Future in Trans-Catheter Heart Valve Treatment

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Conflict of Interest Statement

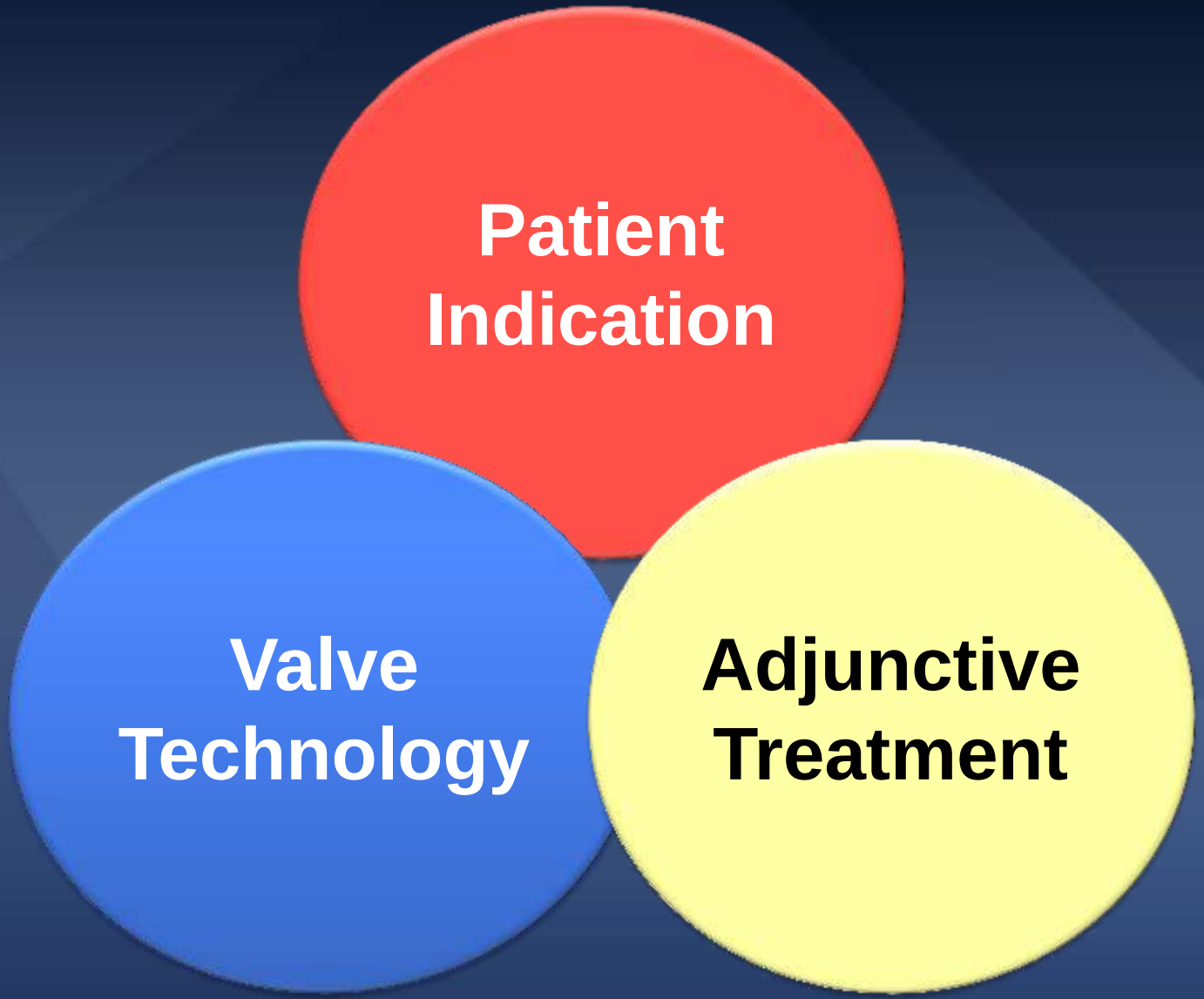
- I have nothing to disclose
- No financial relationships

The Chain of RCT Evidences

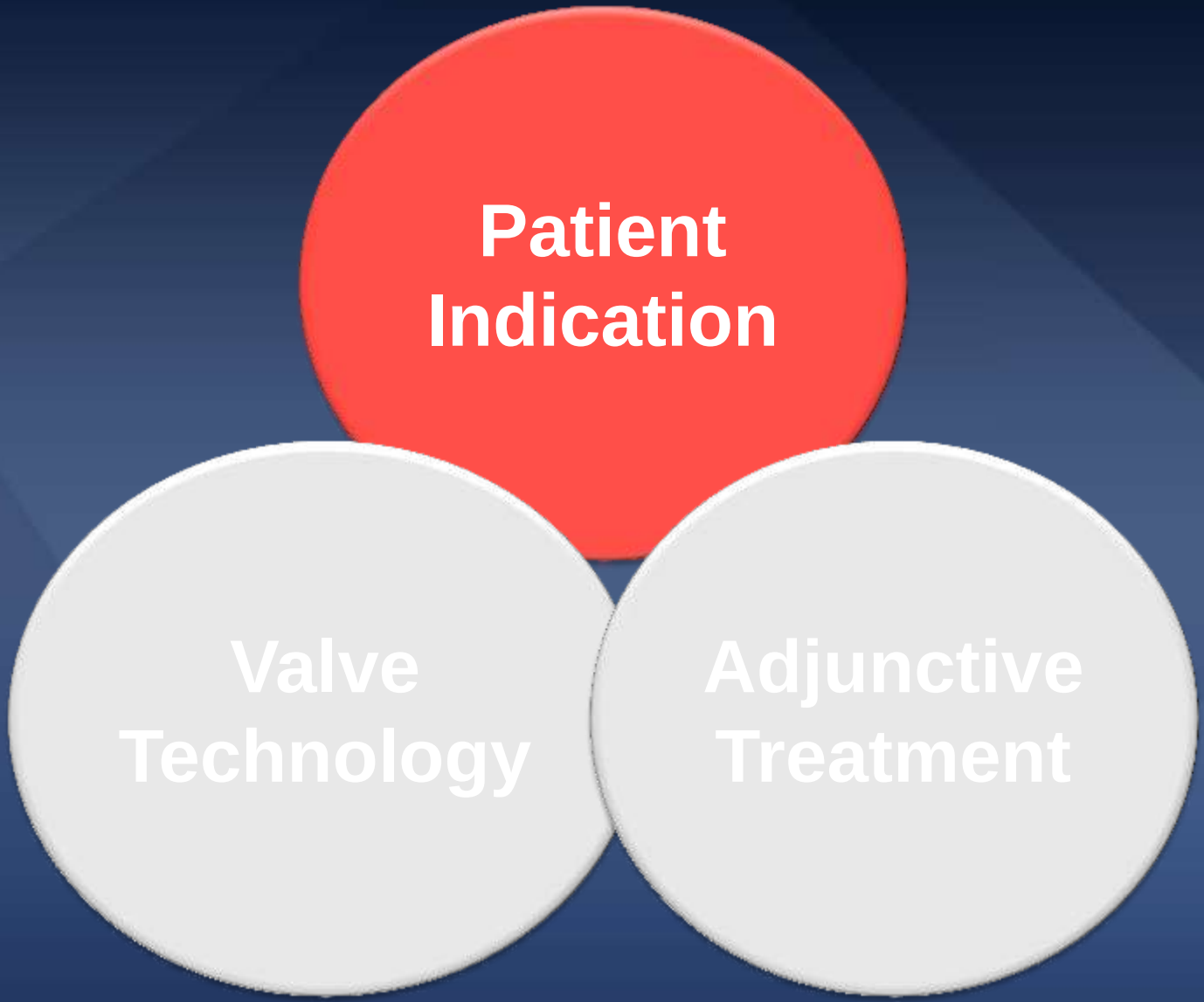
Trial Name	STS Score	Age
Inoperable Population		
PARTNER IB Trial	11.6	83
High Risk Population		
PARTNER IA Trial	11.8	84
CoreValve US Pivotal Trial	7.4	83
Intermediate Risk Population		
PARTNER II Trial	5.8	82
Low Risk Population		
NOTION Trial	3.0	79

TAVR procedure was booming!!!

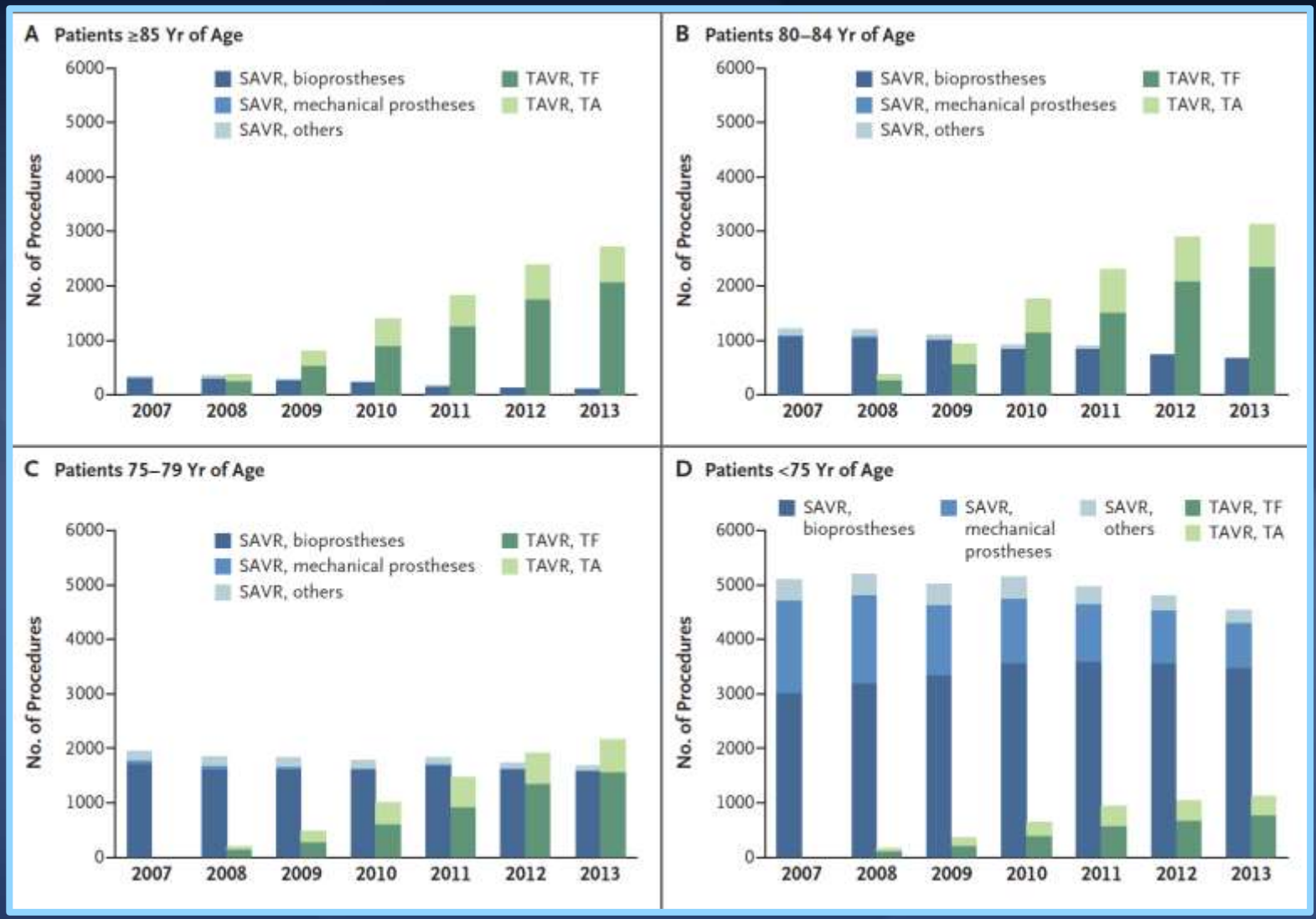
Future Perspective of TAVR



Future Perspective of TAVR

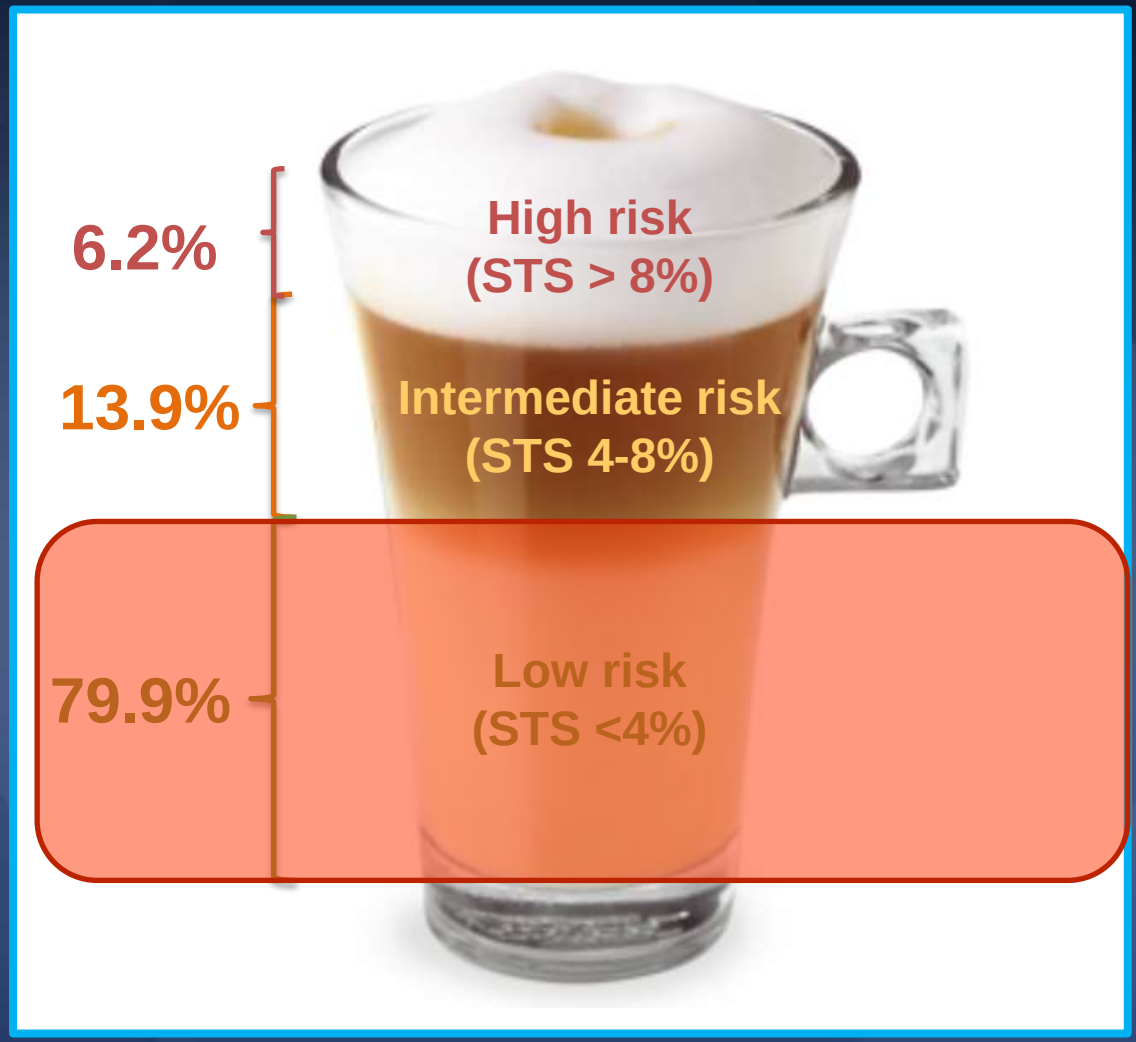


TAVR: "Rapid Applicability in Real World" in Germany from 2007 to 2013.



N Engl J Med 2015;373:2438-47.

STS database 2002-2010
(141,905 pts)



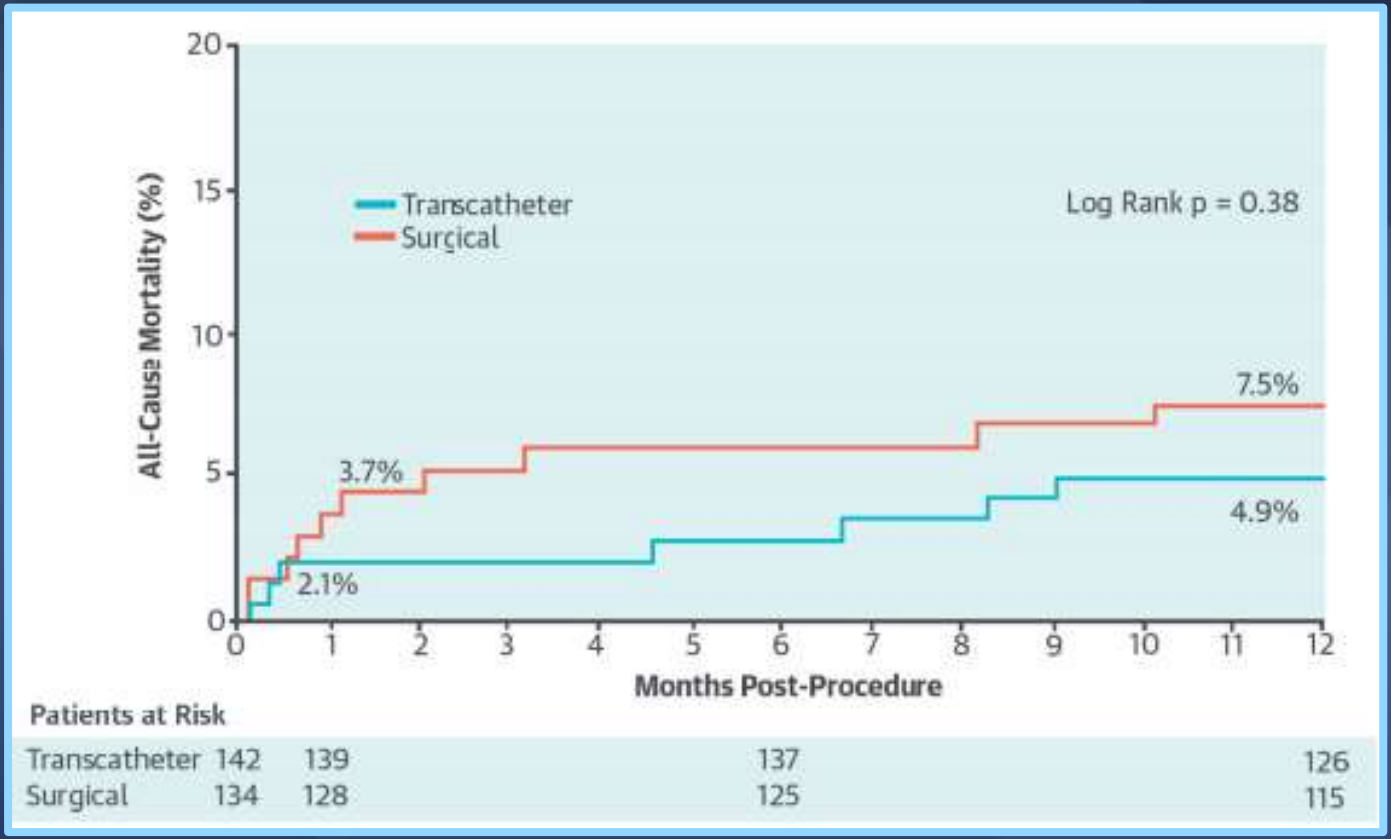
Courtesy of N. Piazza

All-Comers NOTION Trial

Low Risk (N=280) patients

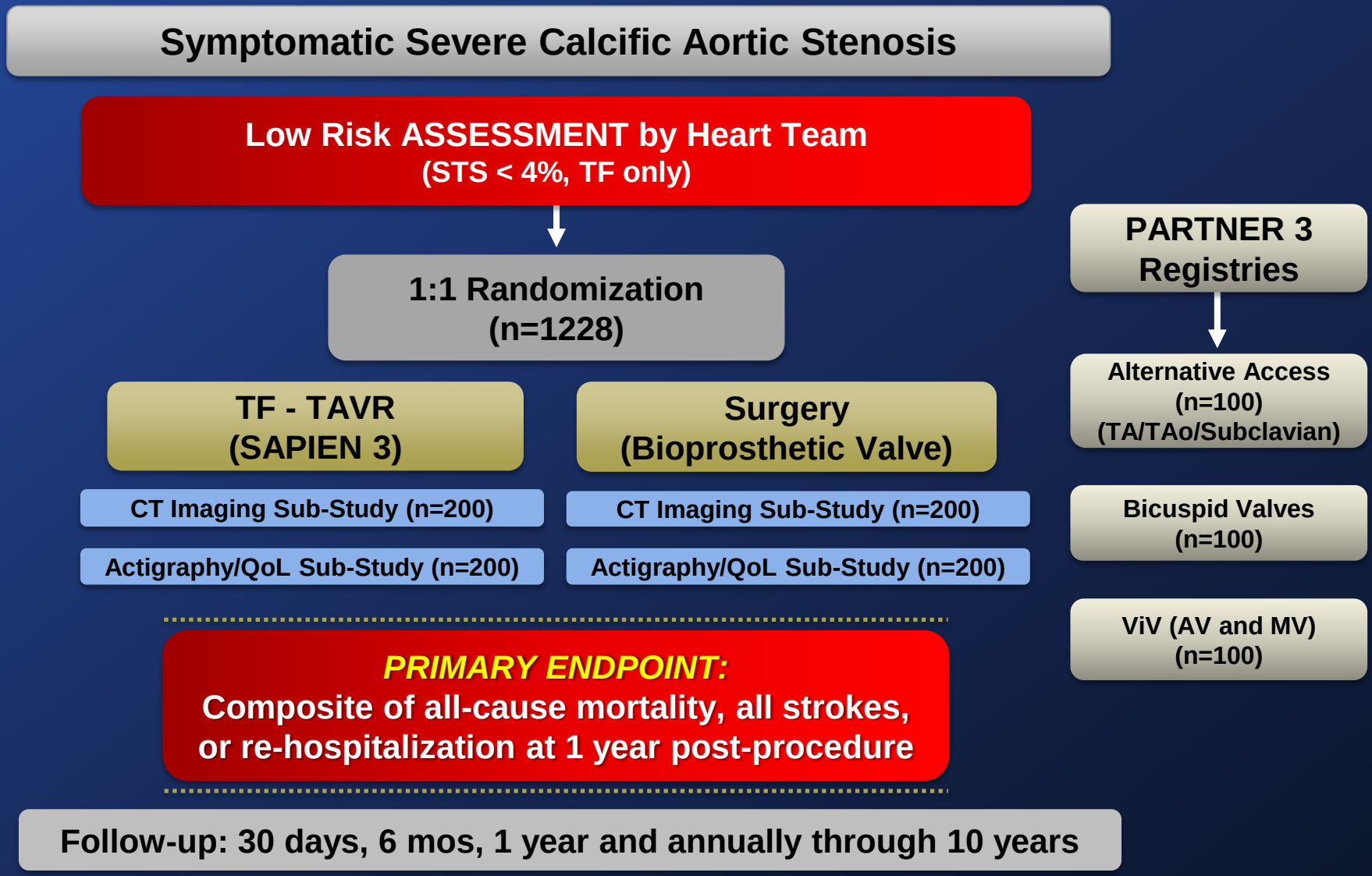
STS = 3.0%, STS < 4% = 81.8%

EuroSCORE I / II = 8.6 / 2.0



Thyregod et al JACC 2015;65:2184–94

The PARTNER 3 Trial
Study Design



EVOLUT R Low-Risk Trial

Heart Team Evaluation
Two Cardiac Surgeons and One Interventional Cardiologist
Low Surgical Risk (predicted mortality risk <3%)

National Screening Committee
One Cardiac Surgeons and One Interventional Cardiologist
Confirm Low Risk for TAVR and SAVR

1:1 Randomization (N=1,256)

TAVR

SAVR

Leaflet sub-study N=200

4D CT for LTI

Leaflet sub-study N=200

In the near future, young age is not an exclusion criteria for TAVR anymore…

Longevity of Artificial Aortic Valve!!!

Mechanical Surgical Valves	Bioprosthetic Surgical Valves	Bioprosthetic TAVR Valves
Lifelong	*>10 Years*	*>10 Years???*

Reduced Leaflet Motion in Bioprosthetic Aortic Valves — The FDA Perspective

John C. Laschinger, M.D., Changfu Wu, Ph.D., Nicole G. Ibrahim, Ph.D., and Jeffrey E. Shuren, M.D., J.D.

Related article, p. 2015

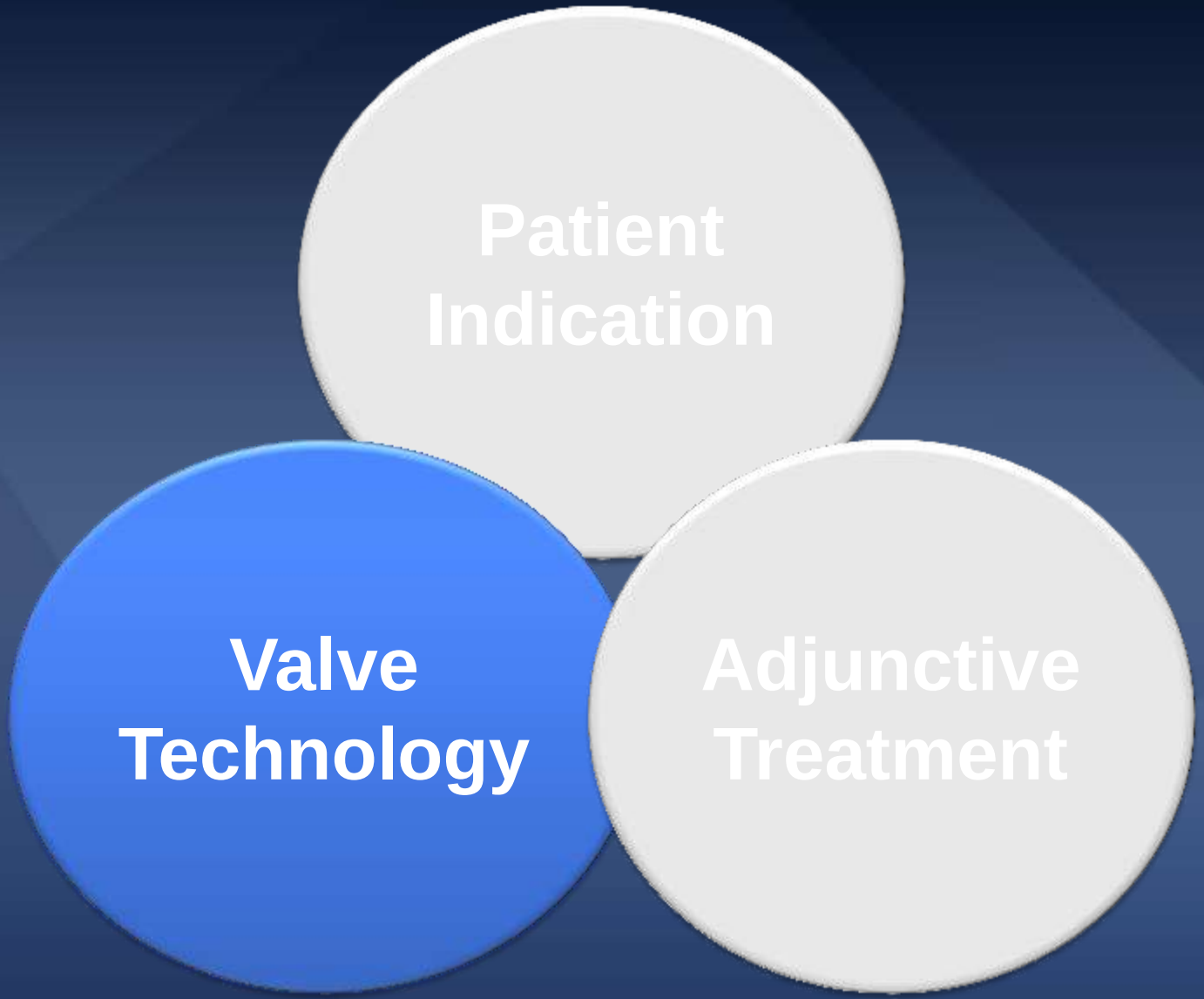
Whether reduced leaflet motion is clinically meaningful or represents a subclinical advanced-imaging phenomenon, the loss of leaflet mobility renders the valve dysfunctional and demands additional investigation.

2007 Oscar of the most viewed slide during cardiology meetings !

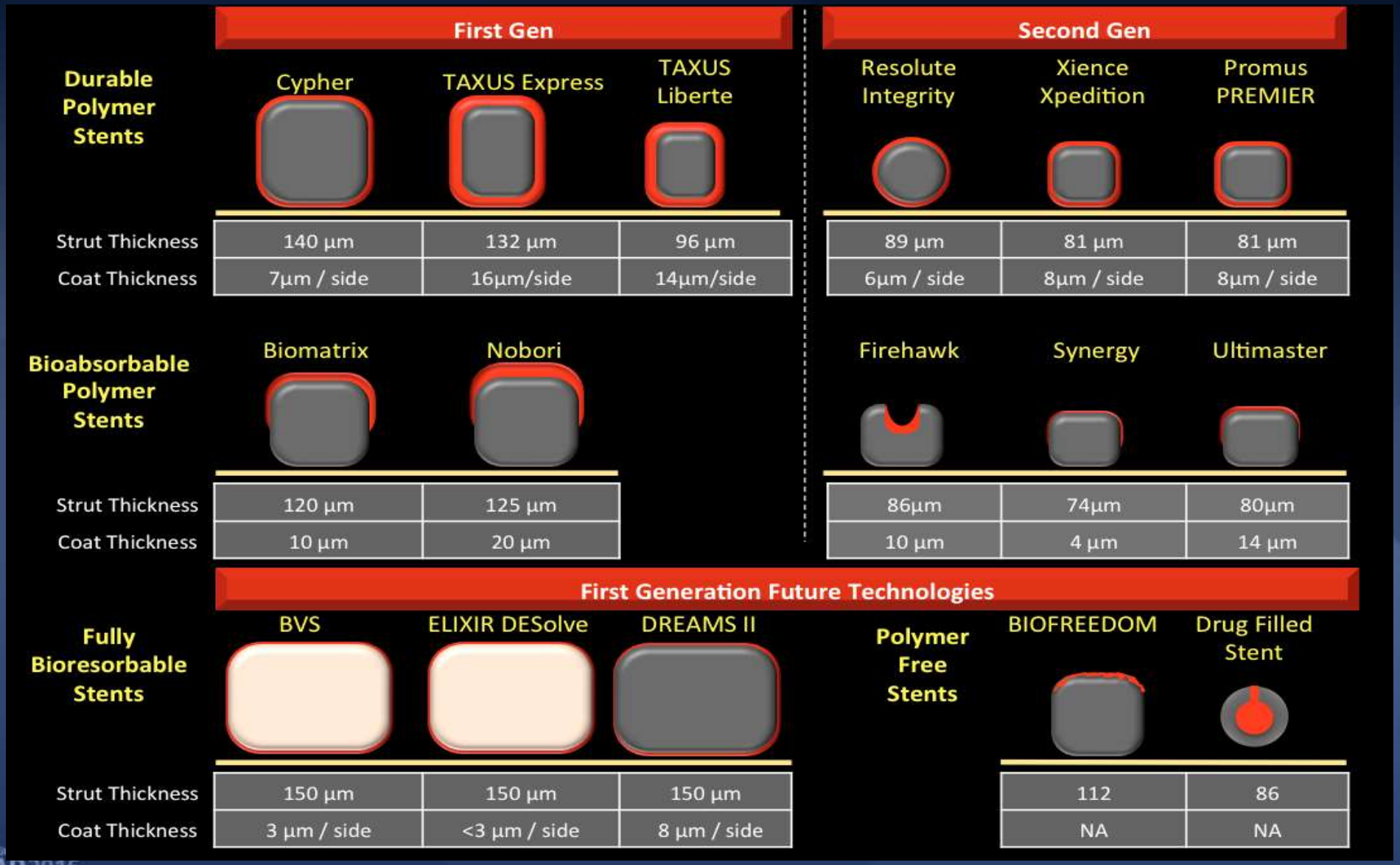
We should not follow previous Camenzind's curse for early-DES device

Without compelling evidence for long-term durability of contemporary TAVR devices!!!!

Future Perspective of TAVR

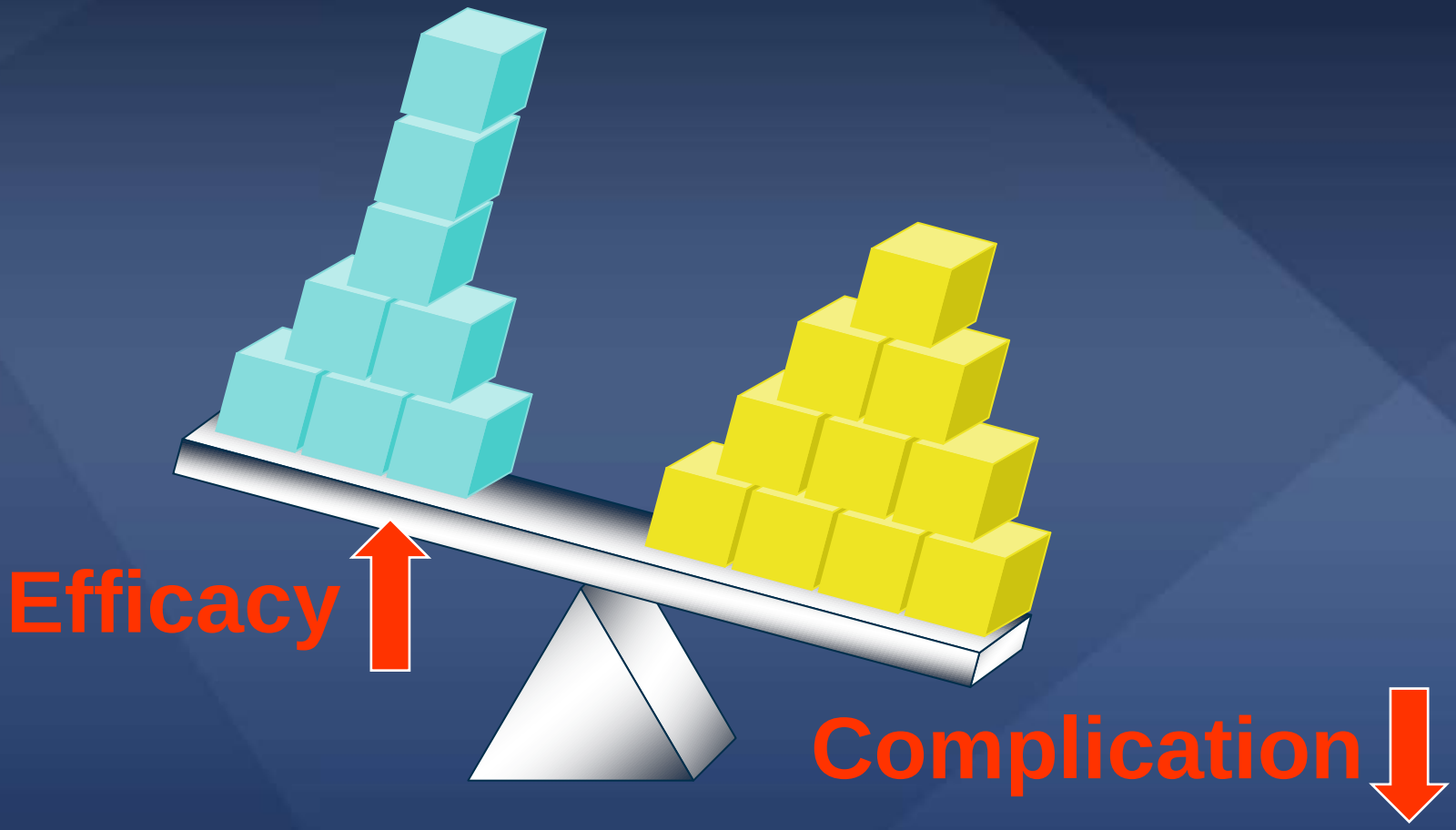


Evolution of DES Technology



Evolution of TAVR Technology

Never-Stop and Newer TAVR Systems!!!



Evolution of TAVR Technology

- **Valve:** tissue components, processing, construction, coaptation, and tissue engineering.
- **Frame:** composition, shape, and geometry.
- **Delivery system:** profile, design, access possibility.
- **Deployment method:** balloon/self-expansion, other designs, and retrievable/repositionable.
- **PVL reduction:** frame/positioning, sub-annular fixation, external skirts/covers, and novel features.

Evolution of TAVR Technology

Current Leaders!

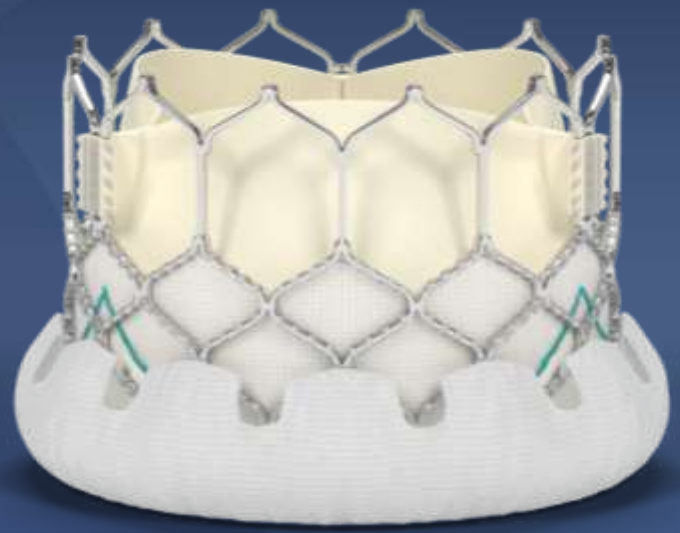
- Sapien 3
- Evolut R
- Lotus
- Portico
- Symetis
- Direct Flow
- Engager
- Jena Valve
- Centera
- Venus A Valve

Future Candidate!

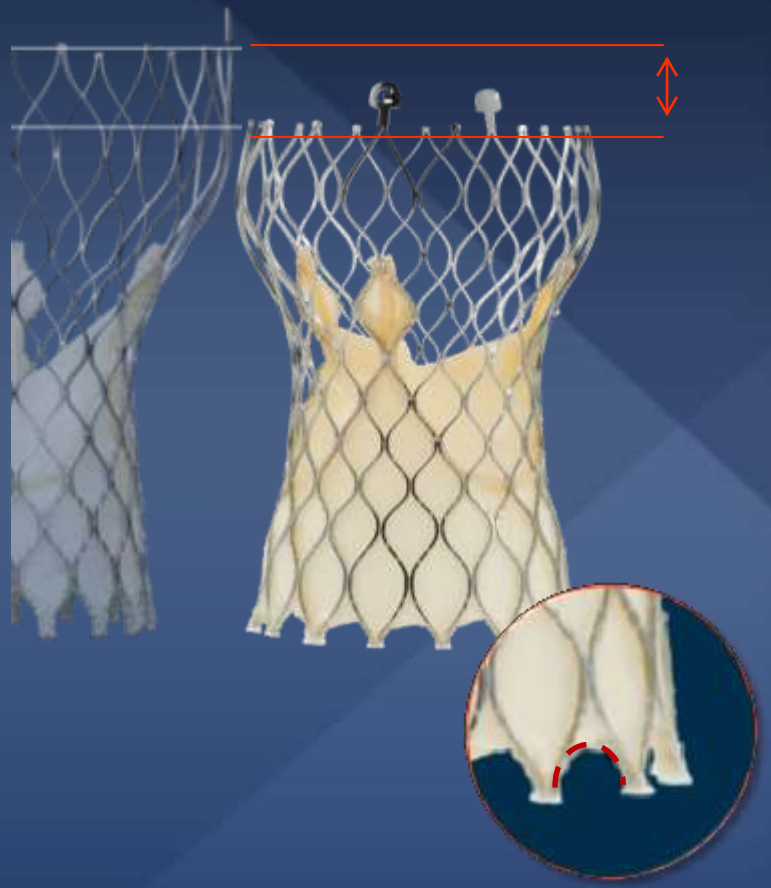
- Shanghai Valve
- Trinity
- Colibri
- Inovare
- Thubrikar
- Valve Medical
- Syntheon Verso
- Triskele
- BioValve
- MyVal
- HLT
- NVT (Nautilus)
- J - Valve
- Xeltis
- Zurich TEHV

Current "Standards" for TAVR

Edwards Sapien 3



MDT Evolut R



TAVR Systems

- Sapien 3
- Evolut R
- *Lotus*
- *Portico*
- *Symetis*
- *Direct Flow*
- Engager
- Jena Valve
- Centera
- Venus A Valve

CE – approved;
Increasing clinical use

TAVR Systems

- Sapien 3
- Evolut R
- Symetis
- Direct Flow
- Lotus
- Portico
- *Engager*
- *Jena Valve*
- *Centera*
- *Venus A Valve*

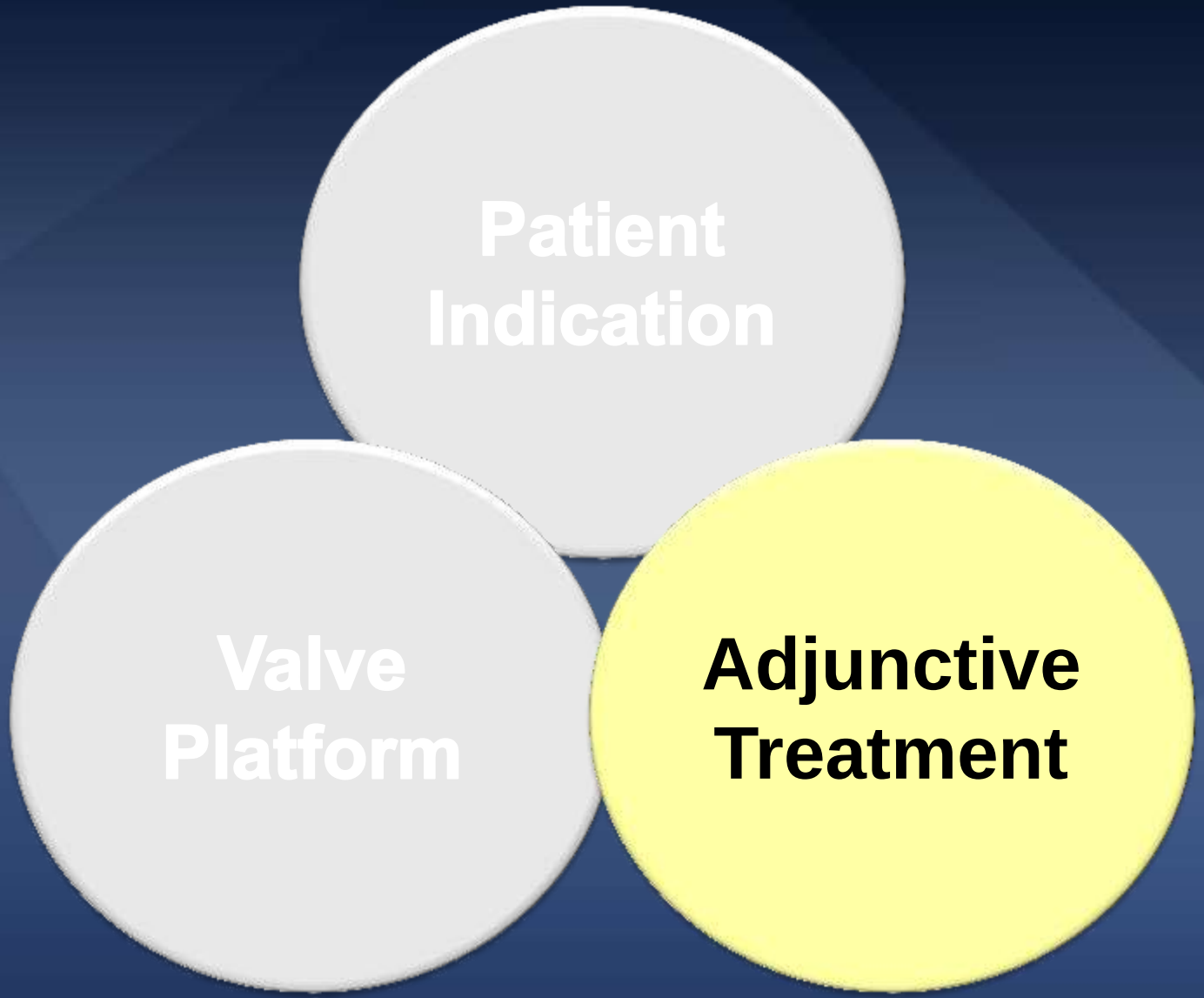
Design modifications, awaiting approval or pivotal experiencing

TAVR Systems

Pre-Clinical or Early Clinical

- *Shanghai Valve*
- *Trinity*
- *Colibri*
- *Inovare*
- *Thubrikar*
- *Valve Medical*
- *Syntheon Verso*
- *Triskele*
- *BioValve*
- *MyVal*
- *HLT*
- *NVT (Nautilus)*
- *J - Valve*
- *Xeltis*
- *Zurich TEHV*

Future Perspective of TAVR

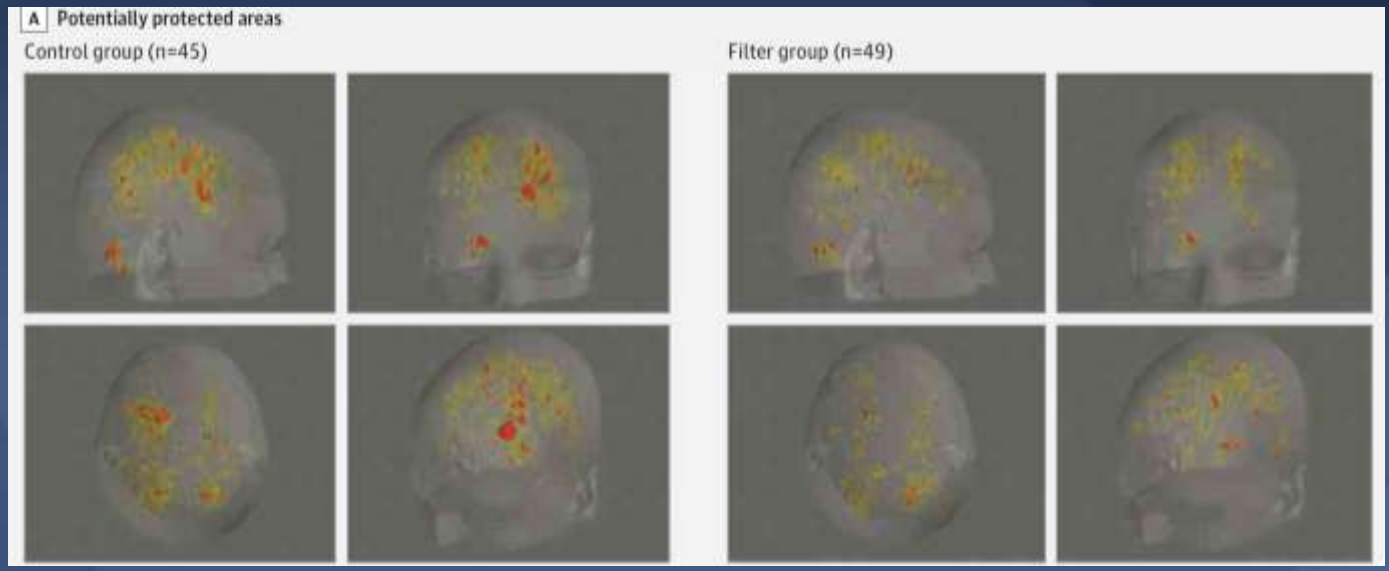


TAVR: Stroke Prevention

JAMA | Original Investigation

Effect of a Cerebral Protection Device on Brain Lesions Following Transcatheter Aortic Valve Implantation in Patients With Severe Aortic Stenosis

The CLEAN-TAVI Randomized Clinical Trial

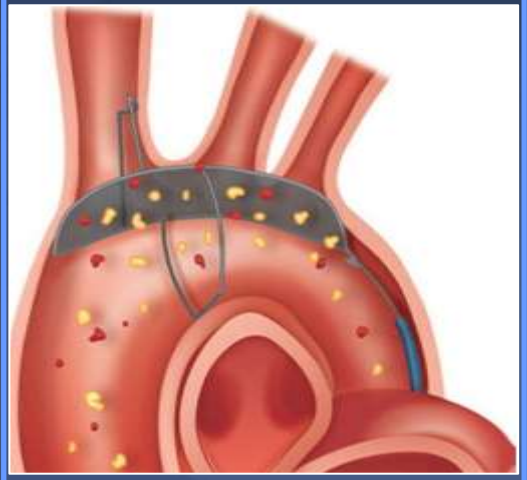


- Those who received the filter had fewer new ischemic cerebral lesions on MRI at 2 days ($P < 0.001$) and 7 days ($P = 0.003$).
- There were no differences in clinical stroke rate between the study groups at 30 days

Haussig S, et al. *JAMA* 2016; 316:592-601.

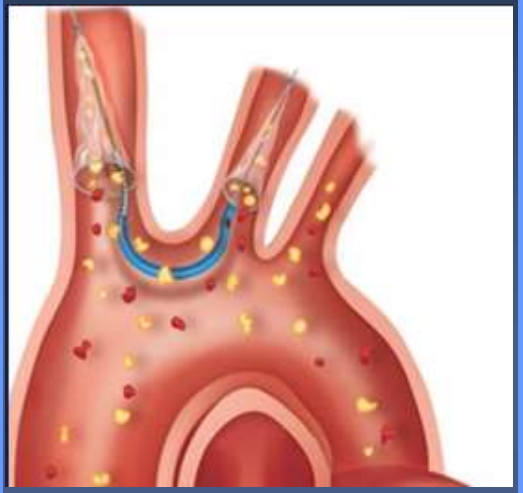
Embolic Protection Devices

TriGuard Embolic Deflection Device (Keystone Heart)[1]



- ✓ Pore Size: 130 µm
- ✓ Delivery Sheath: 9F
- ✓ Access: Transfemoral
- ✓ Coverage: Brachiocephalic, left common carotid, left subclavian

Sentinel Cerebral Protection System (Claret Medical)[2]



- ✓ Pore Size: 140 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial or radial
- ✓ Coverage: Brachiocephalic, left common carotid

Embrella Embolic Deflector System (Edwards Lifesciences)[3]

- ✓ Pore Size: 100 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial
- ✓ Coverage: Brachiocephalic, left common carotid

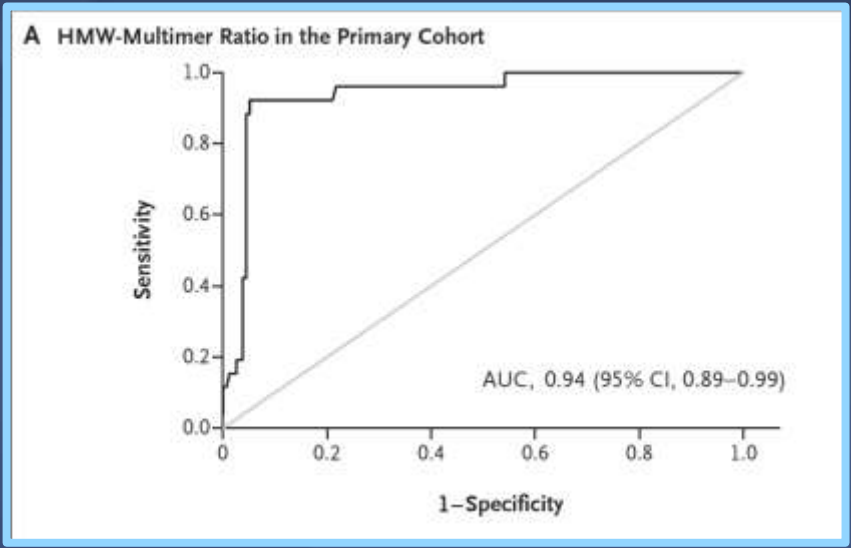
[1]Lansky, et. al. , presented at TCT 2015; [2]Van Mieghem, et al., presented at TCT 2015;
[3]Rodes-Cabau, et al., *J Am Coll Cardiol Intv* 2014;7:1146-55

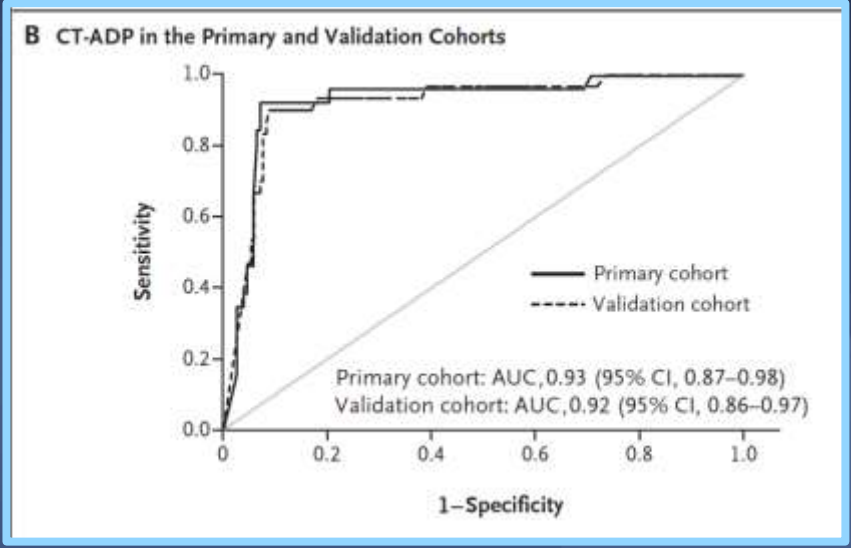
TAVR: AR Prediction

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Von Willebrand Factor Multimers during Transcatheter Aortic-Valve Replacement

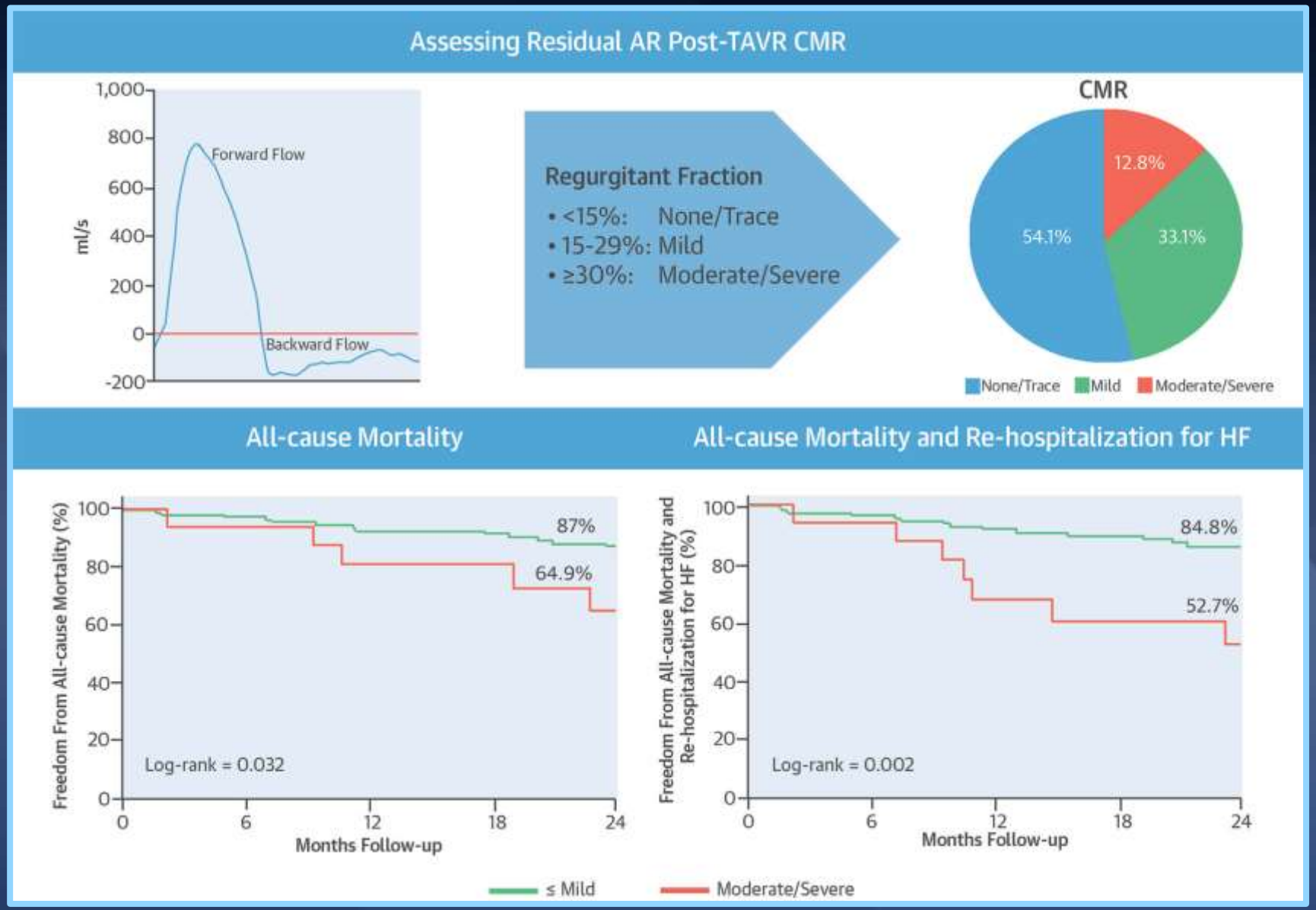




- **The presence of HMW-multimer of von Willebrand factor defects and a high value for a POC hemostatic test, the CT-ADP, were each predictive of the presence of AR after TAVR and were associated with higher 1-year mortality.**

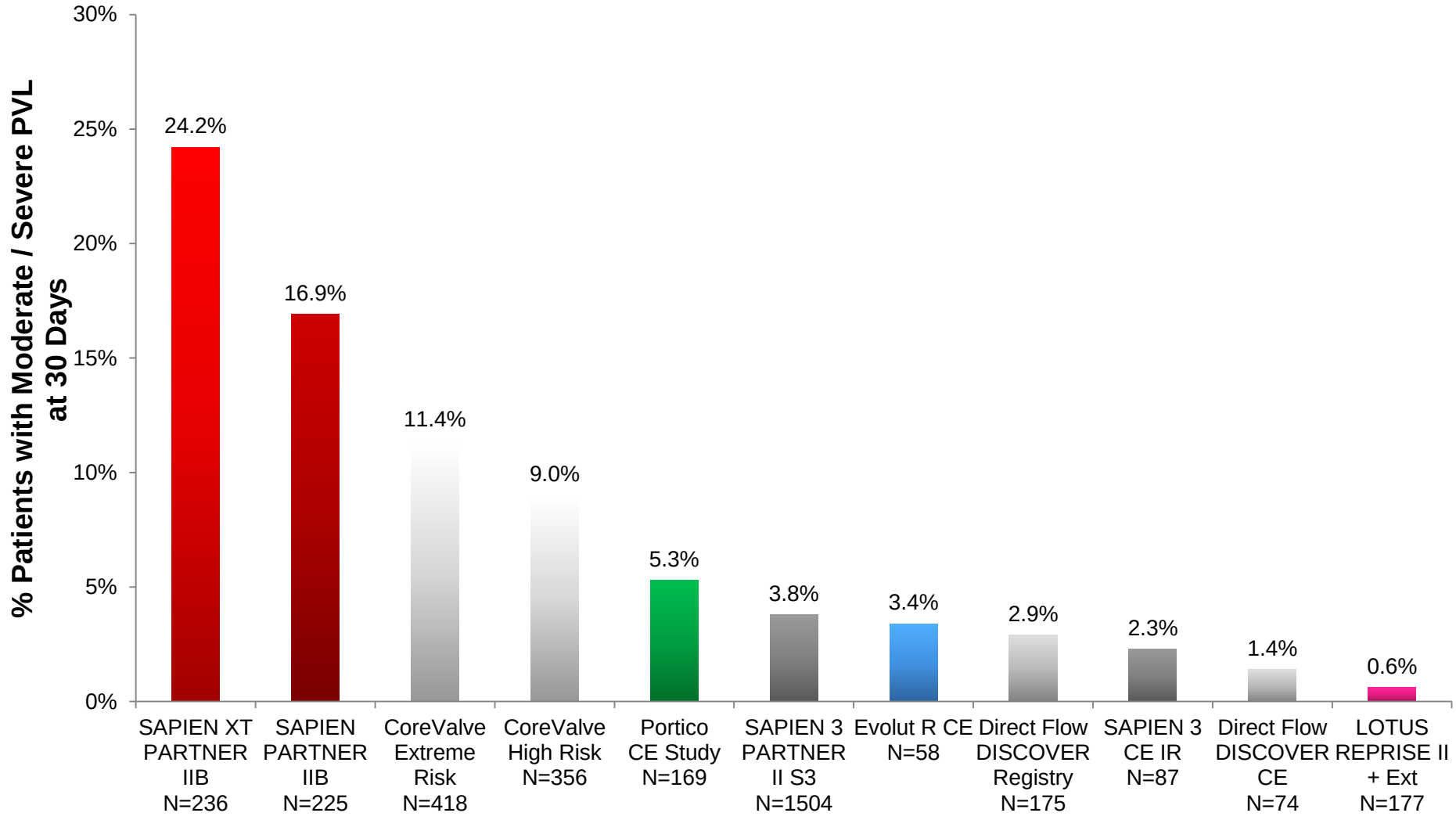
N Engl J Med 2016;375:335-44.

TAVR: AR Prediction



J Am Coll Cardiol 2016;68:577–85

30-Day Moderate and Severe PVL
Current Trends



[1]Leon, et. al. presented at ACC 2013; [2]Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; [3]Adams, et al., *N Engl J Med* 2014; 370: 1790-8; [4]Linke, et. al. presented at PCR London Valves 2015; [5]Kodali, et al., presented at ACC 2015; [6]Meredith, et al., presented at ACC 2015; [7]Naber, et al., presented at EuroPCR 2015; [8]Vahanian, et al., presented at EuroPCR 2015; [9]Schofer, et al., *J Am Coll Cardiol* 2014; 63: 763-8; [10]Meredith, et al., presented at PCR London Valves 2014

Other Adjunctive Strategy Beyond Valve Technology

- TAVR risk score, frailty assessment, and futility modeling are actively developing.
- Adjunctive imaging is actively involving and advancing.
- Antithrombotic therapy after TAVR is the big issue and large trial for optimal antithrombotic strategy (i.e. ATLANTIS, GALILEO) is ongoing.
- Other considerations; cost-effectiveness and QOL.

Summary
Future Perspectives in TAVR

- **Indication;** more widely applied in lower-risk and younger patients.
- **Technology;** more durable and less complicated devices is rapidly evolving.
- **Adjunctive;** adjunctive device, POC test, and risk score can reduce/monitor complication risks and would be helpful to classify “high-risk” patients.
- **Finally;** innovation in device technology and optimization of procedure/patient care is worth pursuing to achieve “**From Great to Greater”** performance.