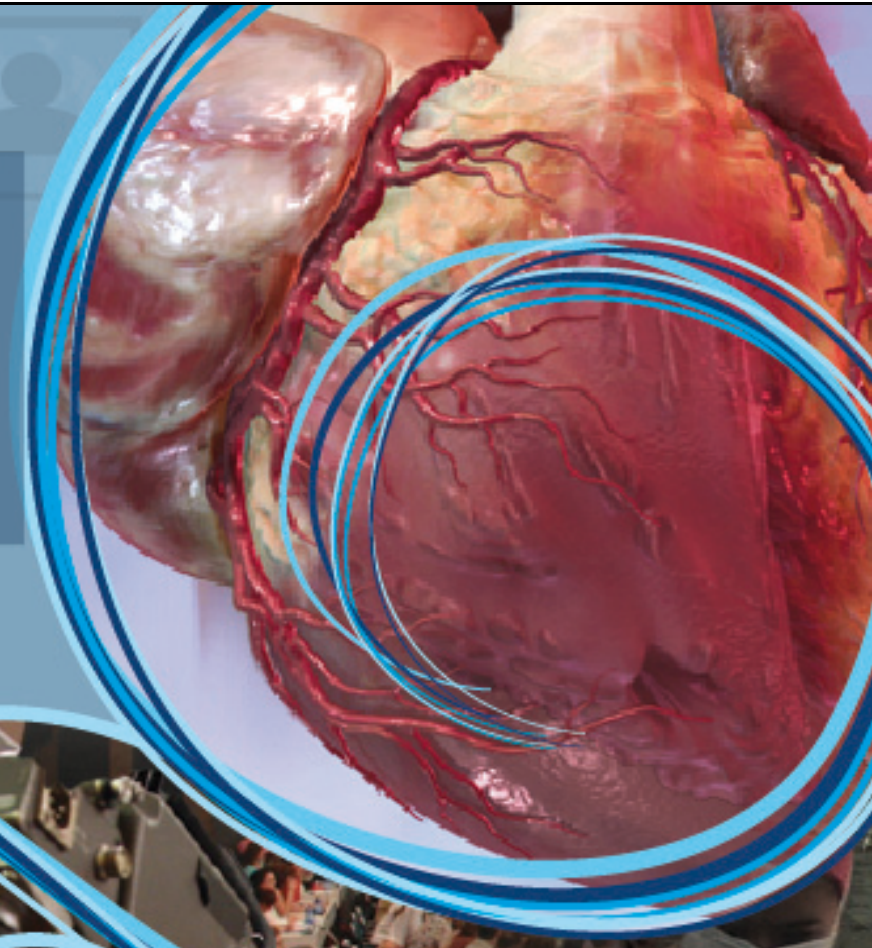


# ***TAVI nei pazienti a rischio intermedio. Nuovi paradigmi clinici e organizzativi nel trattamento della stenosi aortica***

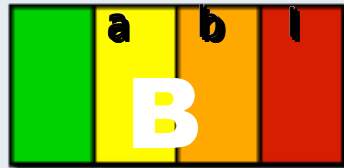
Giuseppe Musumeci

*SC Cardiologia*

*Ospedale Santa Croce e Carle, Cuneo*



# ***Pre-existing market (SAVR)***



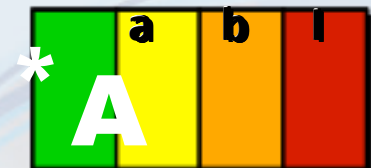
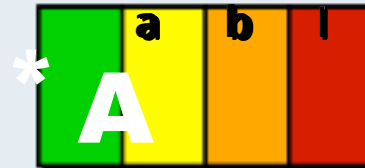
**Low Risk**  
(Must Meet ALL Criteria  
in This Column)

**Intermediate Risk**  
(Any 1 Criterion  
in This Column)

**High Risk**  
(Any 1 Criterion  
in This Column)

**Prohibitive Risk**  
(Any 1 Criterion  
in This Column)

# ***New market***



# The TAVR Path through Risk Categories



Isolated AVR – STS Database 2002 – 2012 (n=141,905)

*Pre-existing market*

6.2% STS > 8



**New market**

*Thourani, Ann Thor Surg 2015*

# TAVI vs SAVR:

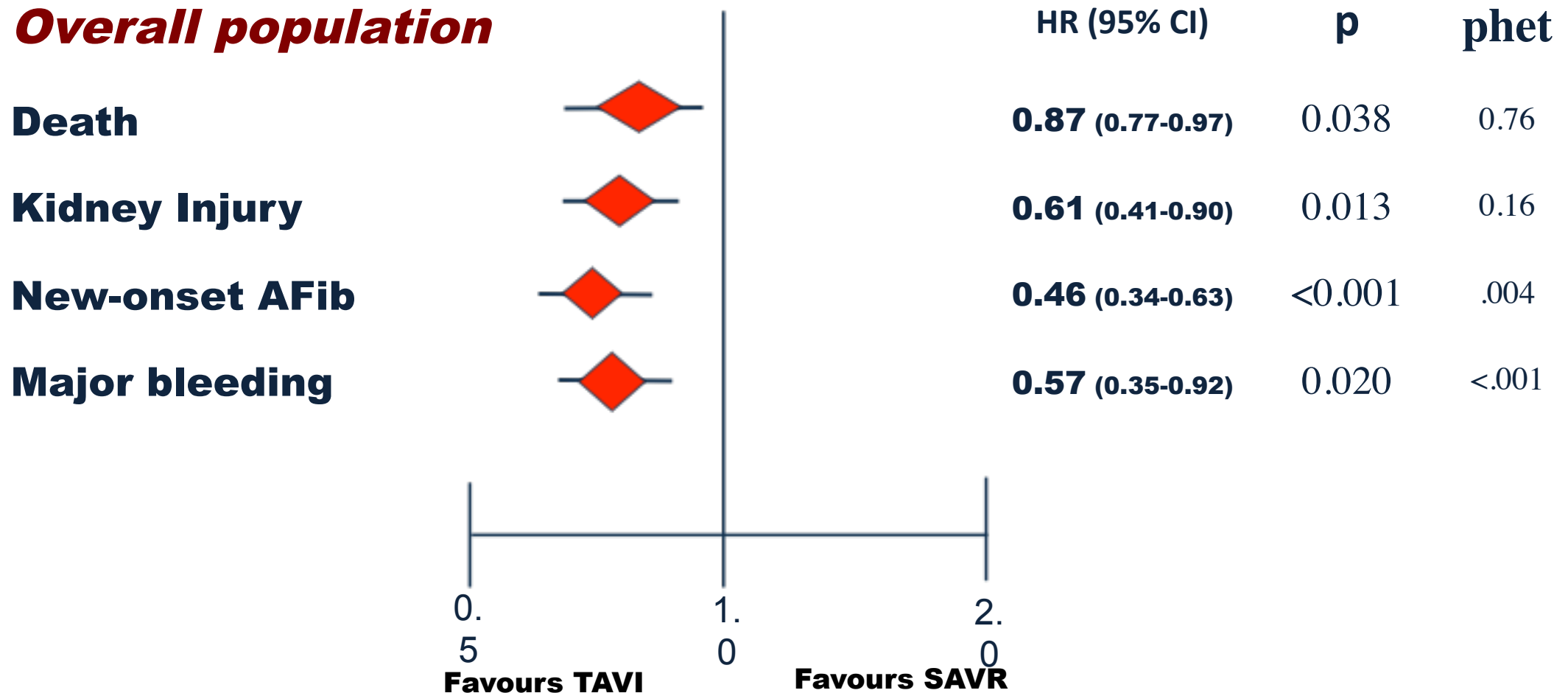
## Meta-Analysis Of 4 Randomized Trials

|                                | PARTNER 1A <sup>1-3</sup> |                 | US CoreValve High Risk <sup>5-7</sup> |                 | NOTION <sup>8</sup> |             | PARTNER 2A <sup>9</sup> |                 |
|--------------------------------|---------------------------|-----------------|---------------------------------------|-----------------|---------------------|-------------|-------------------------|-----------------|
|                                | TAVI                      | SAVR            | TAVI                                  | SAVR            | TAVI                | SAVR        | TAVI                    | SAVR            |
| Number of centres              |                           | 25              |                                       | 45              |                     | 3           |                         | 57              |
| Recruitment period             |                           | 2007–09         |                                       | 2011–12         |                     | 2009–13     |                         | 2011–13         |
| Longest follow-up, year        |                           | 5               |                                       | 3               |                     | 2           |                         | 2               |
| Design                         |                           | Non-inferiority |                                       | Non-inferiority |                     | Superiority |                         | Non-inferiority |
| ITT patients, <i>n</i>         | 348                       | 351             | 394                                   | 401             | 145                 | 135         | 1011                    | 1021            |
| As-treated patients, <i>n</i>  | 344                       | 313             | 391                                   | 359             | 142                 | 134         | 994                     | 944             |
| STS, mean (SD)                 | 11.8 ± 3.3                | 11.7 ± 3.5      | 7.3 ± 3.0                             | 7.5 ± 3.2       | 2.9 ± 1.6           | 3.1 ± 1.7   | 5.8 ± 2.1               | 5.8 ± 1.9       |
| Intervention's characteristics |                           |                 |                                       |                 |                     |             |                         |                 |
| TAVI valve system              | Edwards SAPIEN            | na              | Medtronic CoreValve                   | na              | Medtronic CoreValve | na          | Edwards SAPIEN XT       | na              |
| Access site, <i>n</i>          |                           |                 |                                       |                 |                     |             |                         |                 |
| Transfemoral                   | 244                       | na              | 394                                   | na              | 145                 | na          | 775                     | na              |
| Transthoracic                  | 104                       | na              | 0                                     | na              | 0                   | na          | 236                     | na              |

# TAVI vs SAVR:

## Meta-Analysis Of 4 Randomized Trials

### *Overall population*



# The PARTNER 2A Trial

## Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team

Operable (STS  $\geq 4\%$ ) – **5.8**

**Age – 82**

Randomized Patients n

Yes

ASSESSMENT:  
Transfemoral Access

Transfemoral (TF)

Transapical

1:1 Randomization (n = 1550)

1:1 Randomization

TF TAVR  
(n = 775)

vs.

Surgical AVR  
(n = 775)

TA/TAo TAVR  
(n = 236)

I° EP: All-Cause Mortality or Disabling Stroke at

**SAPIEN XT**



**16-20F**



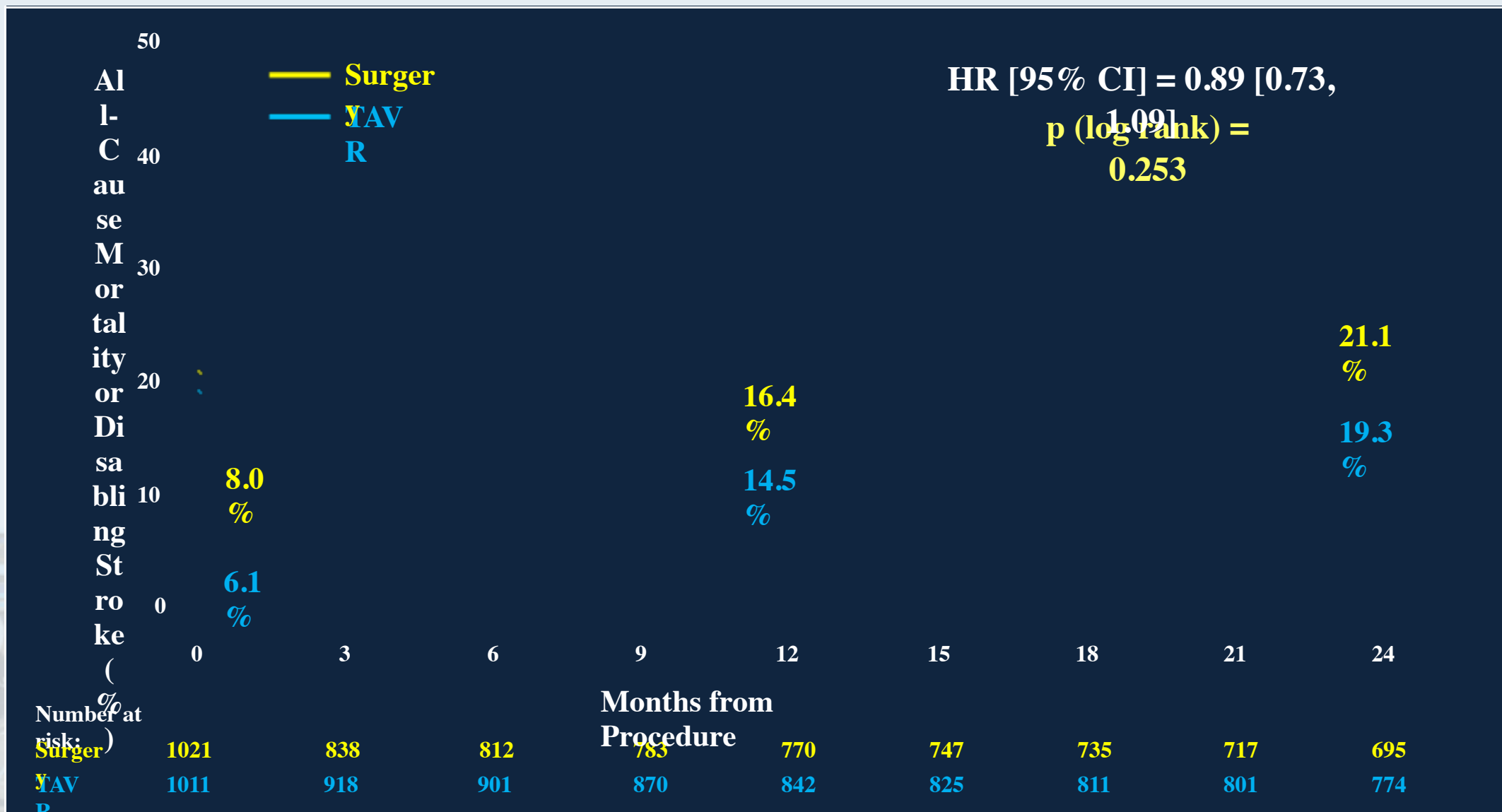
**23mm**

**26mm**

**29mm\***

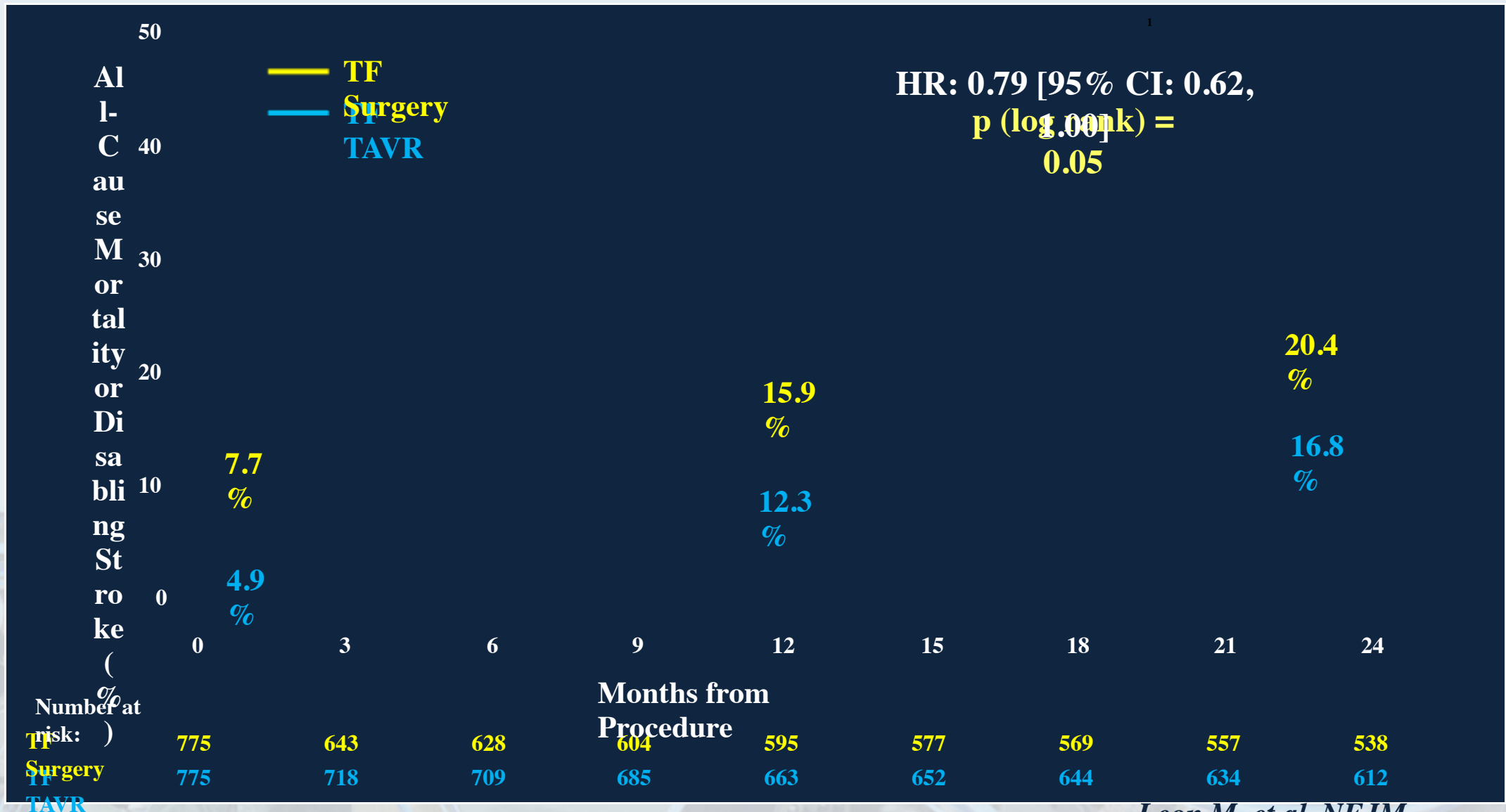
**\*First Implant Oct 30, 2012**

# I° EP (ITT): All-Cause Mortality or Disabling Stroke



# I° EP (ITT) - **TF**

## All-Cause Mortality or Disabling Stroke



Leon M, et al. NEJM

# Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve

## Mortality and Stroke: S3i

At 30 Days (As Treated Patients)

**Mortality**

**Stroke**

**(STS 5.3%)**

%

%

Salvatore<sup>3</sup>, Scott Lin<sup>4</sup>,  
v C. Eisenhauer<sup>8,9</sup>,  
asilis Babaliaros<sup>2</sup>,  
Weissman<sup>14</sup>.



# Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis



## Propensity “**SCORE**” 1-year results

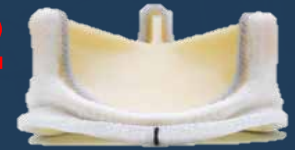
**Sapien 3  
Intermediate Risk  
Registry**

**AGE 82**  
**N=1077**



**Surgical AVR arm  
Partner 2A trial**

**AGE 82**  
**N=944**



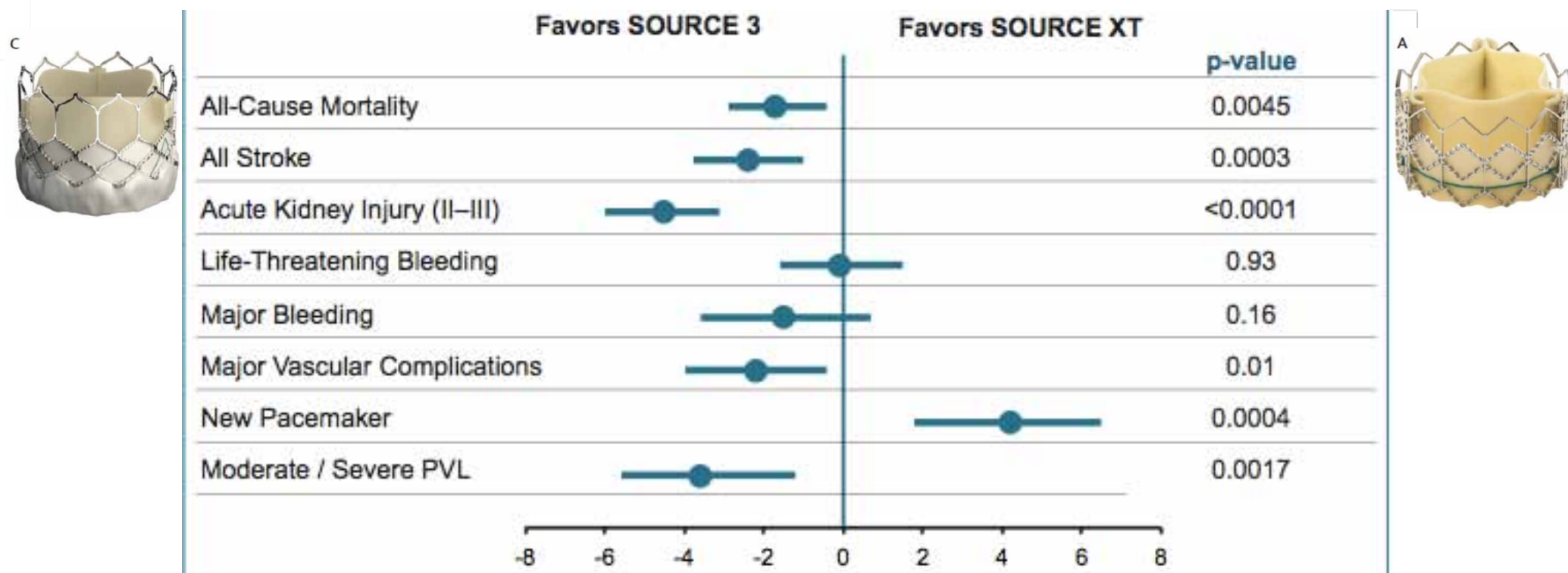
|                      | <b><i>SAPIEN 3 TAVR</i></b> | <b><i>SAVR</i></b> |
|----------------------|-----------------------------|--------------------|
| <b>Cardiac death</b> | <b>4.5%</b>                 | <b>8.1%</b>        |
| <b>Any stroke</b>    | <b>4.6%</b>                 | <b>8.2%</b>        |

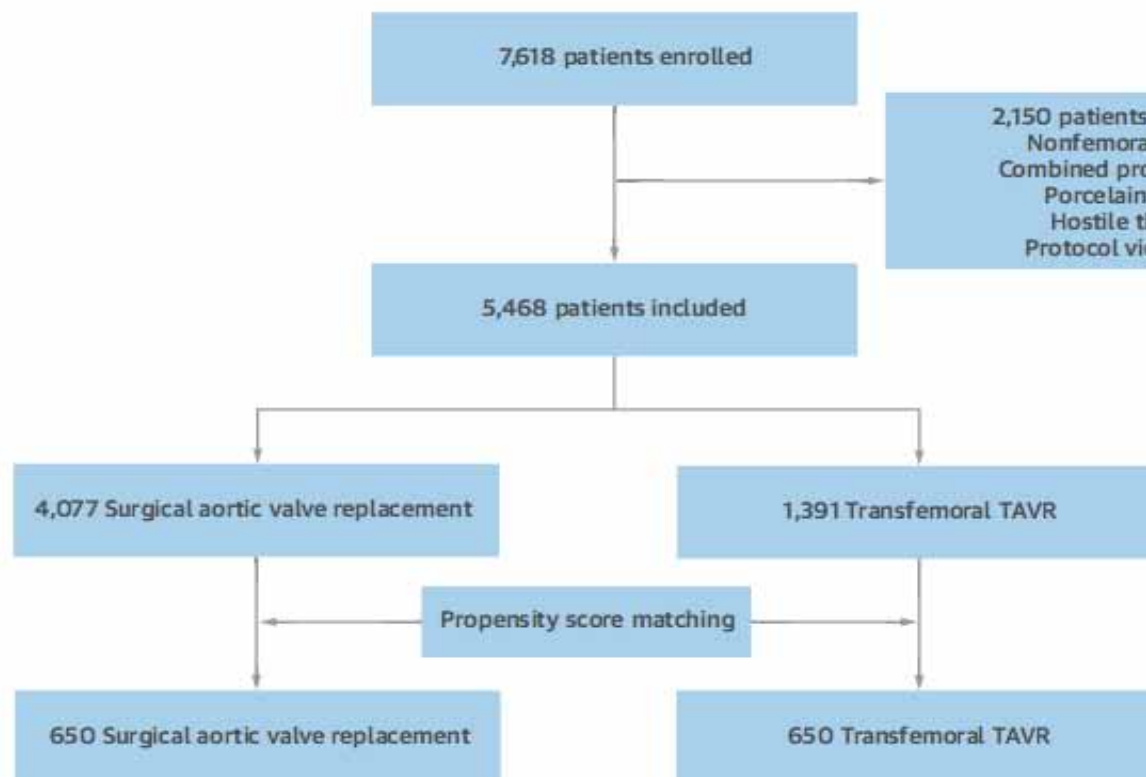
# Large registry # 2

**European SOURCE XT**  
**PLUS SOURCE 3**

**Propensity Adjusted 30-day Outcomes**  
**1947 pts S3 vs 2688 pts XT – Age 82**

**STS – 7**





**Enrollment: Dec 2010-June 2012**

**Country: Italy**

**93 hospitals: 34 cath lab, 59 Surgery**

**THV: ES XT, CV**

**Follow up: 3 years**

VO 66, 7 2 /15  
ISSN 0735-1097/\$36.00  
<http://dx.doi.org/10.1016/j.jacc.2015.06.013>



ment

nucci, MD,§ Francesco Onorati, MD,||  
aro Santoro, MD,\*\*  
ERVANT Research Group

g€score 9.5

# ***EARLY CLINICAL OUTCOMES* OF MATCHED OF PAIRS OF PATIENTS**

**SAVR**

**TAVR**

***Stroke***

**2.2%**

**1.3%** 

***Acute renal  
failure***

**10.9%**

**6.1%** 

***Blood transf.  
unit***

**3.6±3.6**

**2.3±2.2** 

***Major vascular  
complications***

**0.5%** 

**7.9%**

***PM implantation***

**3.6%** 

**15.5%**

# GARY Registry: *intermediate* risk undergoing isolated TAVR or SAVR

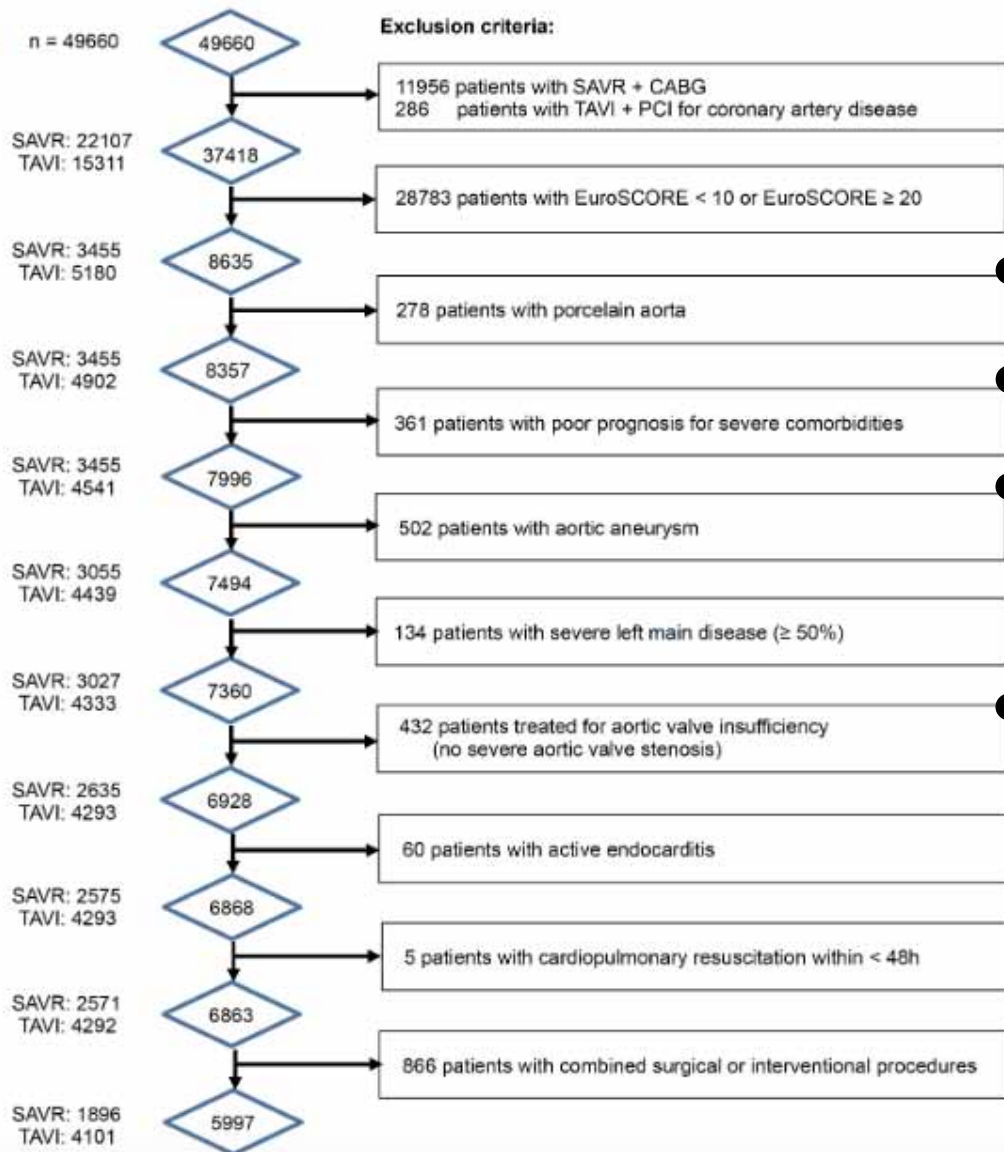
*Large registry # 4*

**Enrollment: 2011-2013**

**Country: Germany**

**Prospective, multicenter,  
all-comers**

**Follow up: up to 5 years**



**5997 pts**

**SAVR 1806 - STS 3.7 – 76 yrs**

**TAVR 4101 (TF 75%) - STS 5.2 – 82 yrs**

**Werner N. AHA 2016**

# ***IN-HOSPITAL CLINICAL OUTCOMES***

## **SAVR**

## **TAVR**

**Major/minor  
stroke**

**1.2/1.3%**

**1.5/1.2%**

**Acute renal  
failure**

**3.6%**

**2.3%** 

**Bleeding  $\geq 2$   
RBC unit**

**51.5%**

**25%** 

**Major vascular  
complications**

**1.1%** 

**7.7%**

**PM implantation**

**5.3%** 

**19.1%**

# SURTAVI Trial

## Study Design

Symptomatic Severe Aortic Stenosis

**Intermediate Surgical Risk**  
STS PROM  $\geq 3\%$  and  $< 15\%$

**Heart Team Evaluation**  
Assess inclusion/exclusion  
Risk classification

**Screening Committee**

Confirmed eligibility

**Randomization n=1,746**  
Stratified by need for revascularization

**Baseline neurological assessments**

**94% TF**

**TAVR N=864**

***age 79.9 – mean STS 4.4%***

TAVR only

TAVR + PCI

**SAVR N=796**

***age 79.6 – mean STS 4.5%***

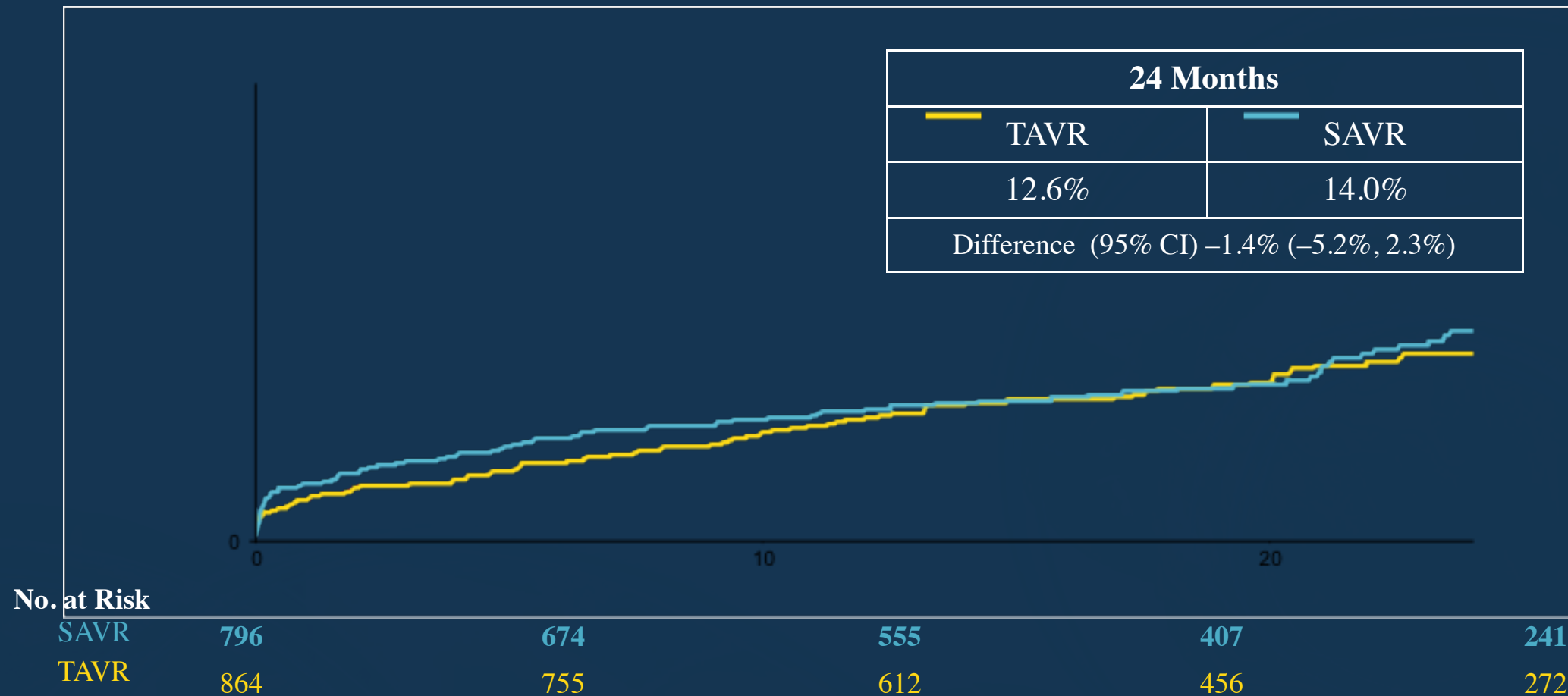
SAVR only

SAVR + CABG

**I° EP: All-Cause Death or Disabling Stroke at 2 Years (non-inferiority)**

Reardon M, ACC

# All-Cause Mortality or Disabling Stroke



# 30-Day Safety and Procedure-related Complications

## SAVR

## TAVR

**Stroke**

**5.6 %**

**3.4%** 

**Shock**

**3.8%**

**1.1%** 

**Acute renal failure  
(stg 2-3)**

**4.4%**

**1.7%** 

**> 2 U blood  
transfusions**

**29.8%**

**9.2%** 

**Major vascular  
complications**

**1.1%** 

**6.0%**

**PM implantation**

**6.6%** 

**25.9%**

# 30-Day Safety and Procedure-related Complications

|                                          | TAVR (N=864) | SAVR (N=796) | 95% CI for Difference |
|------------------------------------------|--------------|--------------|-----------------------|
| All-cause mortality or disabling stroke  | 2.8          | 3.9          | -2.8, 0.7             |
| All-cause mortality                      | 2.2          | 1.7          | -0.9, 1.8             |
| Disabling stroke                         | 1.2          | 2.5          | -2.6, 0.1             |
| All stroke                               | 3.4          | 5.6          | -4.2, -0.2            |
| Overt life-threatening or major bleeding | 12.2         | 9.3          | -0.1, 5.9             |
| Transfusion of PRBCs* - n (%)            |              |              |                       |
| 0 units                                  | 756 (87.5)   | 469 (58.9)   | 24.4, 32.5            |
| 2 – 4 units                              | 48 (5.6)     | 136 (17.1)   | -14.5, -8.5           |
| ≥ 4 units                                | 31 (3.6)     | 101 (12.7)   | -11.7, -6.5           |
| Acute kidney injury, stage 2-3           | 1.7          | 4.4          | -4.4, -1.0            |
| Major vascular complication              | 6.0          | 1.1          | 3.2, 6.7              |
| Cardiac perforation                      | 1.7          | 0.9          | -0.2, 2.0             |
| Cardiogenic shock                        | 1.1          | 3.8          | -4.2, -1.1            |
| Permanent pacemaker implant              | 25.9         | 6.6          | 15.9, 22.7            |
| Atrial fibrillation                      | 12.9         | 43.4         | -34.7, -26.4          |

\*Percentage rates, all others are Bayesian rates

Reardon M, ACC

# Clinical Outcomes\* at 12 and 24 Months

|                                         | 12 Months  |            |                       | 24 Months   |            |                       |
|-----------------------------------------|------------|------------|-----------------------|-------------|------------|-----------------------|
|                                         | TAVR       | SAVR       | 95% CI for Difference | TAVR        | SAVR       | 95% CI for Difference |
| All-cause mortality or disabling stroke | 8.1        | 8.8        | -3.5, 2.1             | 12.6        | 14.0       | -5.2, 2.3             |
| All-cause mortality                     | 6.7        | 6.8        | -2.7, 2.4             | 11.4        | 11.6       | -3.8, 3.3             |
| All stroke                              | 5.4        | 6.9        | -3.9, 0.9             | 6.2         | 8.4        | -5.0, 0.4             |
| Disabling stroke                        | 2.2        | 3.6        | -3.1, 0.4             | 2.6         | 4.5        | -4.0, 0.1             |
| TIA                                     | 3.2        | 2.0        | -0.4, 2.8             | 4.3         | 3.1        | -0.9, 3.2             |
| Myocardial infarction                   | 2.0        | 1.6        | -0.9, 1.8             | 2.8         | 2.2        | -1.1, 2.4             |
| Aortic valve re-intervention            | 2.1        | 0.5        | 0.4, 2.7              | 2.8         | 0.7        | 0.7, 3.5              |
| <b>Aortic valve hospitalization</b>     | <b>8.5</b> | <b>7.6</b> | <b>-1.8, 3.6</b>      | <b>13.2</b> | <b>9.7</b> | <b>0.1, 7.0</b>       |
| MACCE                                   | 13.2       | 12.8       | -2.9, 3.7             | 18.6        | 18.6       | -4.2, 4.2             |

\*All are reported as Bayesian rates

Reardon M, ACC

# NOTION Randomized Trial:

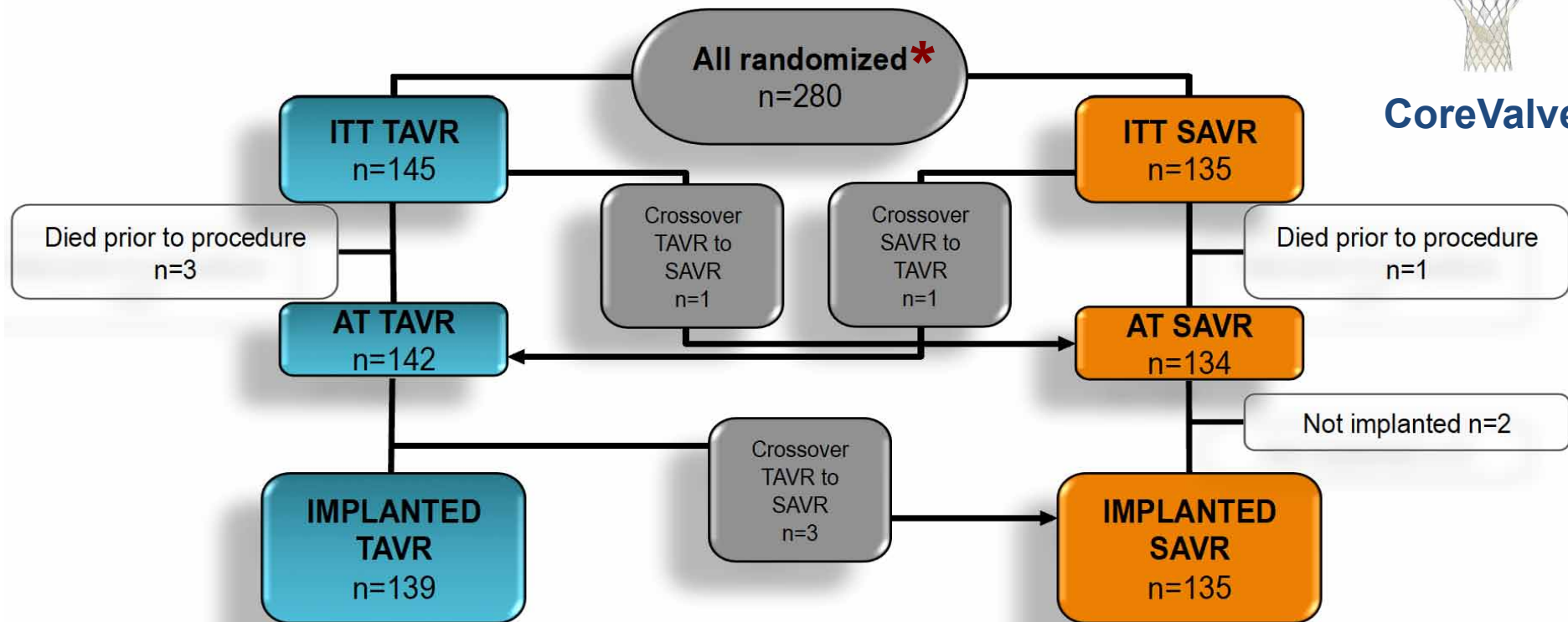
**TAVI (Core valve) Vs. SAVR IN ALL COMERS PTS >70 years old**



## PATIENTS FLOW



CoreValve



|                                          |            |            |     |
|------------------------------------------|------------|------------|-----|
| Age (yrs)                                | 79.2 ± 4.9 | 79.0 ± 4.7 | 0.7 |
| Male                                     | 53.8       | 52.6       |     |
| Society of Thoracic Surgeons (STS) Score | 2.9 ± 1.6  | 3.1 ± 1.7  |     |
| STS Score < 4%                           | 83.4       | 80.0       | 46  |

**P = NS**

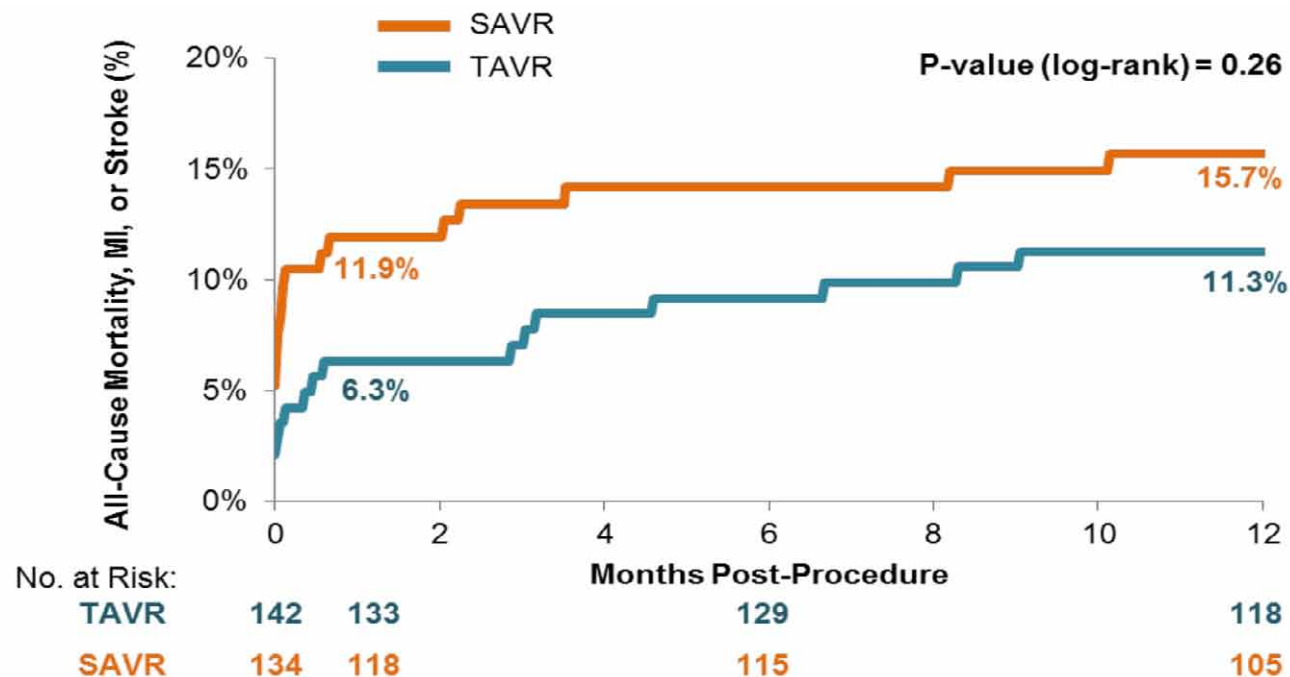
\* **Randomization stratified for age ( $\leq$  OR > 74 yrs), study site, CAD**

# **NOTION Trial - Clinical Outcomes**

## **PRIMARY EP - ITT population**

**TAVR 13.1% vs. SAVR 16.3%,  $p=0.43$**

### **PRIMARY EP -- As Treated population**



## **NOTION Trial – 2ary EP @ 30 Days**

**SAV**

**TAVR**

**Major Bleeding**

**20.9%**

**11.3%** 

**Shock**

**10.4%**

**4.2%** 

**Acute renal  
failure**

**6.7%**

**0.7%** 

**New-onset AFib**

**57.8%**

**16.9%** 

**PM implantation**

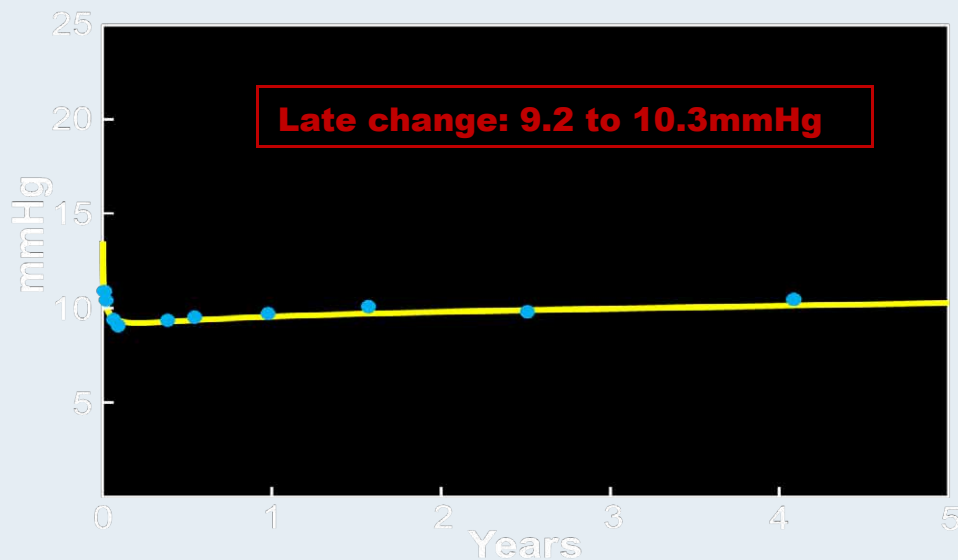
**1.6%** 

**34.1%**



# ***DURABILITY (PARTNER 1 - 5 years)***

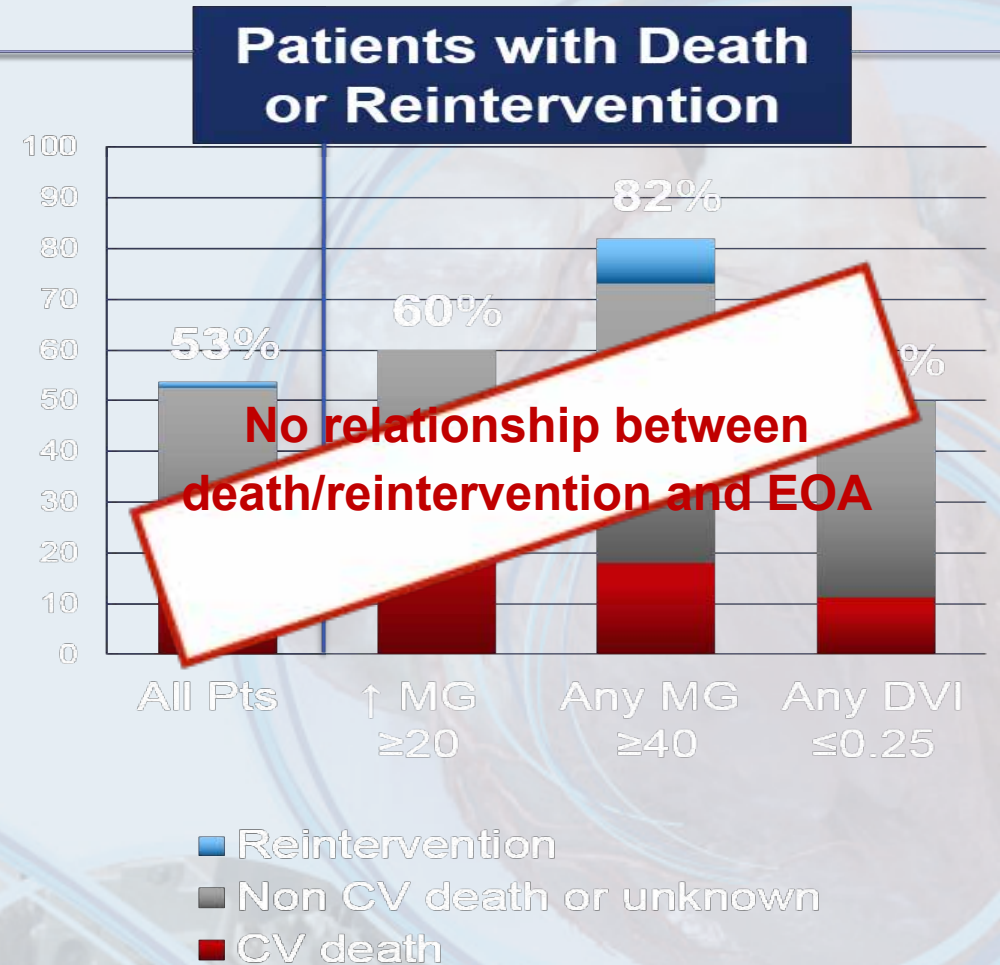
## **AV mean gradient – 5 years**



### **2404 TAVR patients**

- **↑ AV mean gradient  $\geq 20$  mmHg N=10 (0.45%)**
- **Any mean gradient  $\geq 40$  mmHg N=11 (0.46%)**
- **Any DVI  $\leq 0.25$  N=44 (1.8%)**

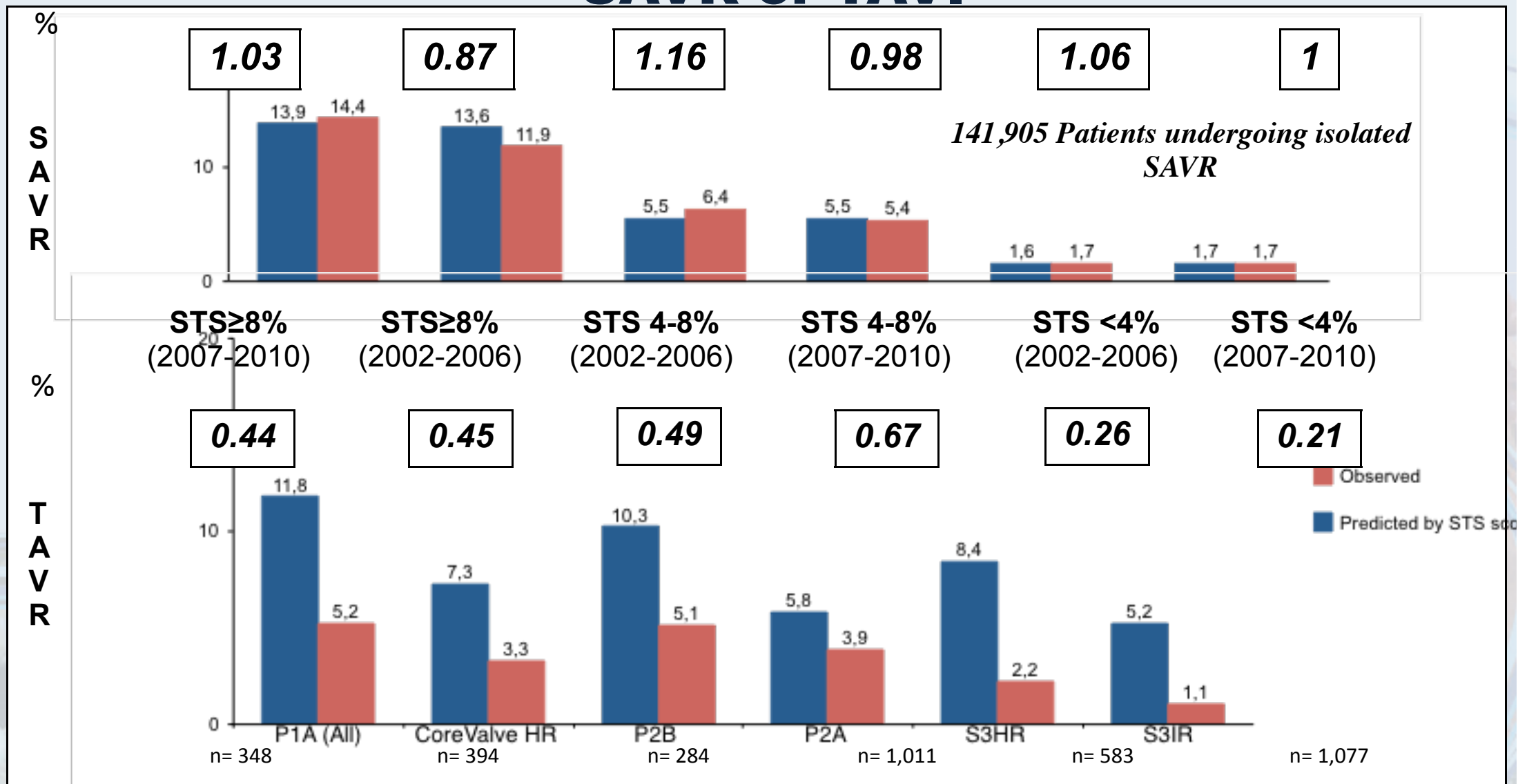
## **Hemodynamic “Outliers”**



The background of the slide is a light blue collage of various medical and scientific images. On the right, there is a close-up of a person's face, possibly a patient, with a focus on the eye area. On the left, there are images of medical equipment, including what looks like a patient in a hospital bed and some technical machinery. The overall theme is healthcare and medical technology.

# ***Scoring insights***

# Observed vs. predicted mortality at 30 days after SAVR or TAVI



# ***SURGICAL RISK AND AGE***

**Mean Age across studies:**

**83**

**84**

**83**

**83**

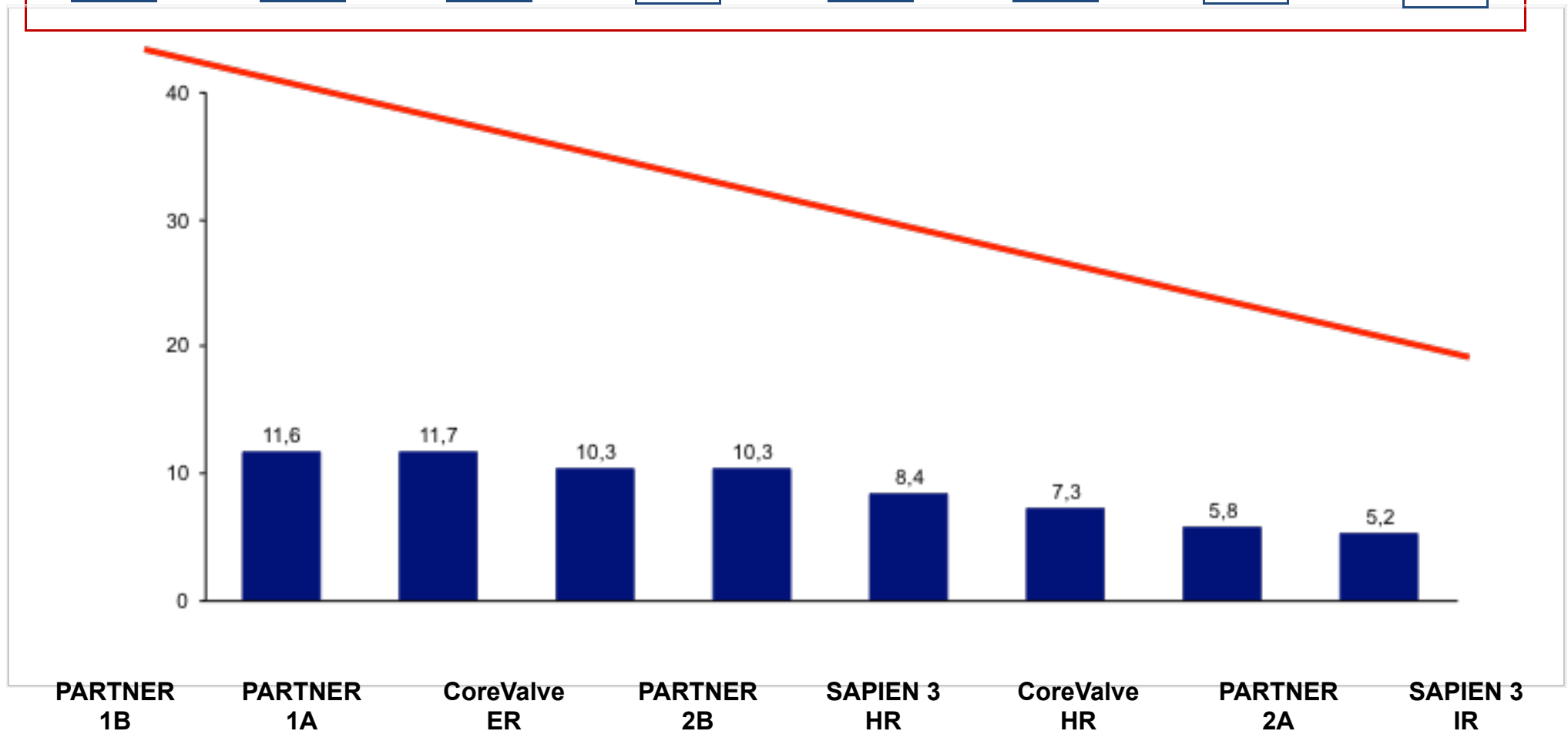
**84**

**82**

**83**

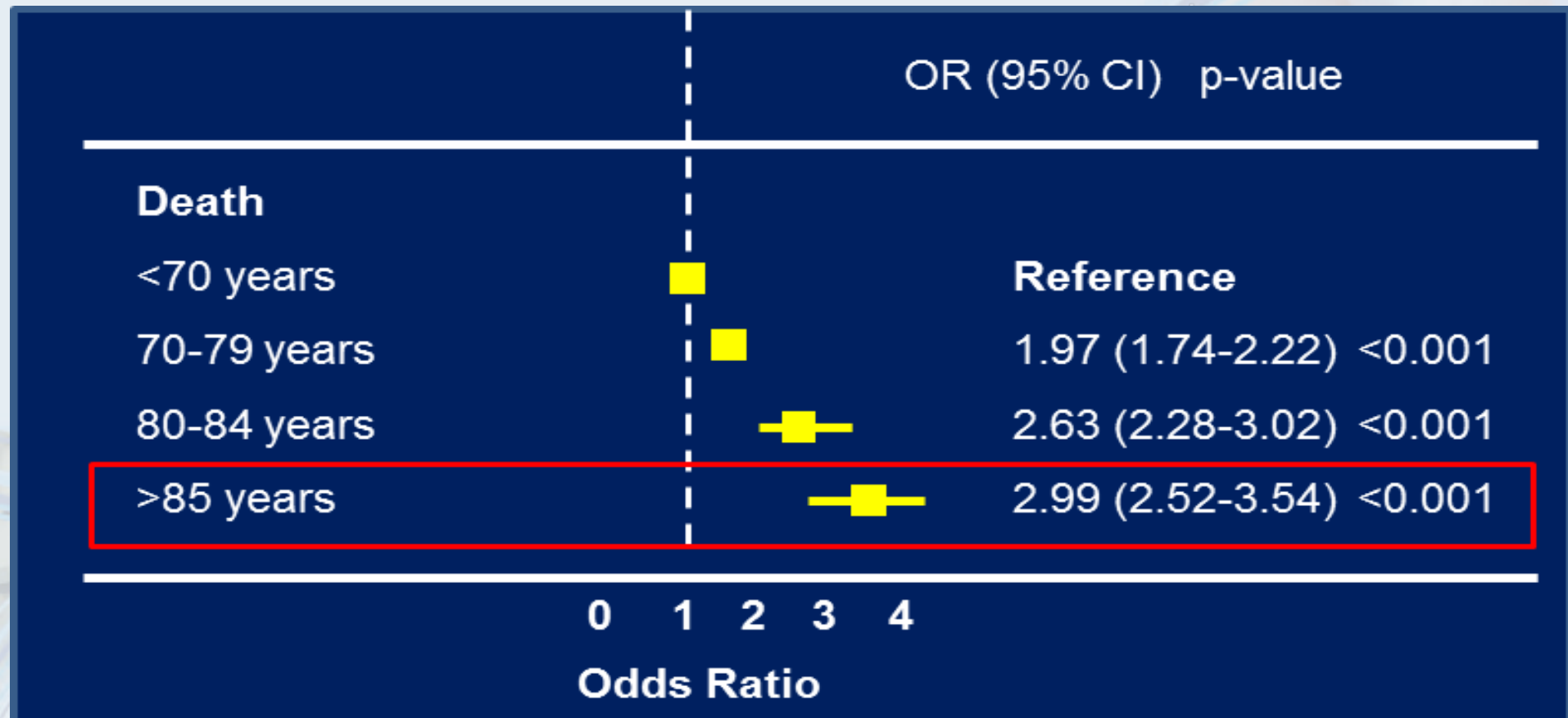
**82**

**S  
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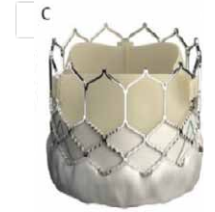


# FACTORS FAVORING TAVR VS. SAVR

**SAVR – US Registry - 104,699 pts**  
Mean age 70 yrs



# SOURCE 3 Registry – Risk analysis



n = 1945

## SURGICAL RISK

**Age – 78**  
**LOW**  
**29.0%**

**HIGH**  
**32.2%**



**Age – 82**

**INTERMEDIATE**  
**38.7%**

**MORE THAN 2/3 INTERMEDIATE OR LOW RISK**

**IR/LR 70% IN TF vs. 60% IN NON-TF (p < 0.01)**

## Log EuroScore

**LR**

**IR**

**HR**

**6.8 ± 2**

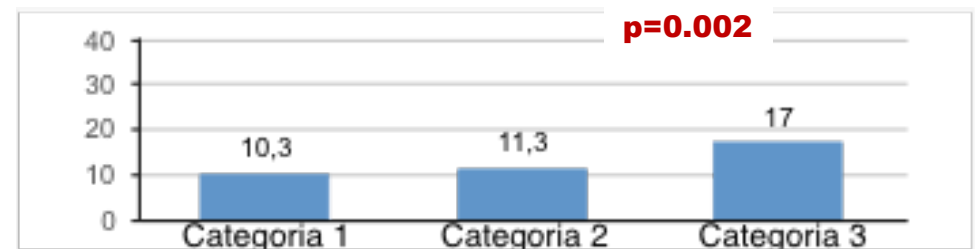
**14 ± 3**

**33.5 ± 12.4**

## 12-mo All-Cause Mortality

**p=0.00**

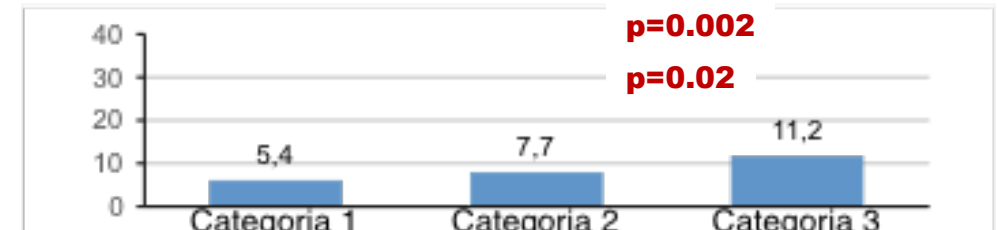
**p=0.002**



## 12-mo Cardiac Mortality

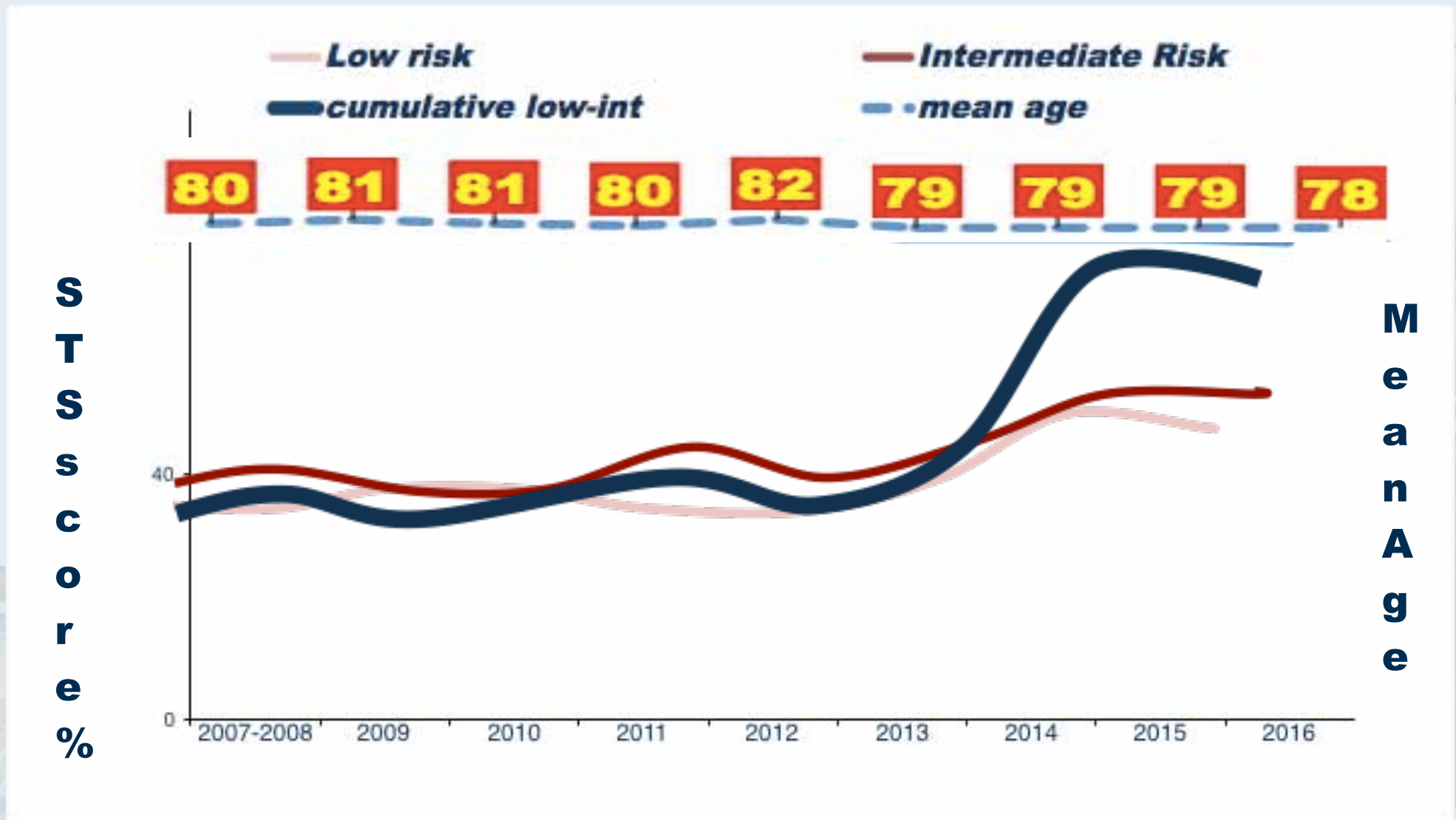
**p=0.002**

**p=0.02**



*Tarantini et al. submitted*

## ***PURE VALVE Registry 2007-2015 – 752 TAVR pts***

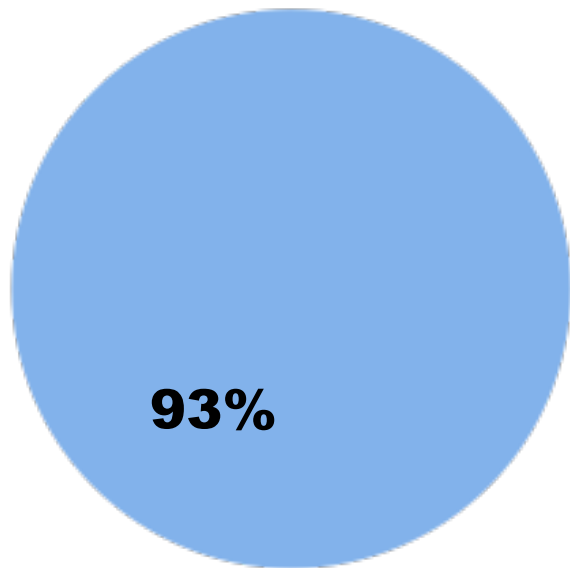


# Severe aortic stenosis: age distribution

Severe aortic stenosis in patients undergoing AVR

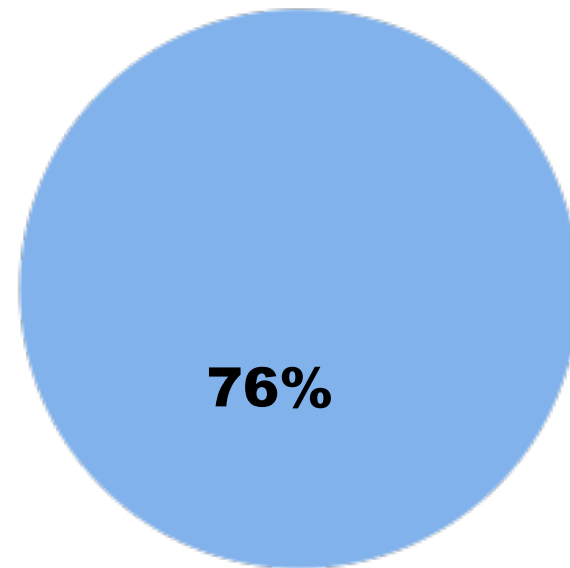
**n=932 pts**

## BICUSPID VALVES



■ Vendite

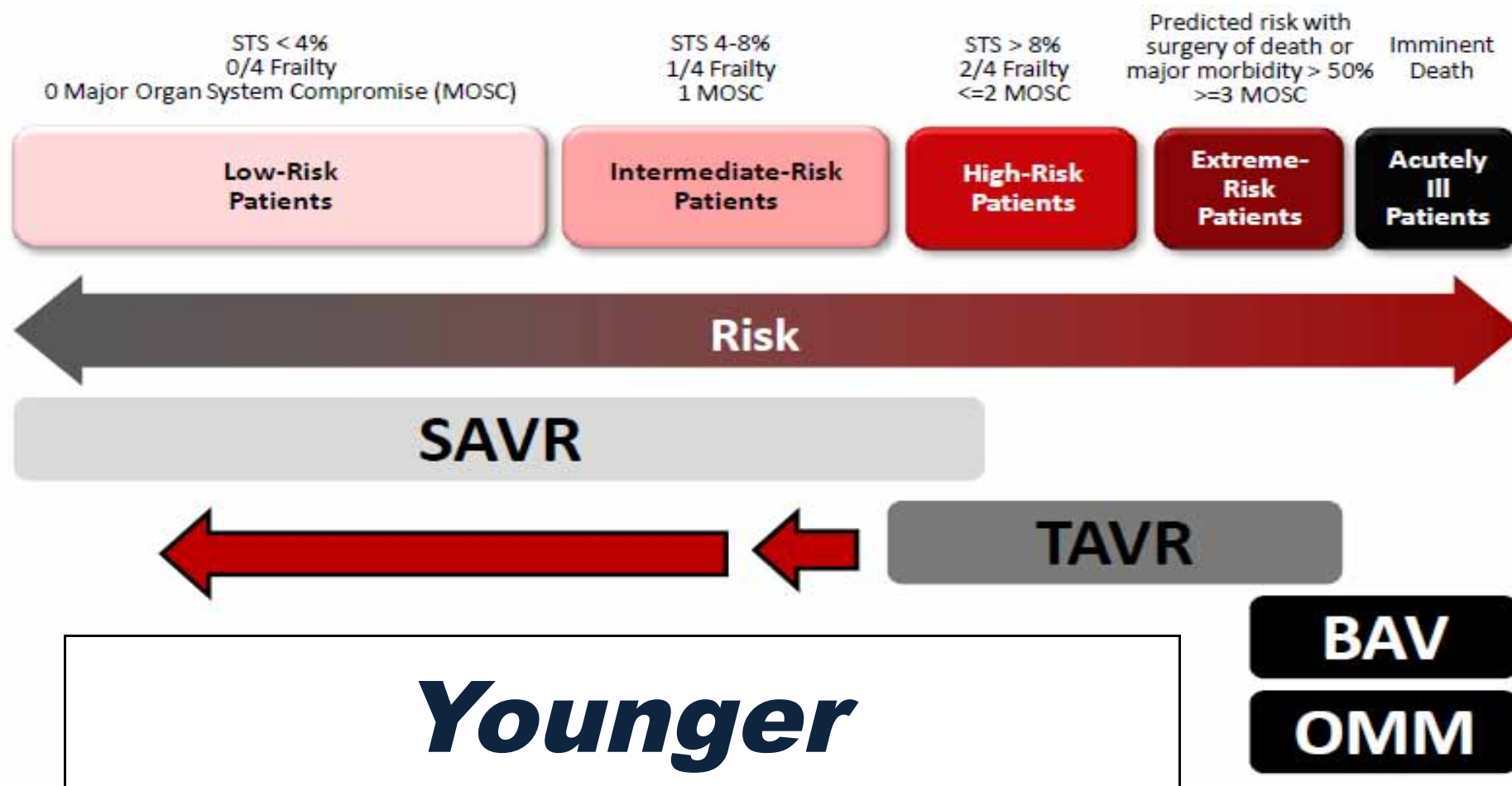
## TRICUSPID VALVES



■ Vendite

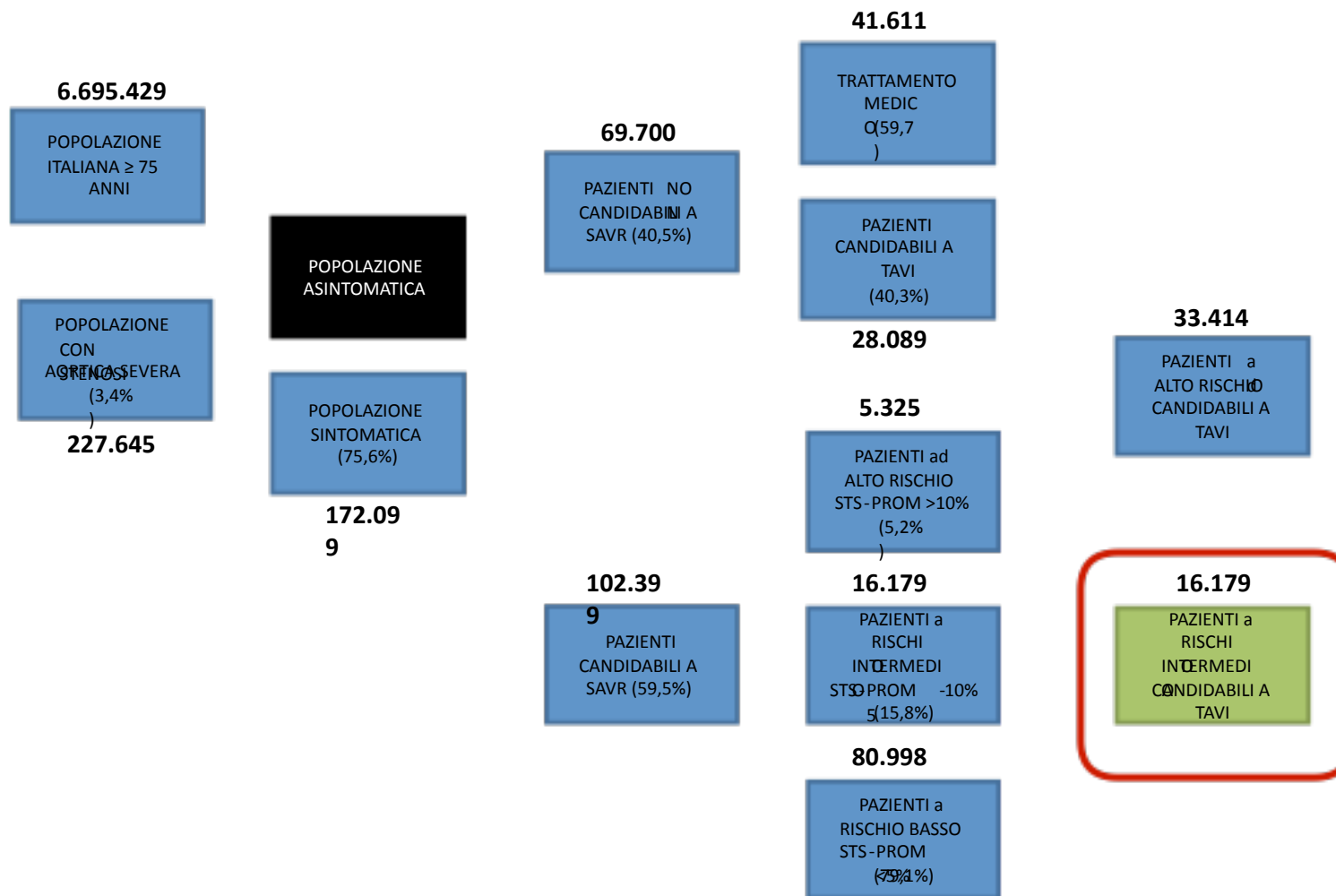
# STENOSI AORTICA

## Modifiche all'attuale algoritmo terapeutico



# EPIDEMIOLOGIA

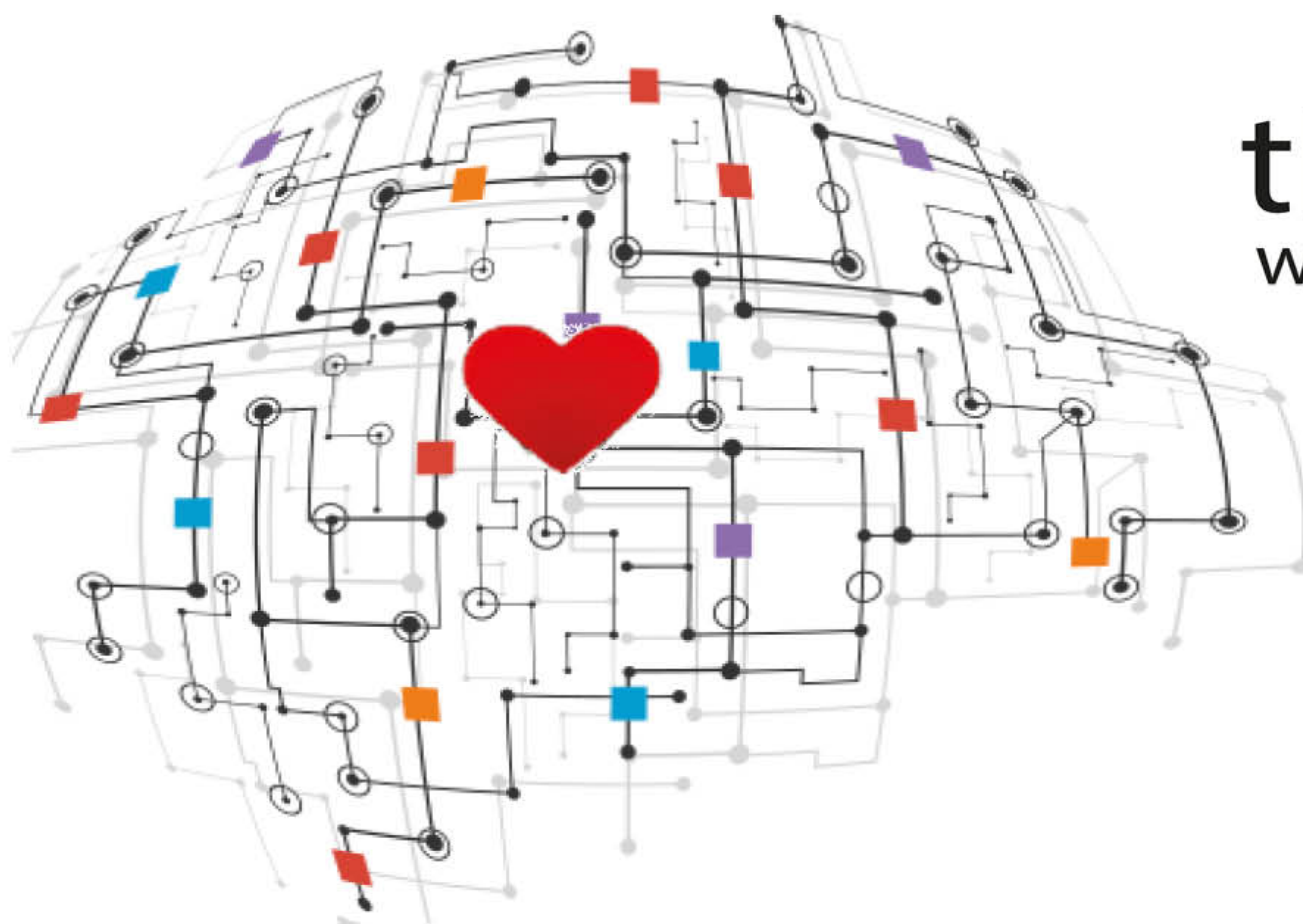
## Bisogno epidemiologico attuale in Italia



FONTE: Osnabrugge RL et al., Aortic stenosis in the elderly: disease prevalence and number of candidates for transcatheter aortic valve replacement: a meta-analysis and modeling study. J Am Coll Cardiol. 2013 Sep 10;62(11):1002-12.

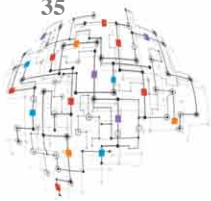


thinkheart  
with GISE



thinkheart

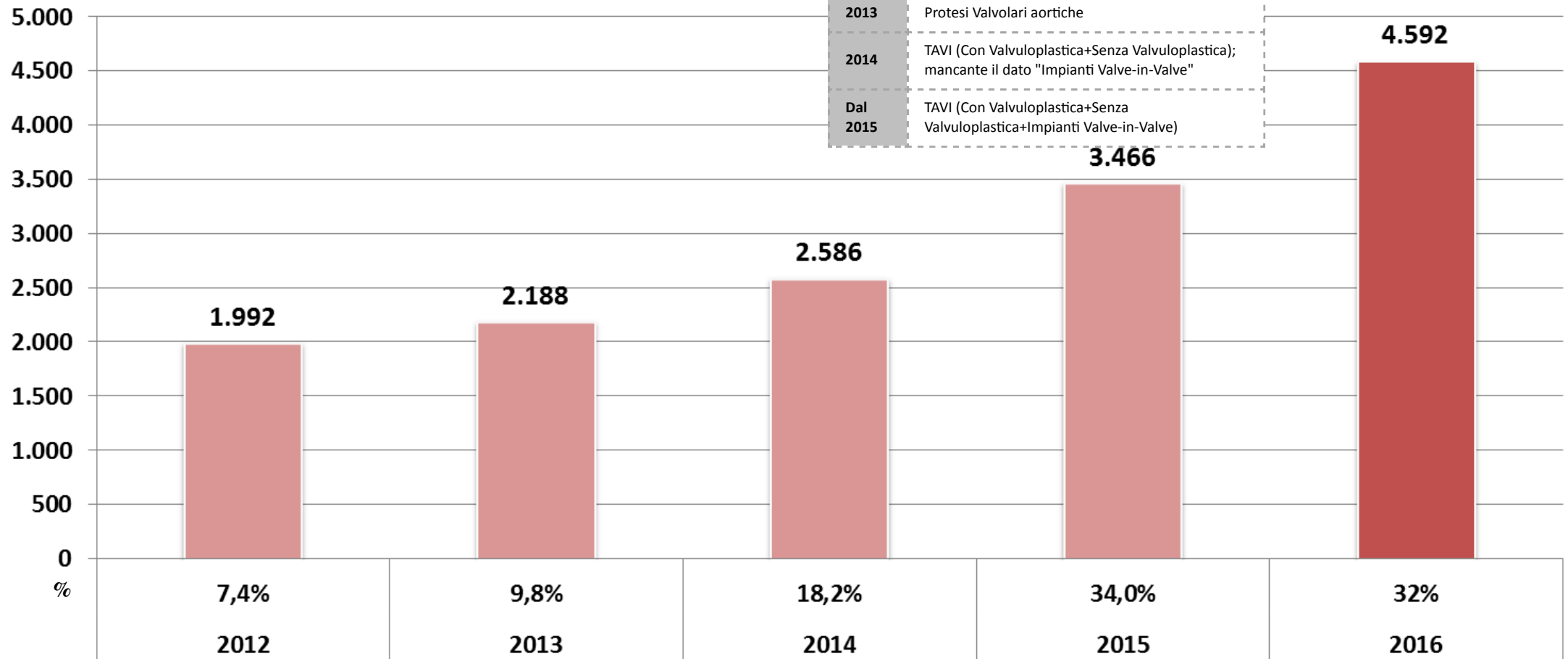
20 - 21 APRILE 2017  
Stazione Leopolda - FIRENZE



# TAVI

## SERIE STORICA

| EVOLUZIONE RACCOLTA DATI TAVI NEGLI ANNI |                                                                                              |
|------------------------------------------|----------------------------------------------------------------------------------------------|
| 2011                                     | Impianto Protesi Percutanee Aortiche                                                         |
| 2012                                     | Protesi Valvolari aortiche                                                                   |
| 2013                                     | Protesi Valvolari aortiche                                                                   |
| 2014                                     | TAVI (Con Valvuloplastica+Senza Valvuloplastica); mancante il dato "Impianti Valve-in-Valve" |
| Dal 2015                                 | TAVI (Con Valvuloplastica+Senza Valvuloplastica+Impianti Valve-in-Valve)                     |



# ORGANIZZAZIONE

## Problematiche attuali

### FASE PREOPERATORIA

- Gestione del flusso di pazienti da parte di Cardiologi ambulatoriali e MMG
- Gestione organizzativa del paziente con SA
- Heart team
- Logica di silos (ospedale e territorio)
- Capacity dei centri (posti letto, CCH on-site)

### FASE OPERATORIA E POST-OPERATORIA

- Approccio terapeutico (es. anestesia generale vs locale)
- Stand-by chirurgico
- Durata della degenza ospedaliera (ICU + general ward)
- Percorso di riabilitazione post-intervento



“ *Non mi preoccupo mai del futuro, arriva  
sempre abbastanza presto* ”

ALBERT EINSTEIN

## **AHA STATISTICAL UPDATE**

---

# **Heart Disease and Stroke Statistics—2017 Update**

**A Report From the American Heart Association**

**From US-TVT registry – 26414 TAVR pts**

*Holmes JACC  
2015*

**2011 to 2014 ≈70% of TAVR pts were ≥80 years,**

**In 2014 median STS was 6.7% and 95% deemed at "extreme" or  
"high" risk**

*Benjamin E et al, Circulation  
2017*

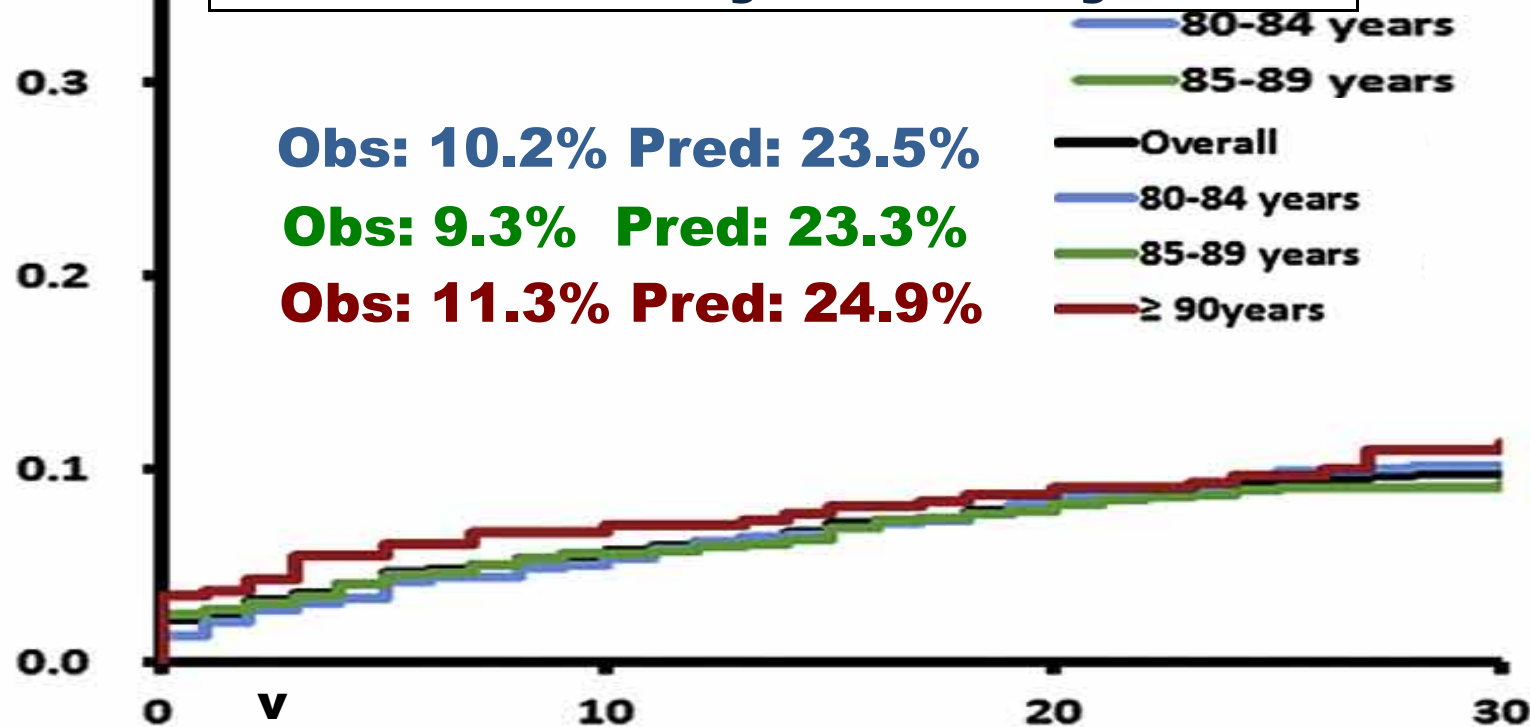
# Factors favoring **TAVR** vs. **SAVR**

B

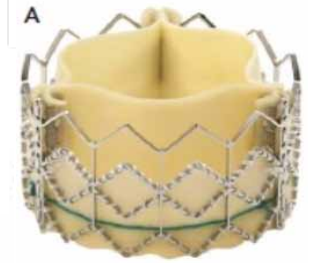


## **TAVR - FRANCE-2 Registry - 2254 pts**

### Mortality at 30-day



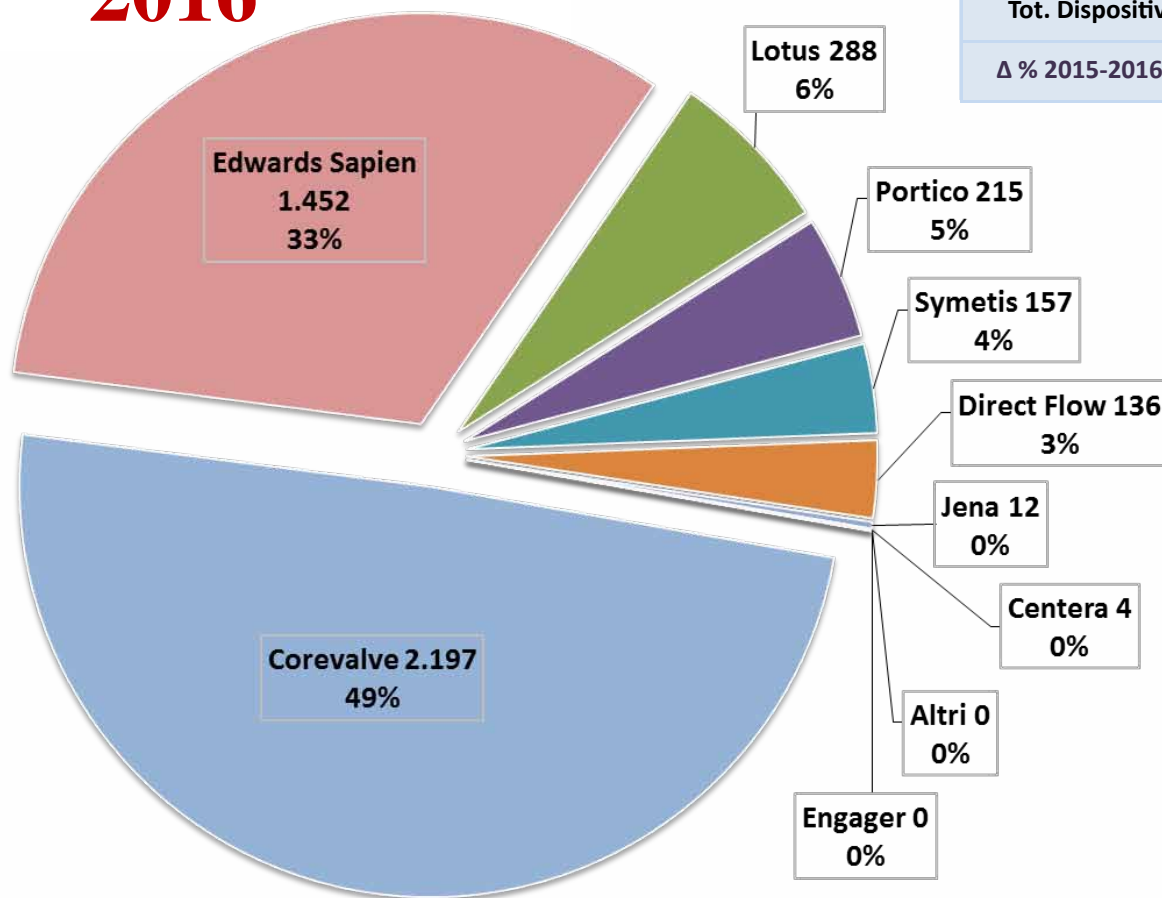
A



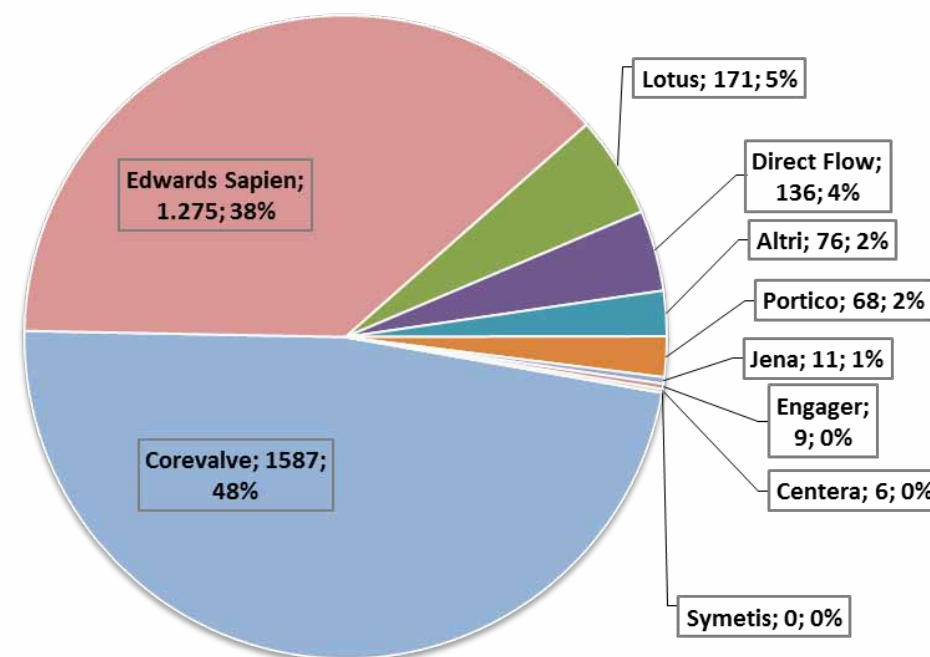


# DISPOSITIVI TAVI UTILIZZATI 2016

|                              |       |
|------------------------------|-------|
| Tot. Dispositivi 2015        | 3.339 |
| Tot. Dispositivi 2016        | 4.461 |
| $\Delta$ % 2015-2016 ITALIA: | 33,6% |



Dispositivi TAVI Italia 2015



# GOVERNANCE

## Variabilità Regionali

### Meccanismi di finanziamento

FONTE: Callea G et al. Il governo dell'innovazione tecnologica in sanità. Il caso dell'impianto di valvola aortica transcateretere: stato dell'arte delle indicazioni e della rimborsabilità nelle regioni italiane. MECOSAN 95/2015, pp. 137-160, DOI:10.3280/MESA2015-095007

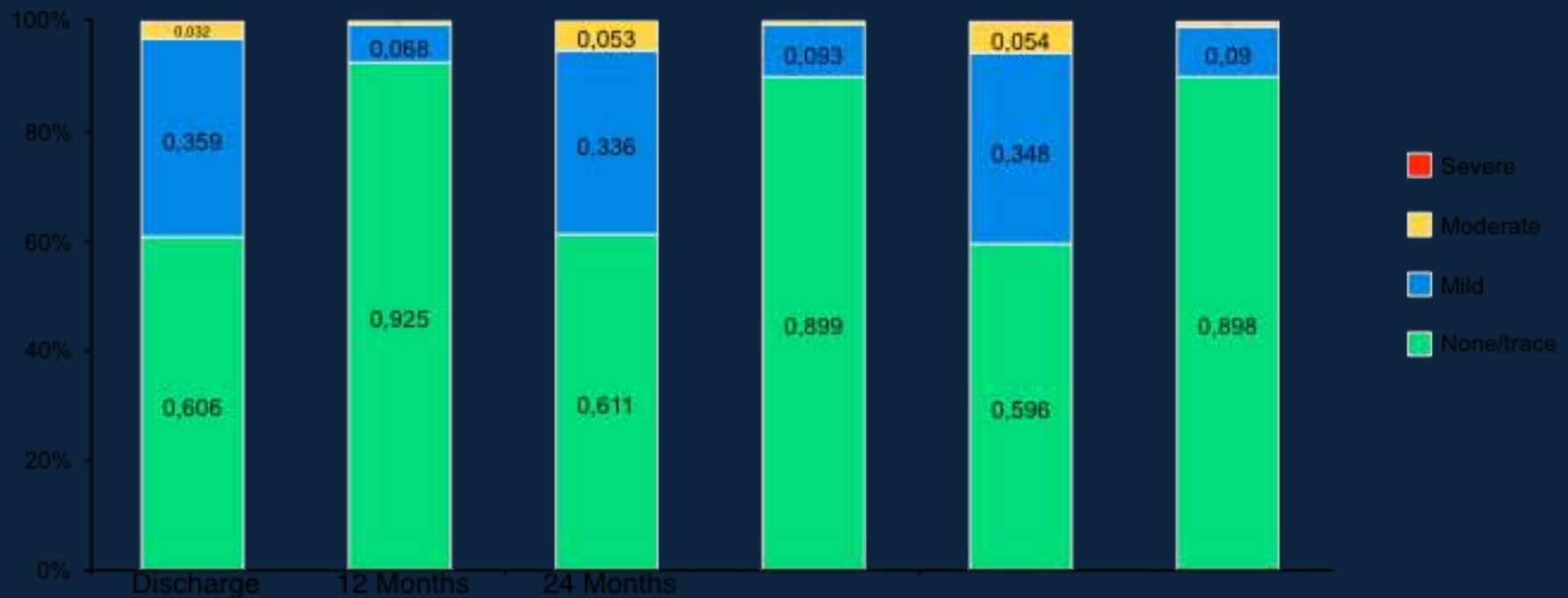
|                       | Quota<br>capitaria | Tariffa<br>base DRG | Add-on | Lump-sum | Budget | Tariffa 2013 <sup>4</sup>  |
|-----------------------|--------------------|---------------------|--------|----------|--------|----------------------------|
| Piemonte              |                    | X                   |        |          |        | 20.487-24.675              |
| Valle D'Aosta         |                    |                     |        |          |        | N/A <sup>5</sup>           |
| Lombardia             |                    |                     | X      |          |        | 25.522                     |
| Prov. Aut. Bolzano    |                    |                     |        |          |        | N/A <sup>6</sup>           |
| Prov. Aut. Trento     | X                  |                     |        |          |        | N/A <sup>7</sup>           |
| Veneto                | X                  | X                   |        |          |        | 27.476-34.179              |
| Friuli Venezia Giulia |                    | X <sup>8</sup>      |        |          |        | 21.551-25.492              |
| Liguria               |                    | X                   |        |          |        | 15.775-20.160              |
| Emilia Romagna        | X                  | X                   |        |          | X      | 21.101-25.415 <sup>9</sup> |
| Toscana               |                    | X                   |        |          |        | 18.237-19.910              |
| Umbria                |                    | X                   |        |          |        | 20.487-24.675              |
| Marche                |                    | X                   |        |          |        | 25.373                     |
| Lazio                 |                    | X                   |        |          |        | 20.487-24.675              |
| Abruzzo               | X                  |                     |        |          |        | N/A <sup>10</sup>          |
| Molise                |                    |                     |        |          |        | N/A <sup>11</sup>          |
| Campania              |                    |                     |        | X        |        | 25.000                     |
| Puglia                |                    |                     |        | X        |        | 20.487-24.675              |
| Basilicata            |                    |                     | X      |          |        | 28.487-32.675              |
| Calabria              |                    | X                   |        |          |        | 20.487-24.675              |
| Sicilia               |                    |                     | X      |          |        | 28.487-32.675              |
| Sardegna              | X                  | X                   |        |          |        | 17.043-21.184              |

### Raccomandazioni & Report HTA

FONTE: Callea G et al. Il governo dell'innovazione tecnologica in sanità. Il caso dell'impianto di valvola aortica transcateretere: stato dell'arte delle indicazioni e della rimborsabilità nelle regioni italiane. MECOSAN 95/2015, pp. 137-160, DOI:10.3280/MESA2015-095007

|                       | Report di HTA  | Delibere regionali di<br>indirizzo | Delibere regionali di<br>rimborsabilità |
|-----------------------|----------------|------------------------------------|-----------------------------------------|
| Piemonte              | X              | X                                  |                                         |
| Lombardia             |                |                                    | X                                       |
| Veneto                | X              | X                                  |                                         |
| Friuli Venezia Giulia |                |                                    | X                                       |
| Emilia Romagna        | X              | X <sup>1</sup>                     | X                                       |
| Lazio                 | X              |                                    |                                         |
| Campania              |                |                                    | X                                       |
| Puglia                |                |                                    | X                                       |
| Basilicata            |                |                                    | X                                       |
| Sicilia               |                |                                    | X <sup>2</sup>                          |
| Prov. Aut. Trento     |                |                                    |                                         |
| Liguria               |                |                                    |                                         |
| Toscana               |                |                                    |                                         |
| Umbria                |                |                                    |                                         |
| Marche                |                |                                    |                                         |
| Abruzzo               |                |                                    |                                         |
| Calabria              |                |                                    |                                         |
| Sardegna              |                |                                    |                                         |
| Valle d'Aosta         |                |                                    |                                         |
| Prov. Aut. Bolzano    |                |                                    |                                         |
| Molise                |                |                                    |                                         |
| Agenas                | X <sup>3</sup> |                                    |                                         |

# Total Aortic Regurgitation (core lab adjudication)



# TAVR: Intermediate risk

Expected improvement compared to High Risk patients:

**TAVR**

**$\Delta C$**

**$\Delta E$**

**ICER**

- Mortality
- QoL
- Complications
- Device Cost
- Admission Cost\*
- Follow-up Cost

**AVR**



Big improvement



Slight improvement



No improvement

\* **Length of Stay + Complications**