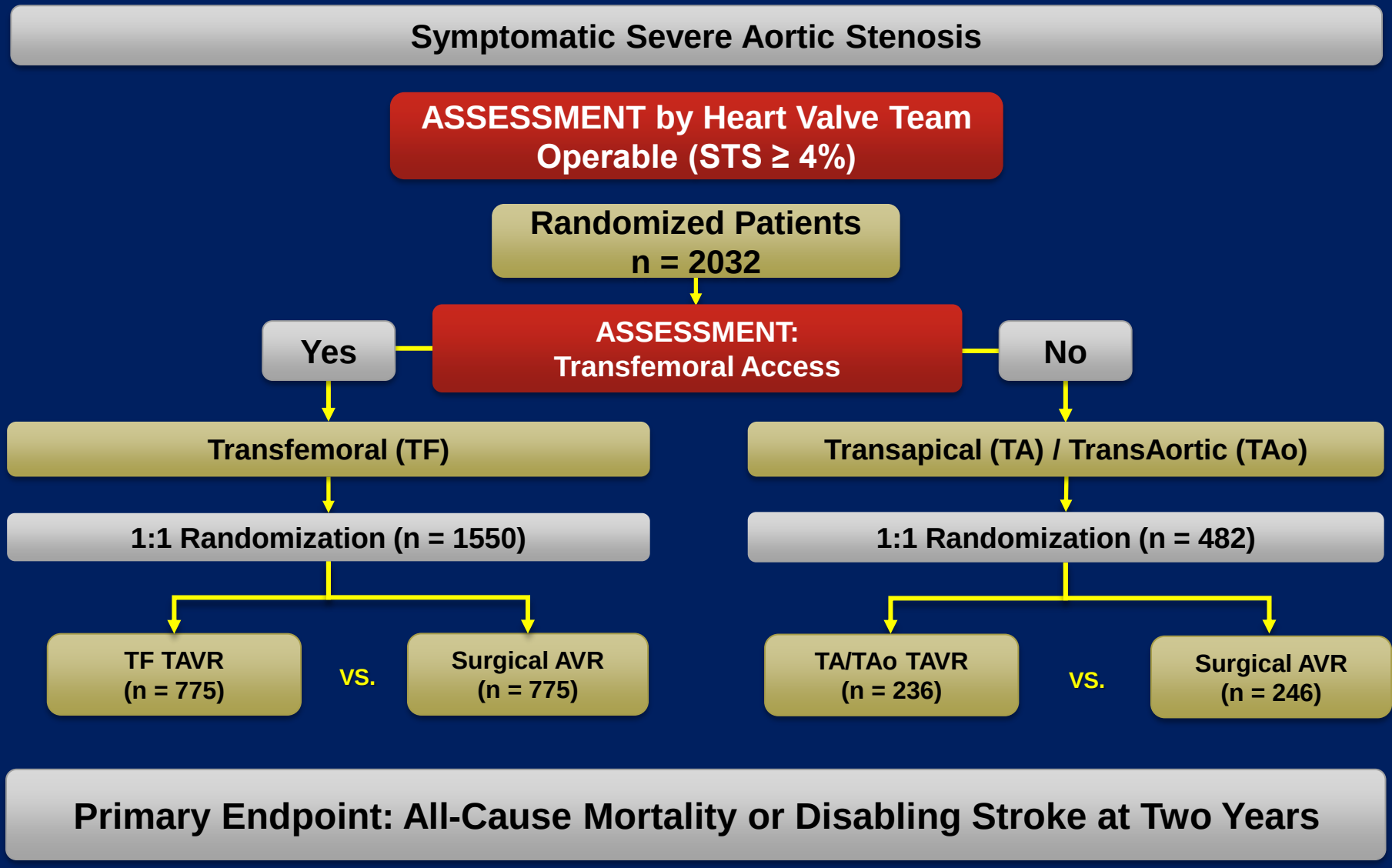


In all multicenter registries, the best results are observed in the subsets of lower risk patients

Piazza et al, JACC Cardiovasculat Int 2013

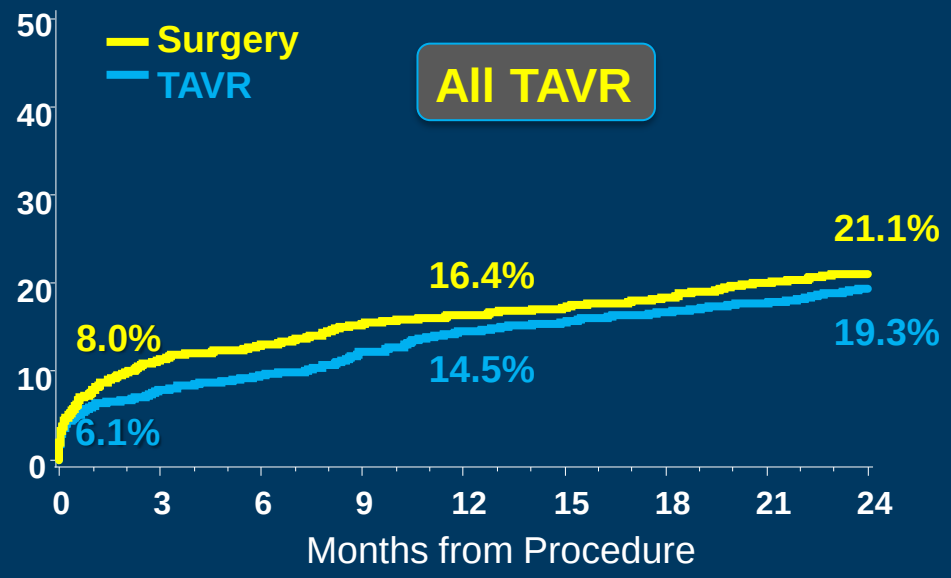
The PARTNER 2A Trial (SAPIEN XT)

Intermediate risk patients

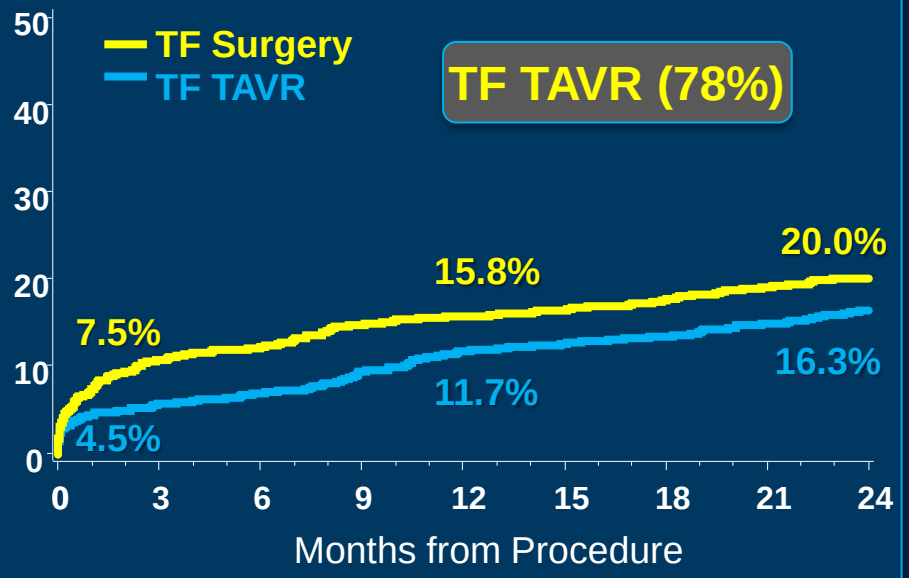


C. Smith et al, ACC 2016. NEJM, 03 2016

Primary Endpoint (ITT) at 2 years
All-Cause Mortality or Disabling Stroke



Primary Non-Inferiority Endpoint Met



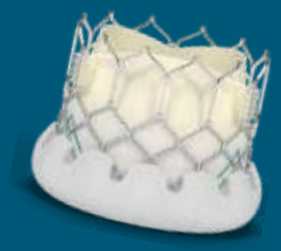
Superiority of TF-TAVR vs Surgery
ITT: p = 0.05, AT: p = 0.04).

TAVR reduced AKI, severe bleeding, new AF and L.O.S.
Surgery reduced vascular complications and PVL

From C. Smith et al, ACC 2016. NEJM 03-2016

The PARTNER 2 S3i Trial

A propensity score comparison of SAPIEN 3 vs SAVR (from PARTNER 2A trial)



BACKGROUND

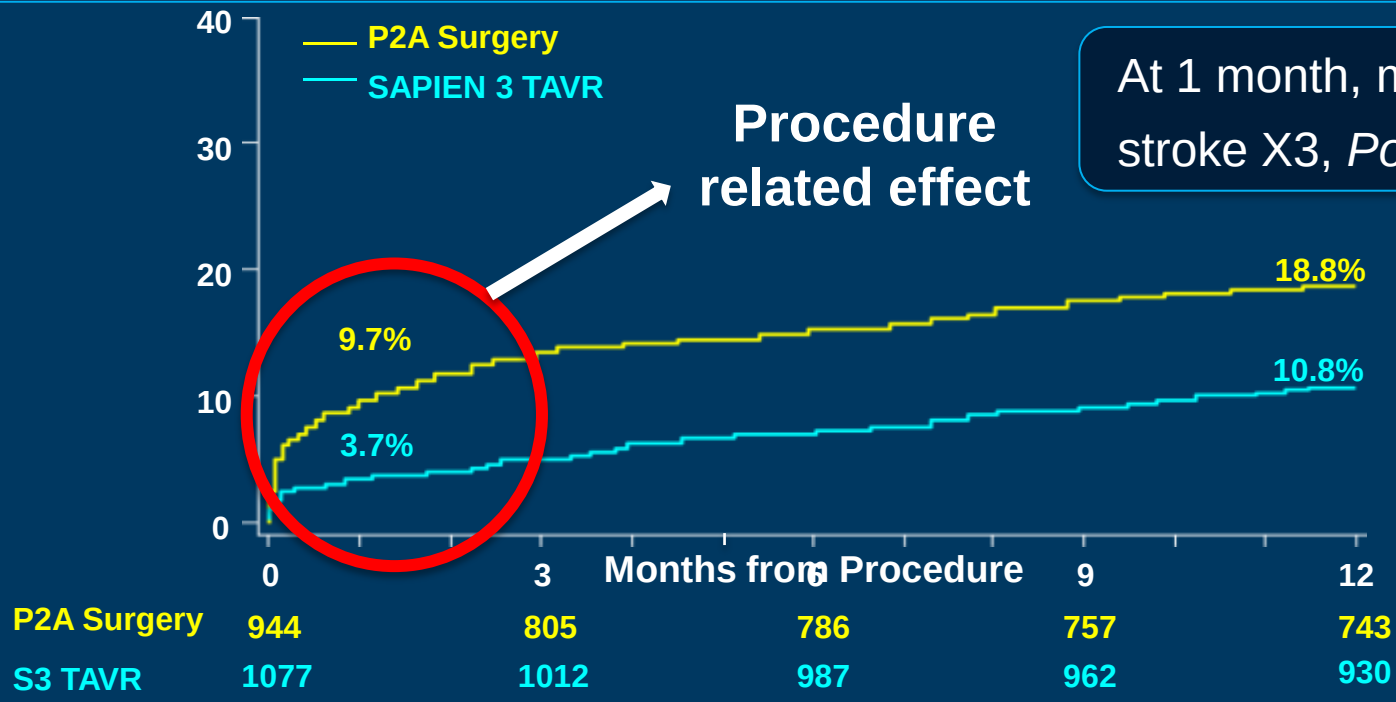
The 30-day outcomes in *intermediate -risk* patients treated with SAPIEN 3 in PARTNER 2 were promising:

All-cause Mortality:	1.1%
Disabling Stroke:	1.0%
PVL ≥ Moderate:	3.8%

Longer term data with SAPIEN 3 and rigourous comparison with SAVR in intermediate risk patients were eagerly expected

The PARTNER S3i Trial

All-Cause Mortality and All Stroke (AT)



Primary Endpoint – Superiority of TAVR achieved (p<0.001)

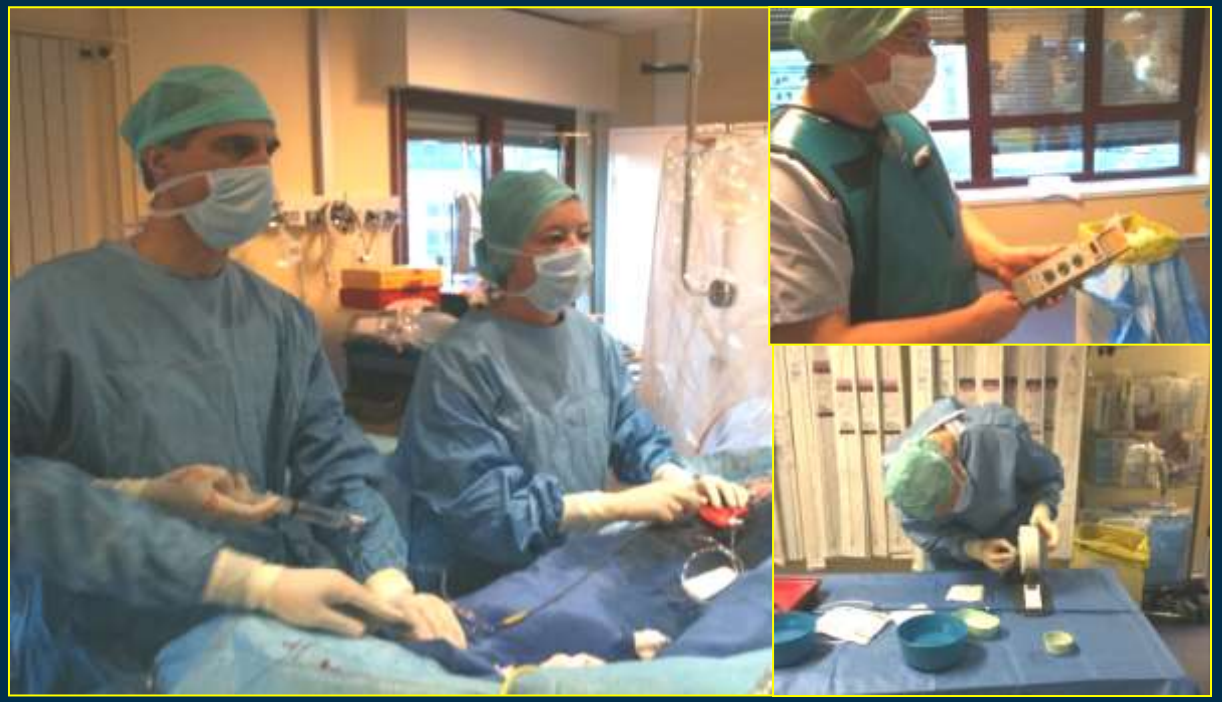
Death, Stroke, or AR ≥ Mod at 1 Year

Superiority of SAVR on PVL (p<0.001) but moderate to severe PVL in only 1.5% at 1 year with TAVR

From V. Thourani et al, ACC 2016. Lancet 03-2016

The minimalist TF-TAVR approach turns TAVR into a « stent-like » procedure

« Near by », aware of the procedure,
Anesthetist
Echocardiographer
Cardiac surgeon



Conscious sedation, local anesthesia
No TEE, Preclosing,
Duration of the procedure: 45 min
Discharge at Day 1 to 3 in 70%

Conversion to surgery and general anesthesia in < 1%

92% of all TAVR cases in Rouen

Minimalist TF-TAVR approach increasingly accepted worldwide

2009 **Standard (Hybrid room)**

2014 **Minimalist (Cath Lab)**

Emory Hospital, Atlanta, USA

- **Same results and outcome**
- **Decreased resource utilization, hospital stay, & cost**

Cost Saving : US$ 15 000

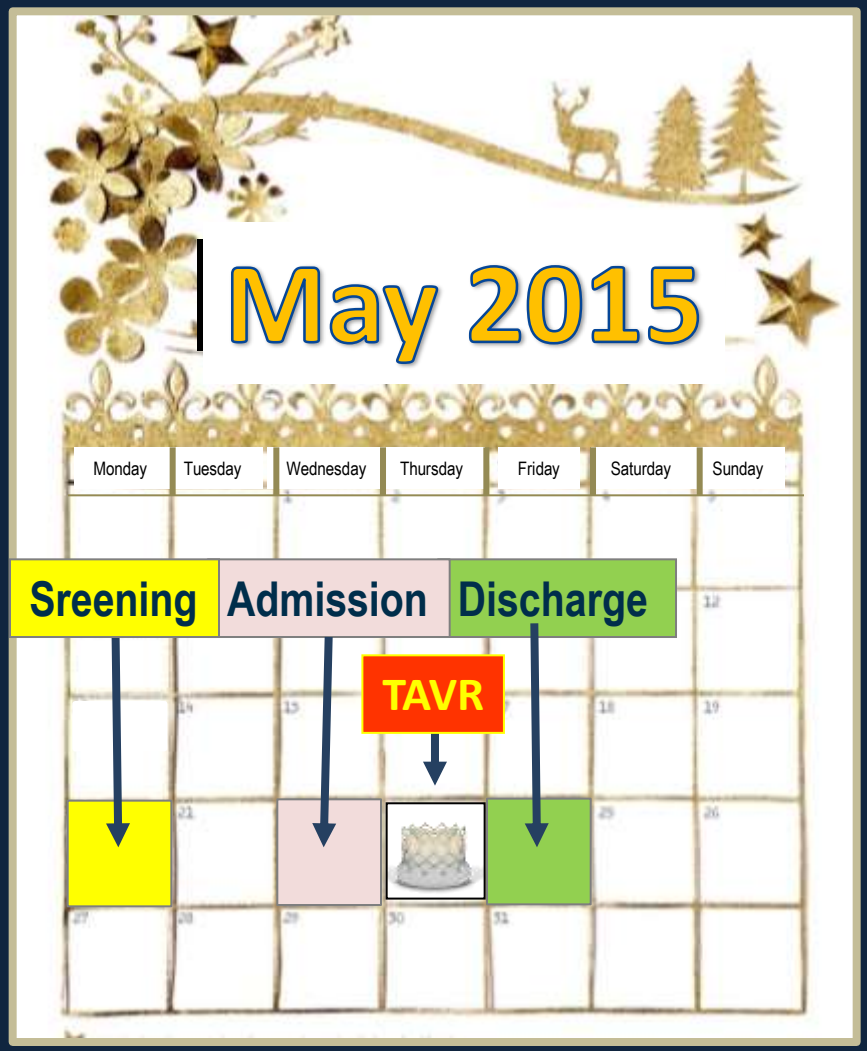
Comparative cost: minimalist vs standard

Babaliaros et al, JACC Interv 2014

In 2015, the “Minimalist Strategy” has Changed the World of TAVR

101 Y/O patient, Sapien 3

Local anesthesia
No scar, no pain
No complication
Back home at D-1



Expansion of TAVR

- Valve in Valve for degenerated bioprothesis
  VIVID Registry: 2012 patients (2015)
- Bicuspid aortic valve
- AS with concomitant diseases (CAD, MR)
- Moderate AS with CHF
- AS with low flow, low gradient
- Asymptomatic patients with severe AS
- TAVR in selected patients with pure AR

- TAVR in all comers
  NOTION Study (2015), PARTNER 3 (ongoing)

How can we see the future of TAVR ?

GUIDELINES
EU 2012
US 2014

NEW GUIDELINES

NEW GUIDELINES

High Risk
Inoperable
Frail

Intermediate

Low Risk > 75y

Low Risk > 65y

Default strategy
for all comers

SAVR in
-Younger patients
(< 65y ?)
-Calcific bicuspid
-Massively calcific AS

2015 | 2016 | 2020

PARTNER II

Prospective ?

PARTNER III

Other randomized ?

New strategies/new devices

ISSUES
-THV durability ?
-PPM, Strokes (EPD?)
-Reaccess Cor Arteries
-Post-TAVR Med Strategy

Minimalist TF-TAVR expanding

- Concept of Heart Team and Scoring revisited
- AGE = major factor
- Well informed patient / relatives at the « heart » of the heart team decision (TAVR or SAVR)

Benchmark
New TAVR systems=
Results comparable to SAVR at ≥ 10 years

My prediction on the future of TAVR

2016 TAVI is indicated in patients who are not optimal candidates to surgery

2020 SAVR is indicated in patients who are not optimal candidates to TAVR !