TAVR in Lower Risk Patients

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Eberhard Grube, MD

Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF LivaNova: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Millipede: E, SB, C, AB Kona: AB, E Abbott Vascular: AB InSeal Medical: AB, E, Valtech: E, SB, Claret: SB Keystone: AB Shockwave: E, AB

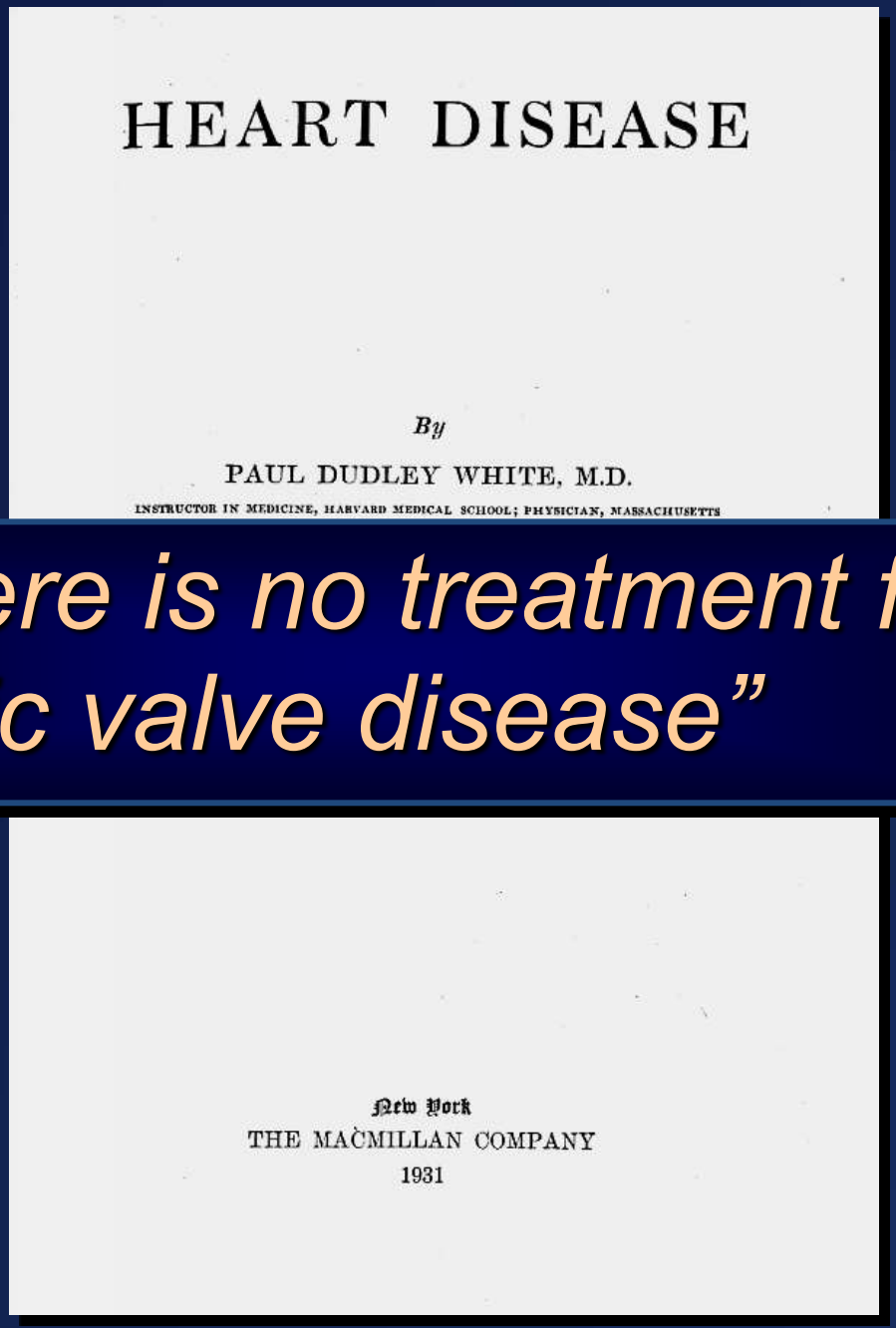
Key

G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits

TAVR Journey - 2016

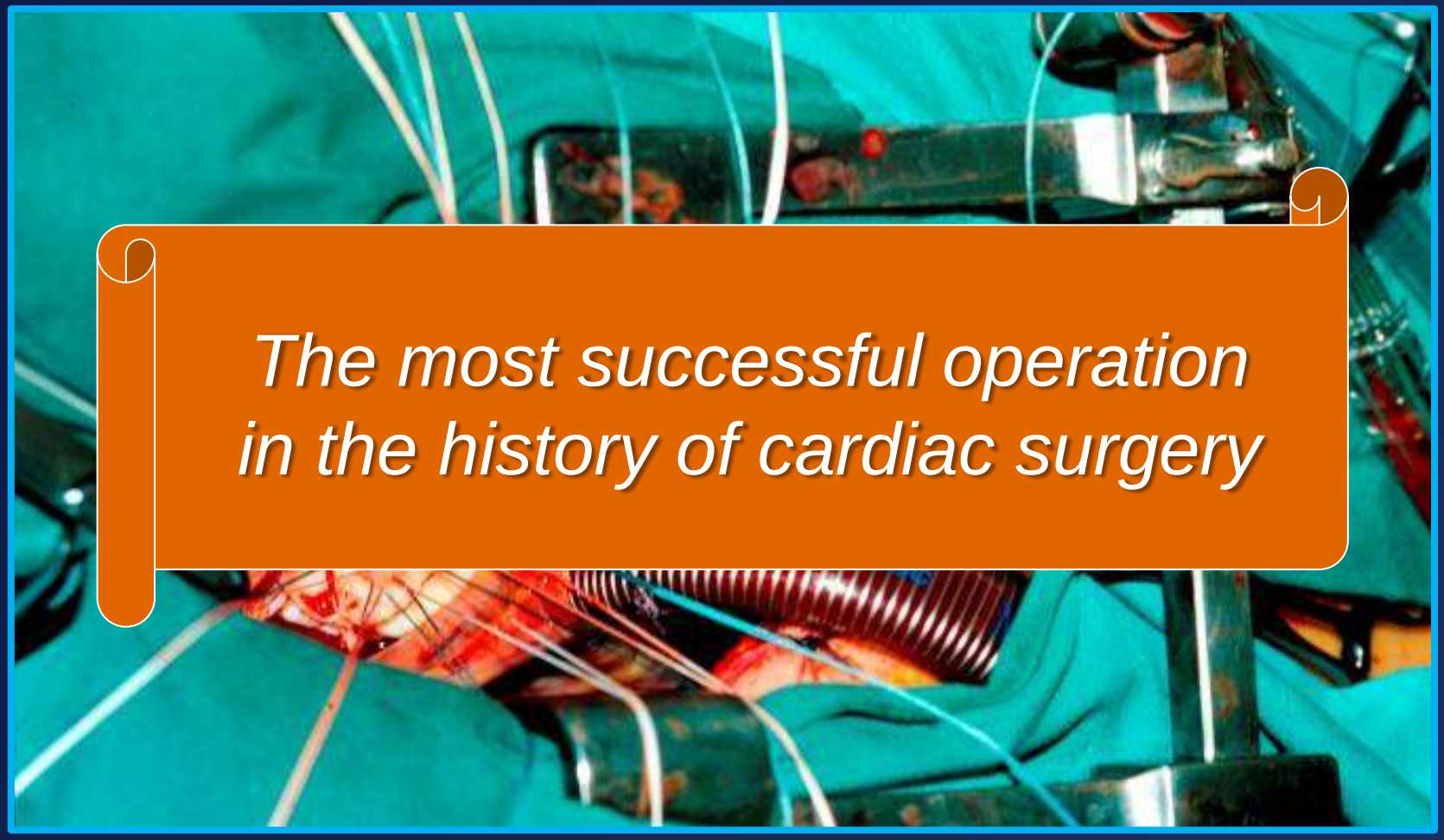
	YES	NO
Survival comparable to or better than SAVR in patients at all levels of surgical risk	X	
Safety and efficacy comparable to or better than SAVR	X	
Safety in common anatomical variations such as bicuspid aortic valve	X	
Ability to perform PCI or valve re-interventions in patients with long life expectancy	X	
Perfect, complication-free performance which is durable for the lifetime of every TAVR patient		XXX

TAVR Journey - 2016



"There is no treatment for aortic valve disease"

Conventional Aortic Valve Surgery



Is there a better way?

92 yo Patient with severe AS…

Which Therapy ?

- Severe COPD
- Creat 2.8
- Prior CABG (patent LIMA)
- EF 30%
- Class IV CHF
- STS 15.5%

…..but still enjoying life.!

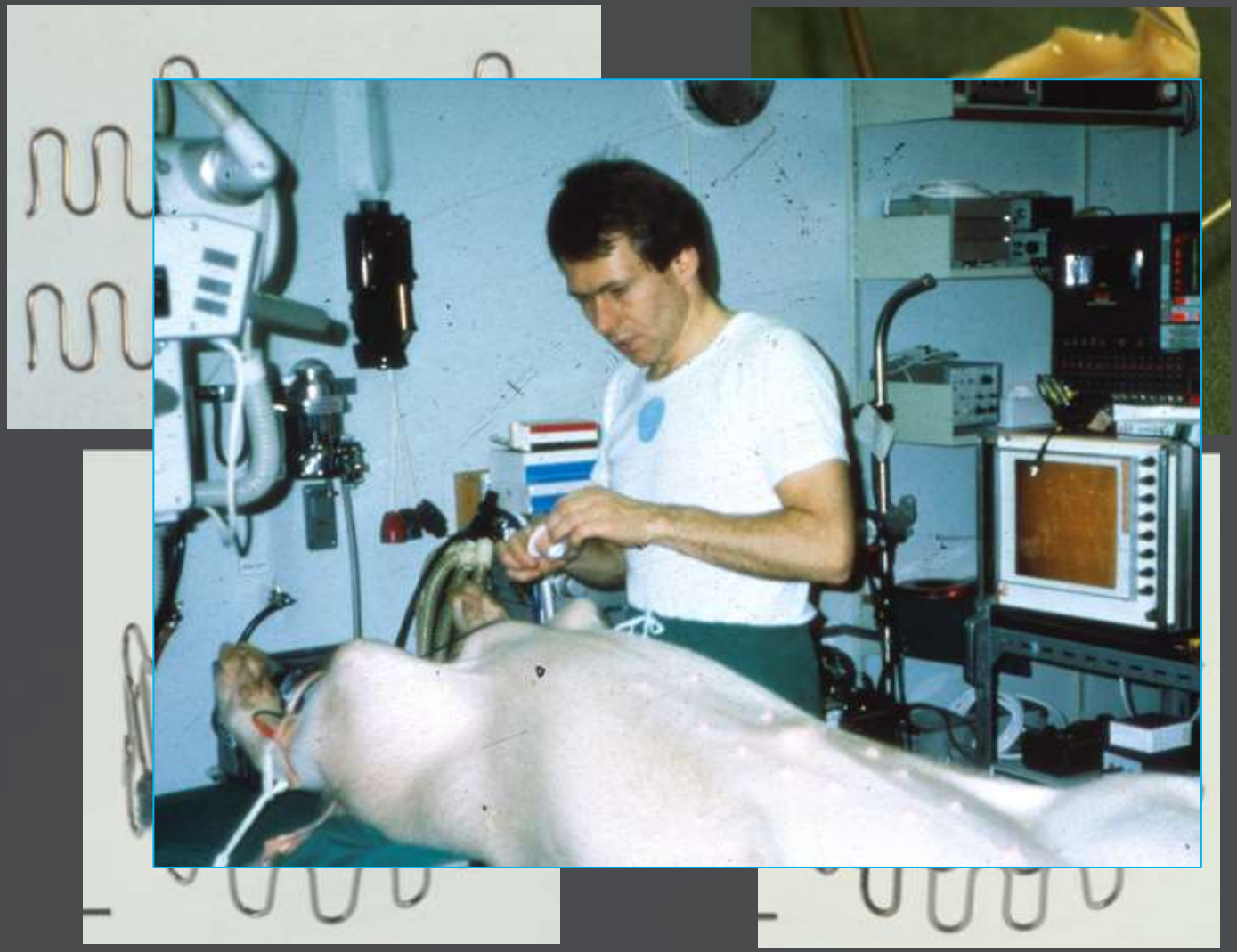
TAVR Journey - 2016

- **The Beginning…**

  With global aging, there is an important unmet clinical need in the treatment of aortic stenosis

  - open surgery is problematic in frail elderly patients with multiple co-morbidities

The Andersen Stent-Valve (1989)



First Sapien and Core Valve Implants

April 16, 2002

July 12, 2004

TAVR - The Early Skeptics

- Strokes
- Aortic rupture
- Coronary occlusion
- Mitral valve injury
- Valve instability – embolization
- Para-valvular regurgitation
- Vascular complications
- Valve durability
- Technical challenges insurmountable

This is a crazy project that will fail!

TAVR Journey - 2016

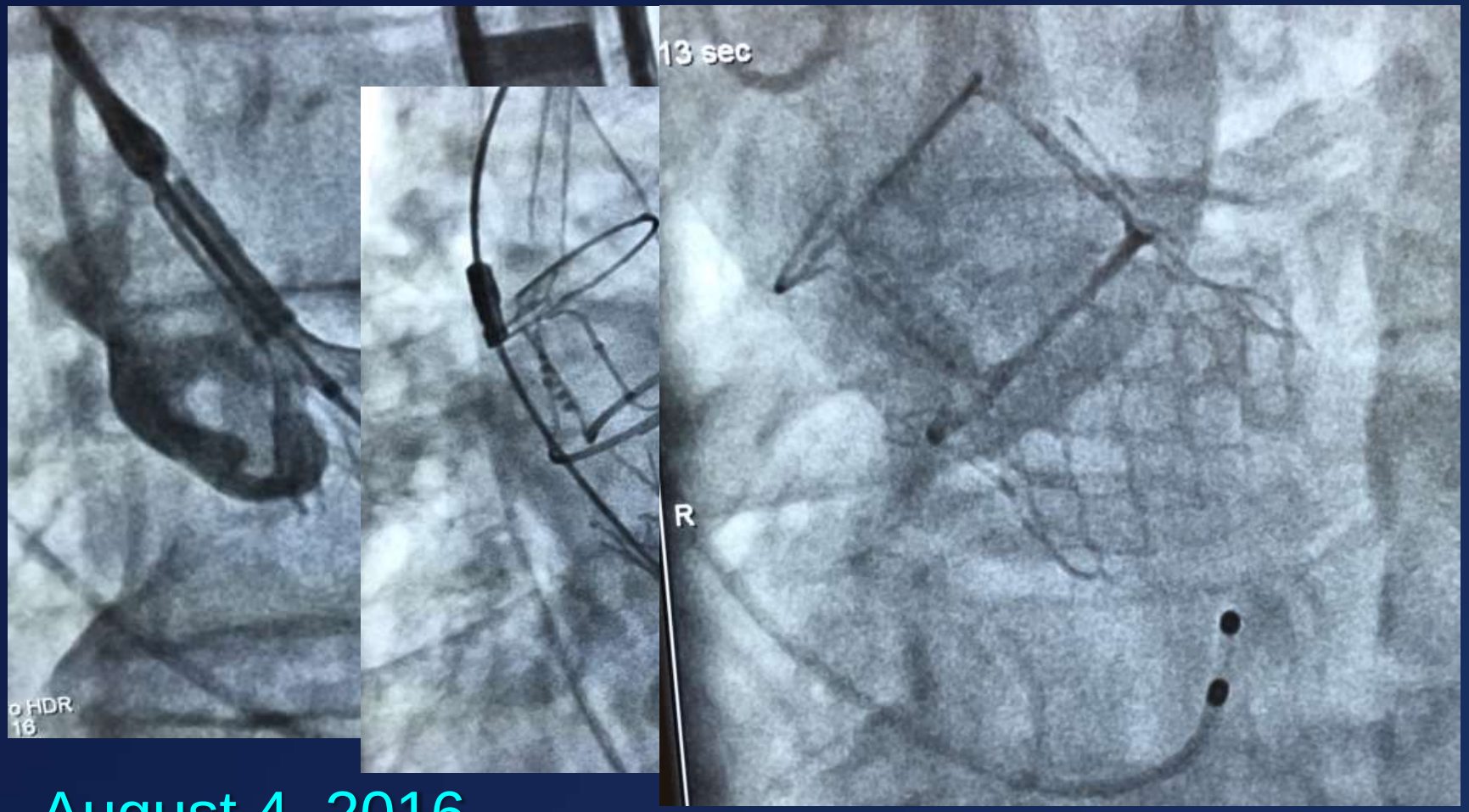
- **The Beginning…**

  With global aging, there is an important unmet clinical need in the treatment of aortic stenosis

  - open surgery is problematic in frail elderly patients with multiple co-morbidities

  The early days of TAVR were tumultuous – crude devices, inexperienced operators, and unstable procedures = frequent complications

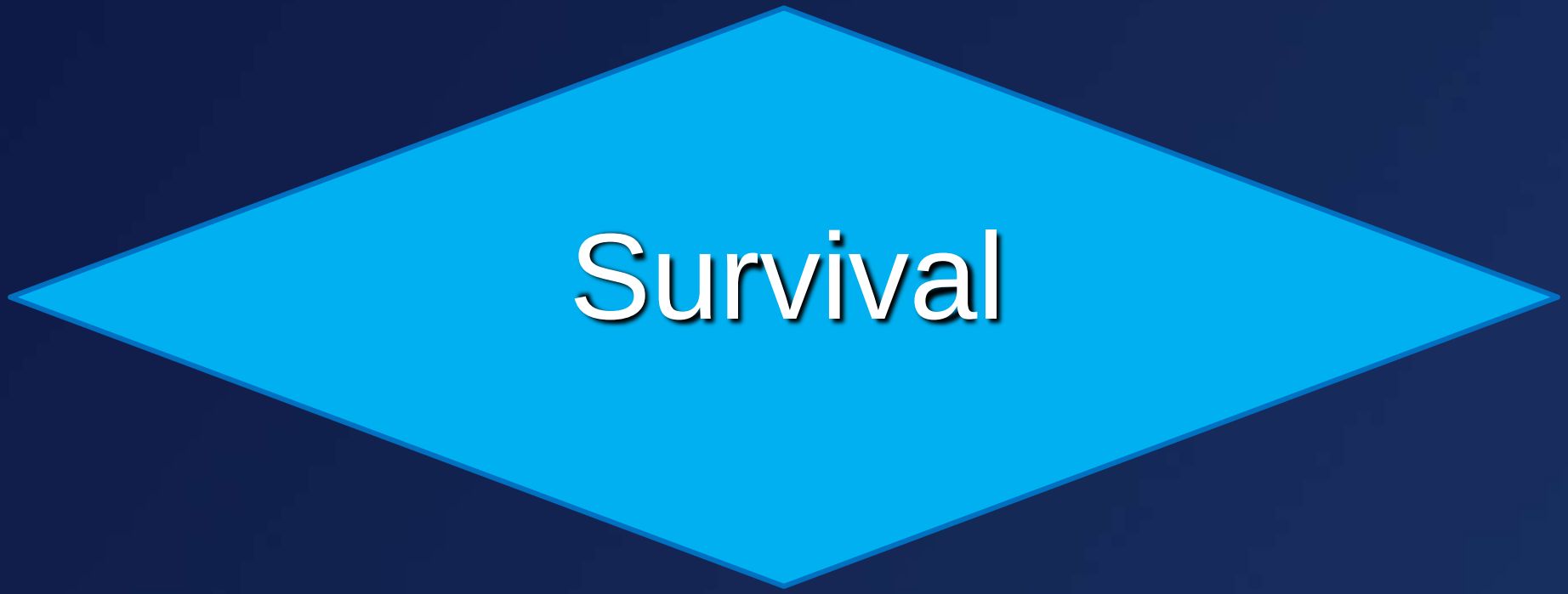
First Successful 12 French Valve Medical TAVR Modular Implant



August 4, 2016

MB Leon, A Abizaid, E Grube

TAVR Journey - 2016



TAVR vs. SAVR

High Risk Patients

We have data from 2 randomized trials comparing TAVR with SAVR in patients at high surgical risk

PARTNER A

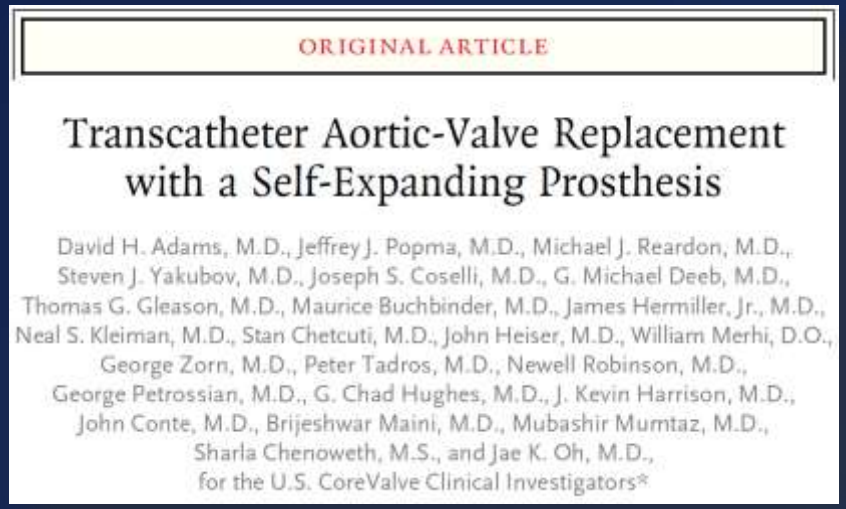
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2011 VOL. 364 NO. 23

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

CoreValve US Pivotal Trial



ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

David H. Adams, M.D., Jeffrey J. Popma, M.D., Michael J. Reardon, M.D., Steven J. Yakubov, M.D., Joseph S. Coselli, M.D., G. Michael Deeb, M.D., Thomas G. Gleason, M.D., Maurice Buchbinder, M.D., James Hermiller, Jr., M.D., Neal S. Kleiman, M.D., Stan Chetcuti, M.D., John Heiser, M.D., William Merhi, D.O., George Zorn, M.D., Peter Tadros, M.D., Newell Robinson, M.D., George Petrossian, M.D., G. Chad Hughes, M.D., J. Kevin Harrison, M.D., John Conte, M.D., Brijeshwar Maini, M.D., Mubashir Mumtaz, M.D., Sharla Chenoweth, M.S., and Jae K. Oh, M.D., for the U.S. CoreValve Clinical Investigators*

SAPIEN, N=348, STS 11.8% vs. SAVR, N=351, STS 11.7%

CoreValve, N=390, STS 7.3% vs. SAVR, N=357, STS 7.5%

TAVR vs. SAVR

PARTNER A

- *The final analysis of PARTNER A showed that ~35% of patients survived to 5 years, regardless of treatment*
- *This study was the first to confirm that TAVR is a reasonable alternative to surgery in high risk patients*

[1]Mack, et al., presented at ACC 2015

TAVR vs. SAVR

CoreValve US Pivotal Trial

Survival in TAVR patients in the CoreValve Pivotal Trial was superior to surgery to 2 years (p=0.04), with continued separation of the curves to 3 years

[1]Deeb, et al., presented at ACC 2016

TAVR vs. SAVR

Lower-than-High Risk Patients

We now also have data from 2 randomized trials comparing TAVR with SAVR in patients at lower surgical risk

PARTNER 2A

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

SAPIEN XT, N=1,011, STS 5.8%
vs. SAVR, N=1,021, STS 5.8%

NOTION

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis

1-Year Results From the All-Comers NOTION Randomized Clinical Trial

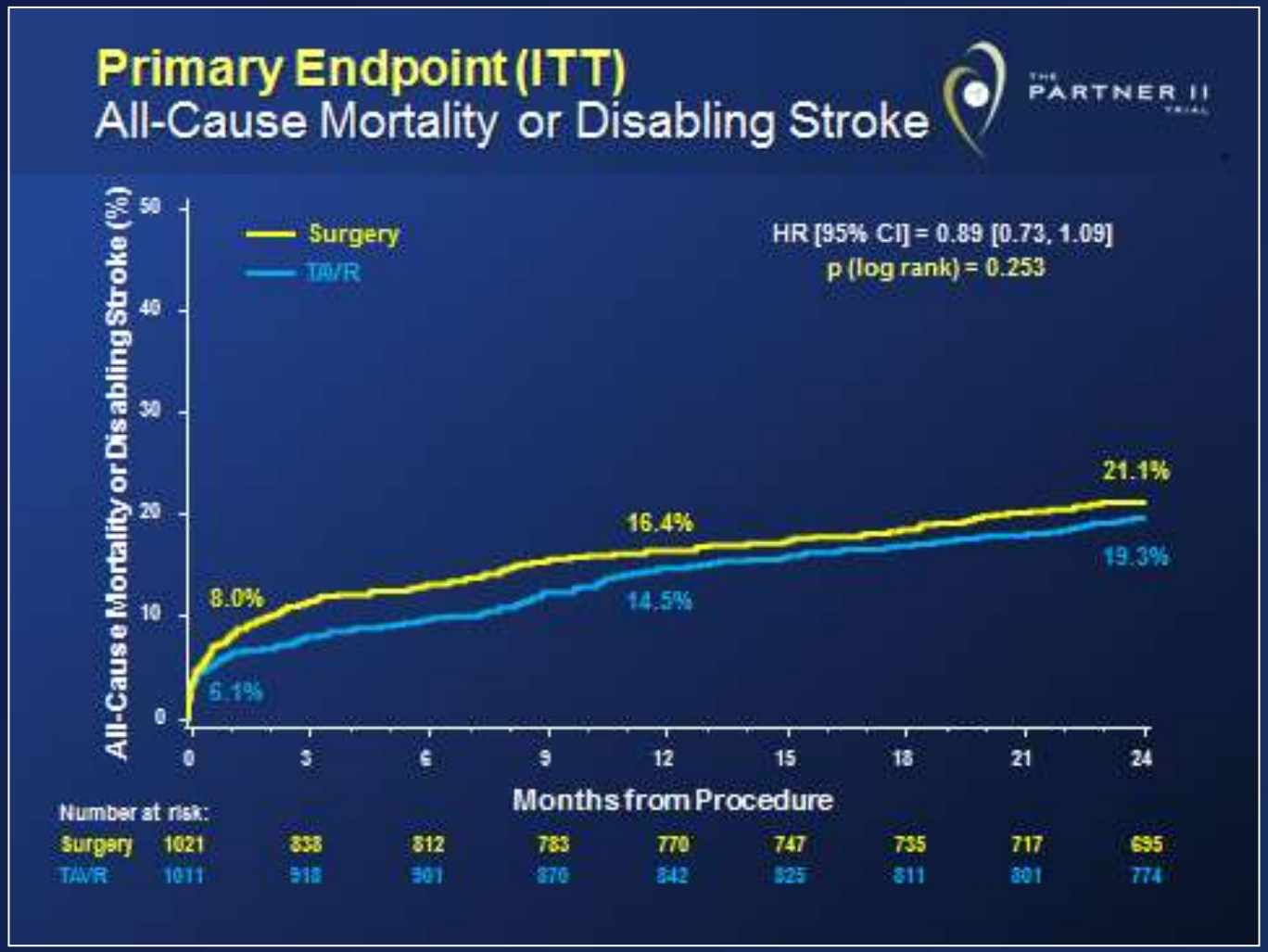
Hans Gustav Hørsted Thyregod, MD,* Daniel Andreas Steinbrüchel, MD, DMSc,* Nikolaj Ihlemann, MD, PhD,† Henrik Nissen, MD, PhD,‡ Bo Juel Kjeldsen, MD, PhD,§ Petur Petursson, MD,‖ Yanping Chang, MS,¶ Olaf Walter Franzen, MD,† Thomas Engstrøm, MD, DMSc,† Peter Clemmensen, MD, DMSc,† Peter Bo Hansen, MD,# Lars Willy Andersen, MD, DMSc,# Peter Skov Olsen, MD, DMSc,* Lars Søndergaard, MD, DMSc†

CoreValve, N=145, STS 2.9%
vs. SAVR, N=135, STS 3.1%

TAVR vs. SAVR

PARTNER 2A

In PARTNER 2A, TAVR using SAPIEN XT was non-inferior to surgery for the primary endpoint (all-cause mortality or disabling stroke) at 2 years

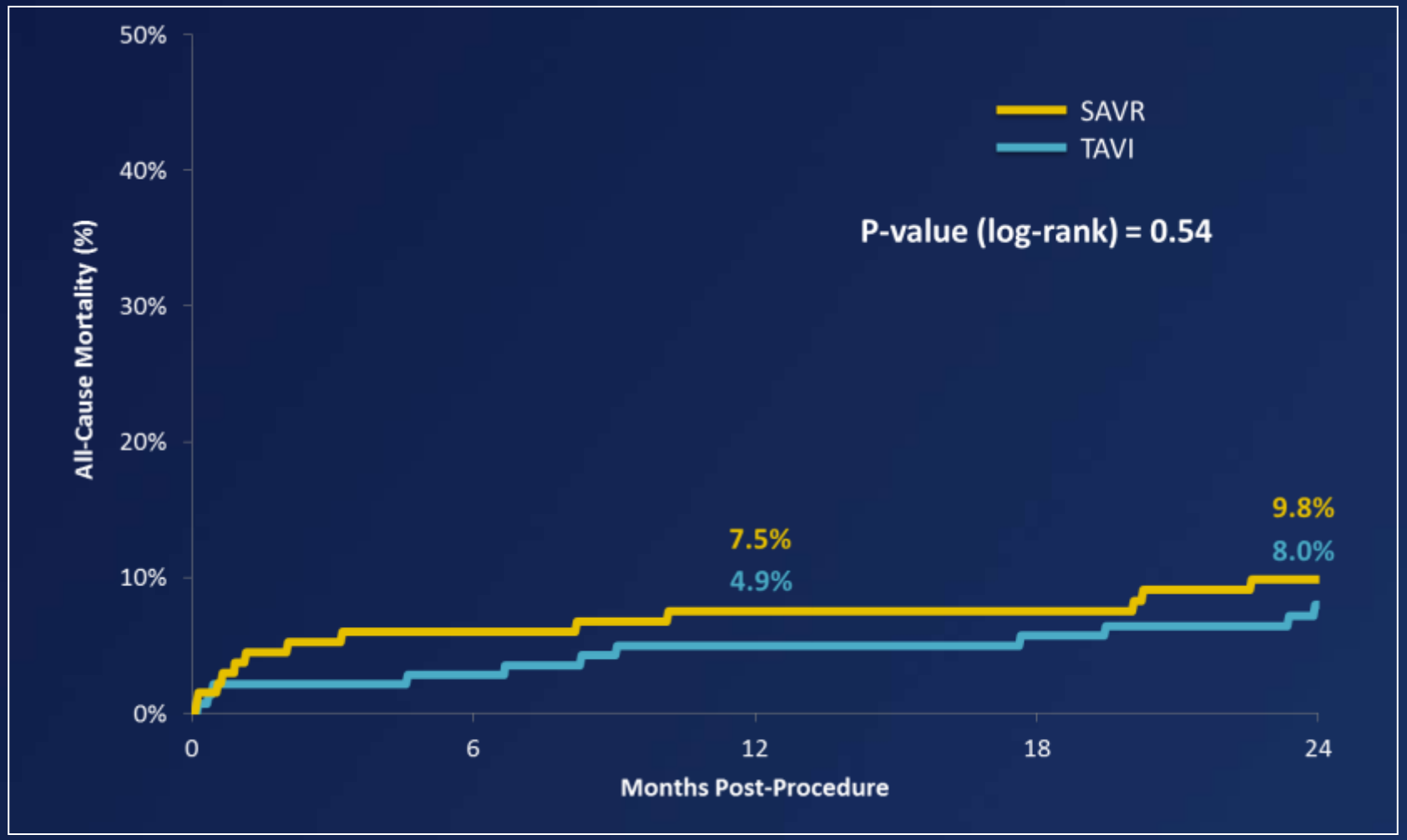


[1]Smith, et al., presented at ACC 2016

TAVR vs. SAVR

The NOTION Trial

The NOTION trial showed all-cause mortality with TAVR to be non-inferior to SAVR



[1]Sondergaard, presented at EuroPCR 2015

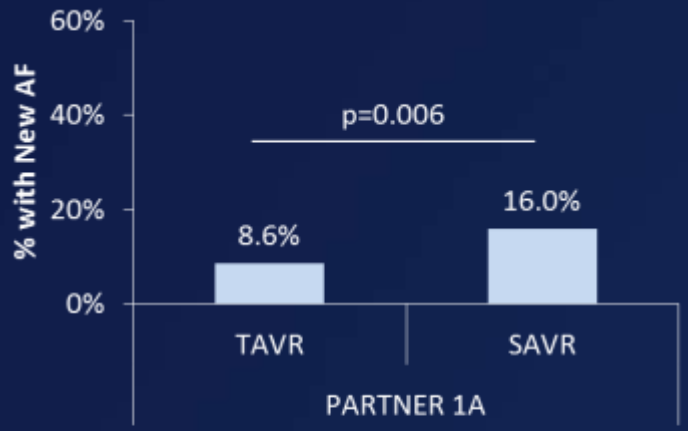
TAVR Journey - 2016

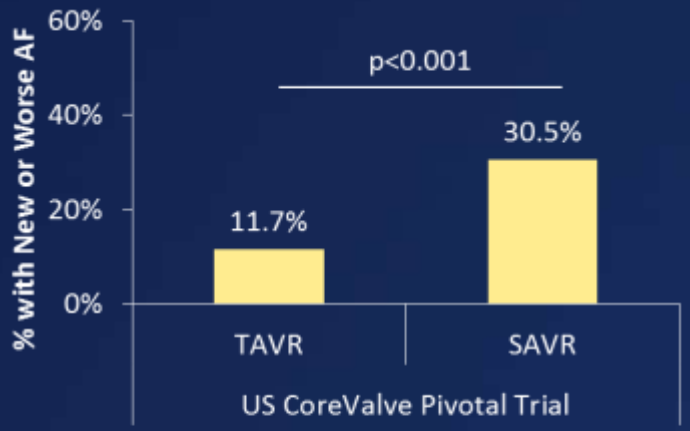
Safety
TAVR vs SAVR

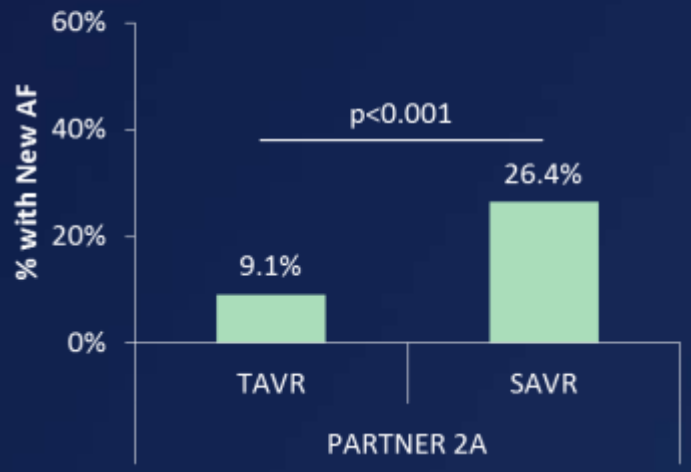
Atrial Fibrillation

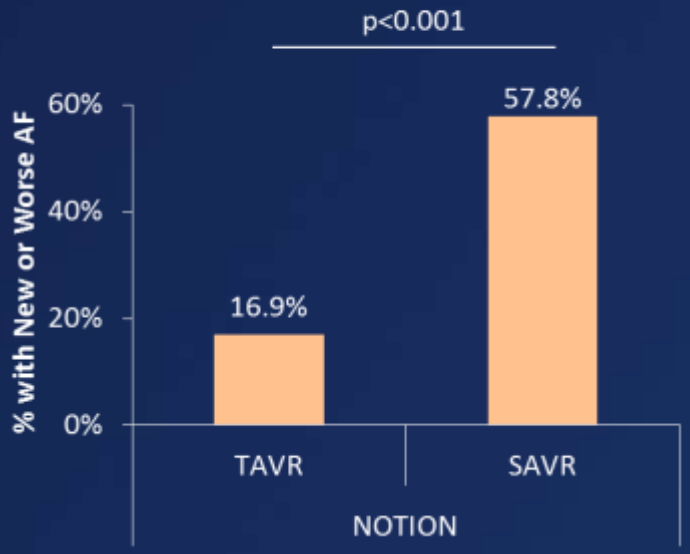
Rates in TAVR vs. SAVR

- *Differing definitions of New Onset Atrial Fibrillation and methods of detection (continuous vs. discrete monitoring) preclude comparison of rates across studies*
- *Within each randomized trial, the rate of NOAF was at least 2x higher with SAVR*







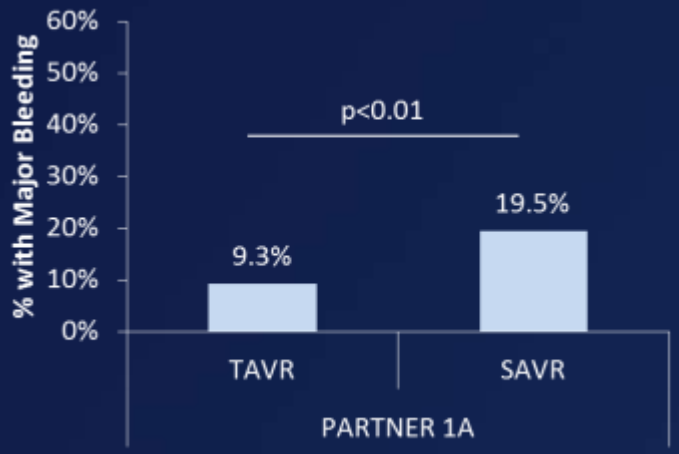


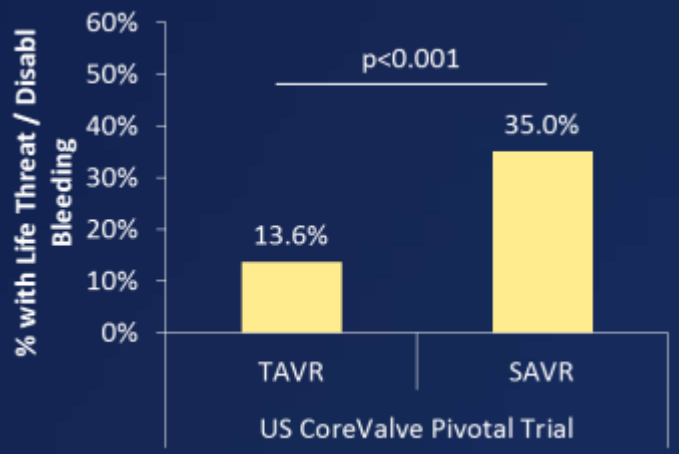
[1]Smith, et al., presented at ACC 2011; [2] Adams, et al., presented at ACC 2014; [3]Thyregod, et al., presented at ACC 2015; [4]Smith, et al., presented at ACC 2016

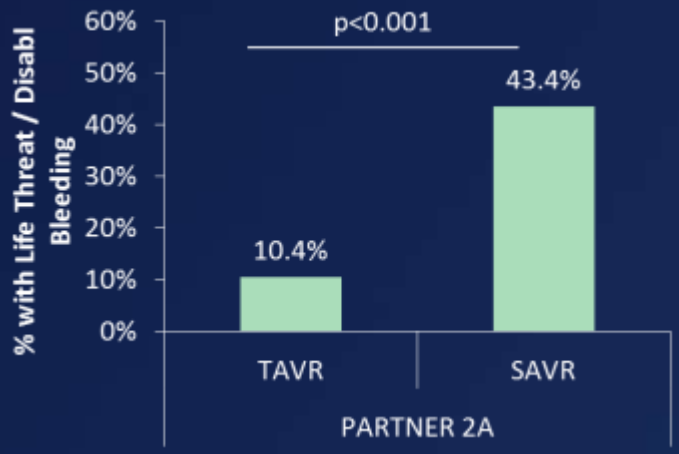
Bleeding

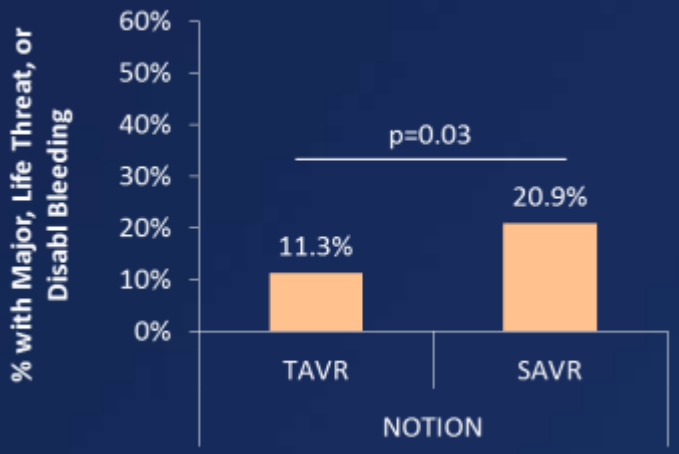
Rates in TAVR vs. SAVR

- *Differing definitions of bleeding (major vs. life threatening or disabling) preclude comparison of rates across studies*
- *Bleeding was significantly more frequent in SAVR patients within the randomized trials*







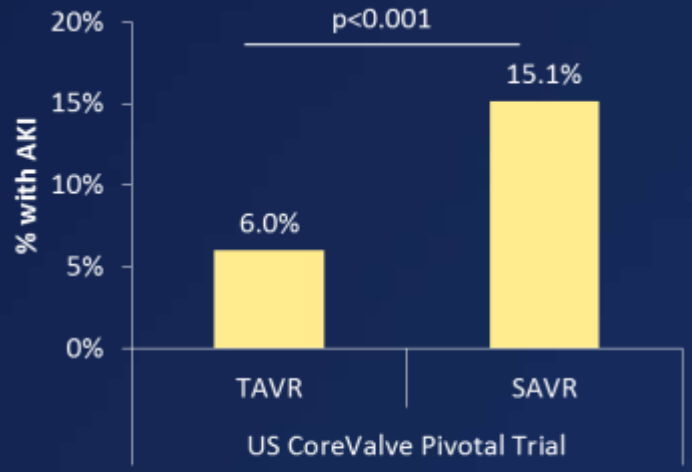


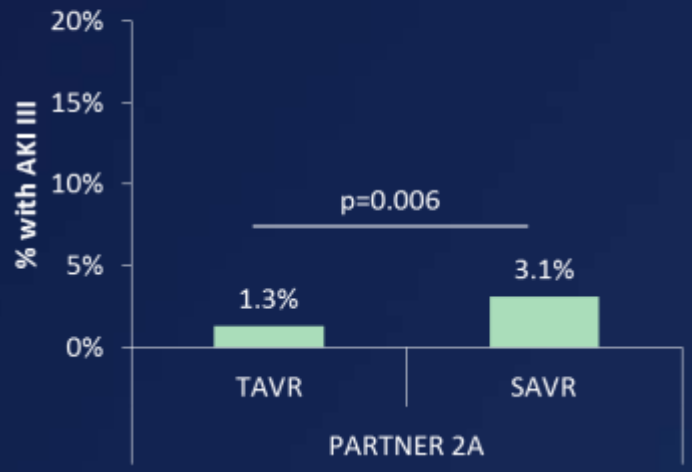
[1]Smith, et al., presented at ACC 2011; [2] Adams, et al., presented at ACC 2014; [3]Thyregod, et al., presented at ACC 2015; [4]Smith, et al., presented at ACC 2016

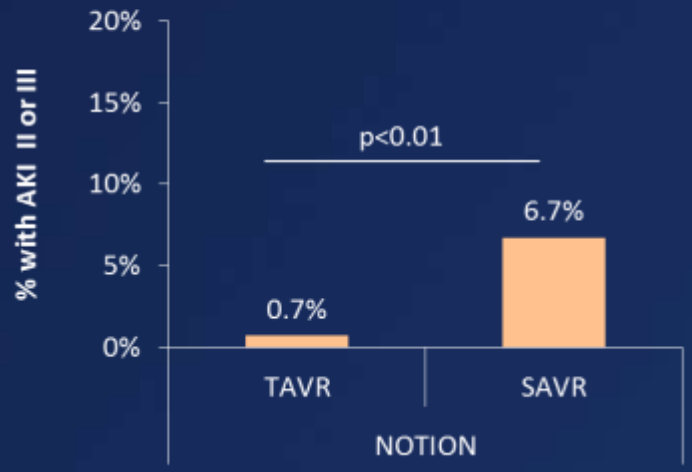
Acute Kidney Injury

Rates in TAVR vs. SAVR

- *Differing definitions of Acute Kidney Injury (total AKI vs. certain stages only) preclude comparison of rates across studies*
- *AKI was significantly more frequent in SAVR patients within the randomized trials*





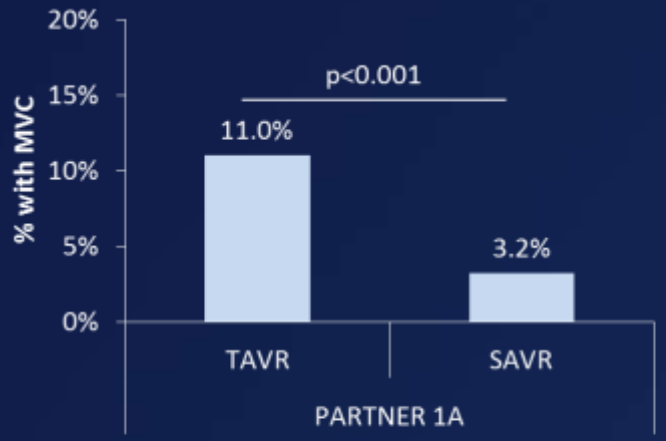


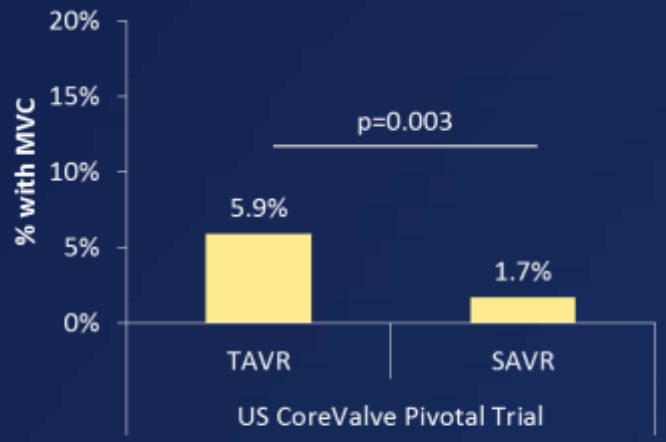
[1]Smith, et al., presented at ACC 2011; [2] Adams, et al., presented at ACC 2014; [3]Thyregod, et al., presented at ACC 2015; [4]Smith, et al., presented at ACC 2016

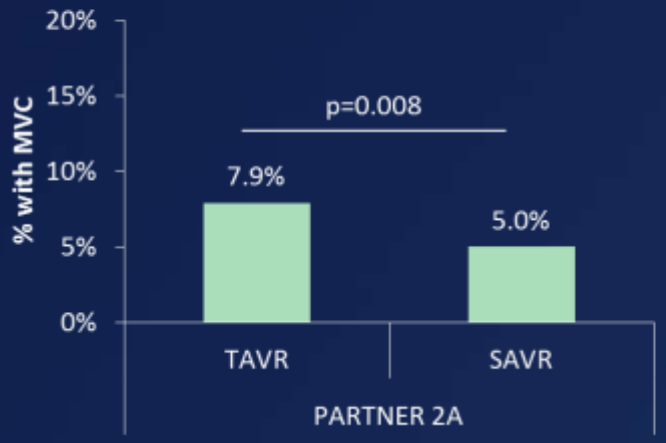
Major Vascular Complications

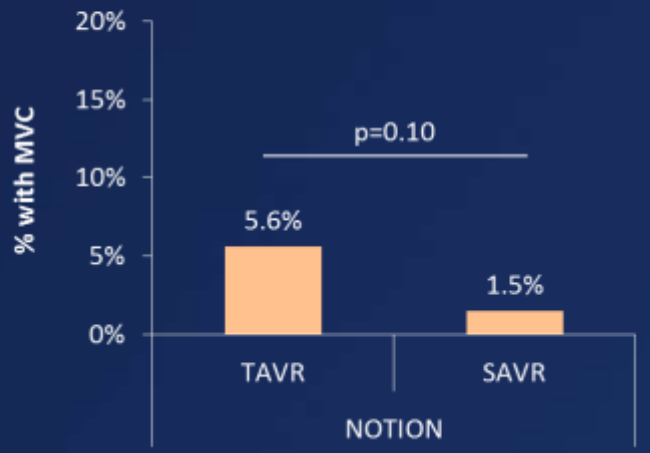
Rates in TAVR vs. SAVR

- *Differing definitions of Major Vascular Complications (modified VARC vs. VARC) preclude comparison of rates across studies*
- *MVCs were significantly more frequent in TAVR patients within the randomized trials*







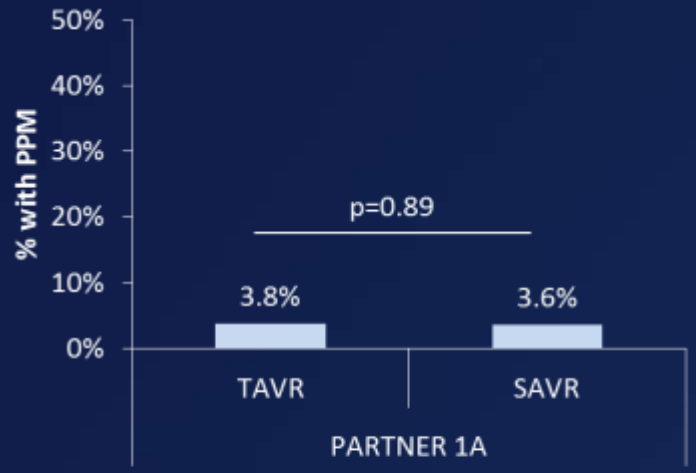


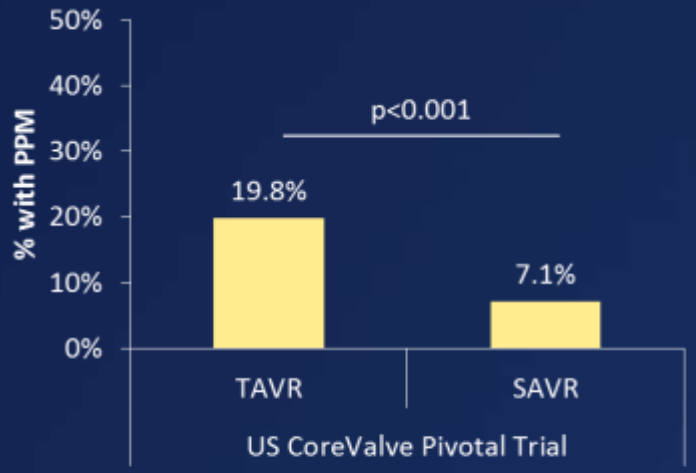
[1]Smith, et al., presented at ACC 2011; [2] Adams, et al., presented at ACC 2014; [3]Thyregod, et al., presented at ACC 2015; [4]Smith, et al., presented at ACC 2016

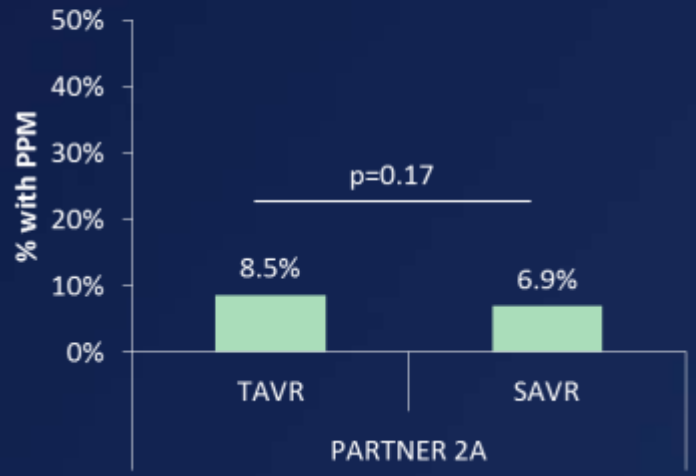
Permanent Pacemakers

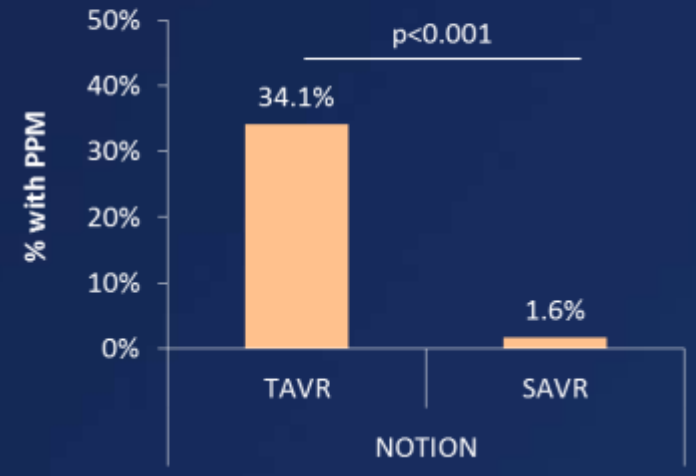
Rates in TAVR vs. SAVR

- *New permanent pacemakers were common after TAVR with the self-expanding valve, however pacemaker rates were similar between SAVR and TAVR with balloon-expandable valves*







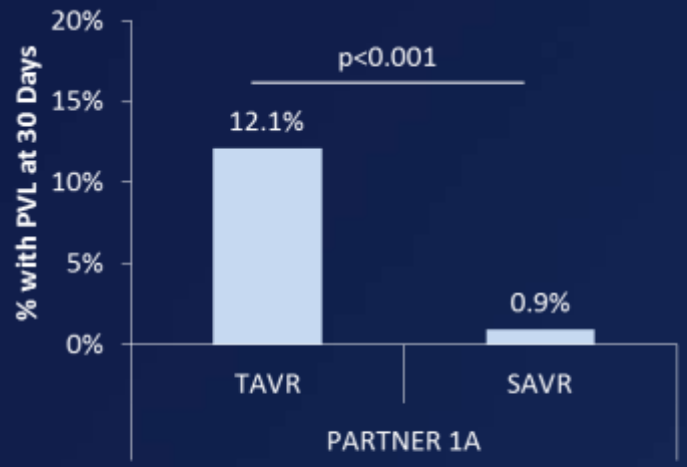


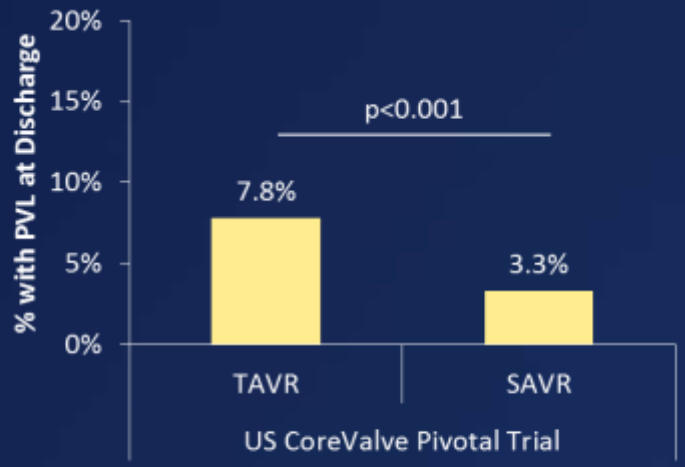
[1]Smith, et al., presented at ACC 2011; [2] Adams, et al., presented at ACC 2014; [3]Thyregod, et al., presented at ACC 2015; [4]Smith, et al., presented at ACC 2016

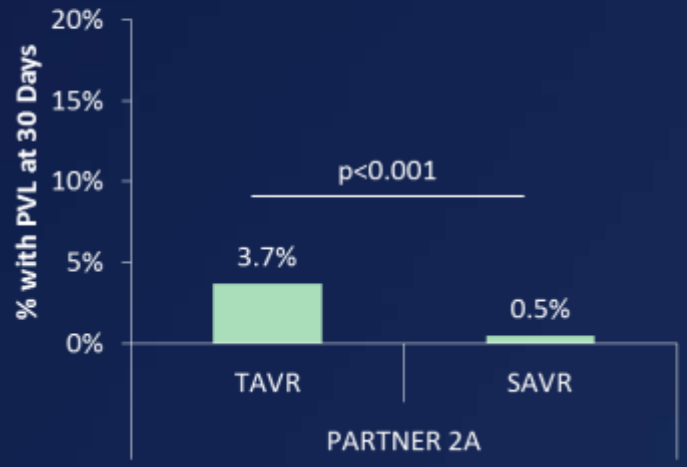
Paravalvular Leak

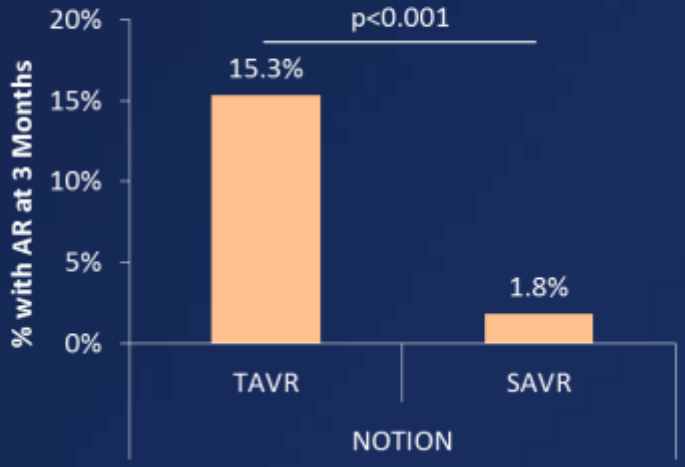
Moderate / Severe Rates in TAVR vs. SAVR

- *Differing definitions of Paravalvular Leak preclude comparison of rates across studies*
- *PVL was significantly more common in TAVR patients across trials*









[1]Smith, et al., presented at ACC 2011; [2] Adams, et al., presented at ACC 2014; [3]Thyregod, et al., presented at ACC 2015; [4]Smith, et al., presented at ACC 2016

Safety Outcomes

Key Points

- Atrial fibrillation, bleeding, and acute kidney injury were all significantly more common with SAVR than TAVR across randomized studies.
- This finding was regardless of TAVR valve type, patient risk profile, or specific outcome definition used.
- Each of these outcomes increased the risk of 1-year mortality by approximately 2 times.
- Major vascular complications, new permanent pacemakers, and paravalvular leak were sometimes more common with TAVR than with SAVR.
- Only PVL strongly impacted mortality, increasing the risk of death at 1 year by 2 times. Major vascular complications were important if they were severe, and permanent pacemakers did not appear to have a meaningful clinical impact.

- *Taken together, the data suggest that common SAVR complications present a higher risk to patients than common TAVR complications.*

TAVR Journey - 2016

The Low-Risk Journey

TAVR Journey - 2016

- **The Low-Risk Journey**

  The relentless evolution of TAVR clinical growth has been driven by:

  - the multi-disciplinary heart team
  - commitment to evidence-based medicine
  - rapid technology enhancement
  - simplification of the procedure
  - striking reduction in complications

The Low-Risk Journey

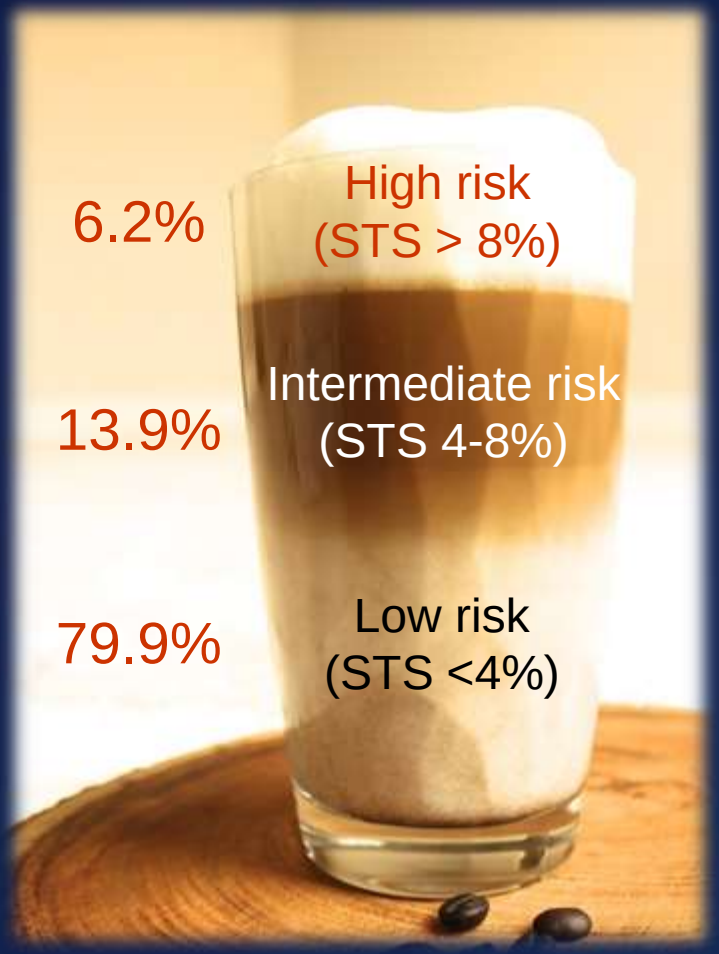
Double-Shot Mocha Latte

The Low-Risk Journey

STS database 2002-2010 (141,905 pts)

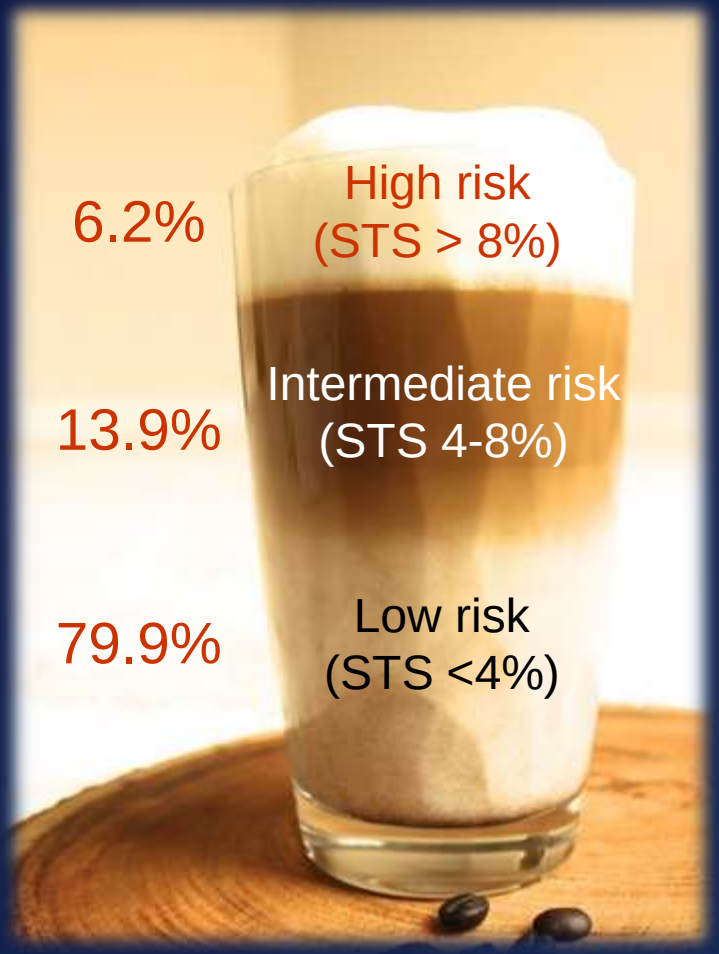
The Low-Risk Journey

STS database 2002-2010 (141,905 pts)



The Low-Risk Journey

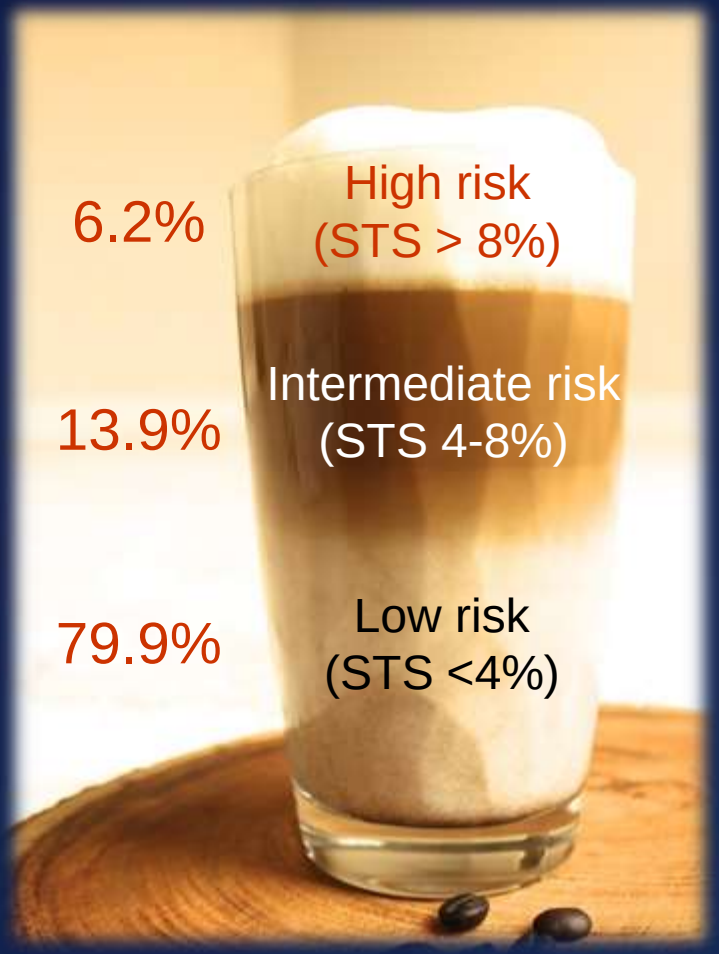
STS database 2002-2010 (141,905 pts)



Since 2007, in the U.S., >15,000 patients have been enrolled in FDA studies (including 6 RCTs) with multiple generations of two TAVR systems!

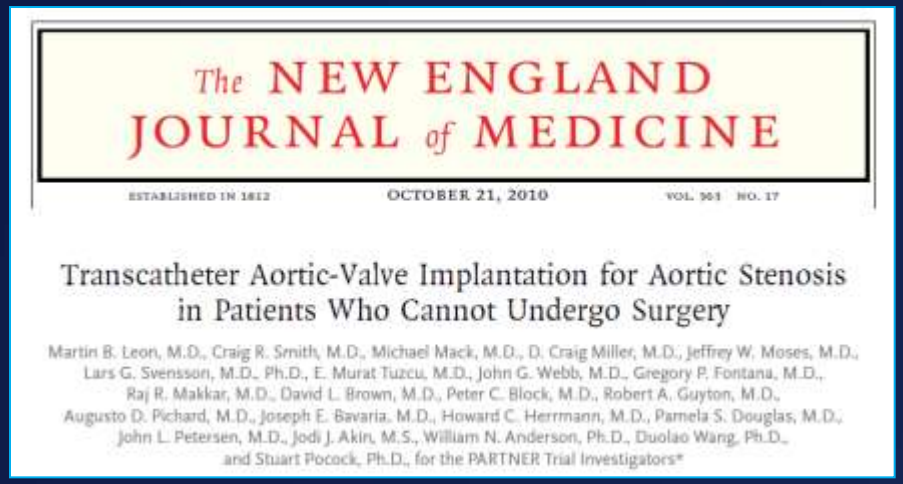
The Low-Risk Journey

STS database 2002-2010 (141,905 pts)



PARTNER 1A, 1B
CoreValve Extreme/High-Risk

PARTNER Manuscripts in NEJM (October, 2010 – May, 2012)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2010 VOL. 363 NO. 17

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2011 VOL. 364 NO. 23

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement for Inoperable Severe Aortic Stenosis

Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Hasan Jilaihawi, M.D., Samir Kapadia, M.D., Augusto D. Pichard, M.D., Pamela S. Douglas, M.D., Vinod H. Thourani, M.D., Vasilis C. Babaliaros, M.D., John G. Webb, M.D., Howard C. Herrmann, M.D., Joseph E. Bavaria, M.D., Susheel Kodali, M.D., David L. Brown, M.D., Bruce Bowers, M.D., Todd M. Dewey, M.D., Lars G. Svensson, M.D., Ph.D., Murat Tuzcu, M.D., Jeffrey W. Moses, M.D., Matthew R. Williams, M.D., Robert J. Siegel, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Stuart Pocock, Ph.D., Craig R. Smith, M.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

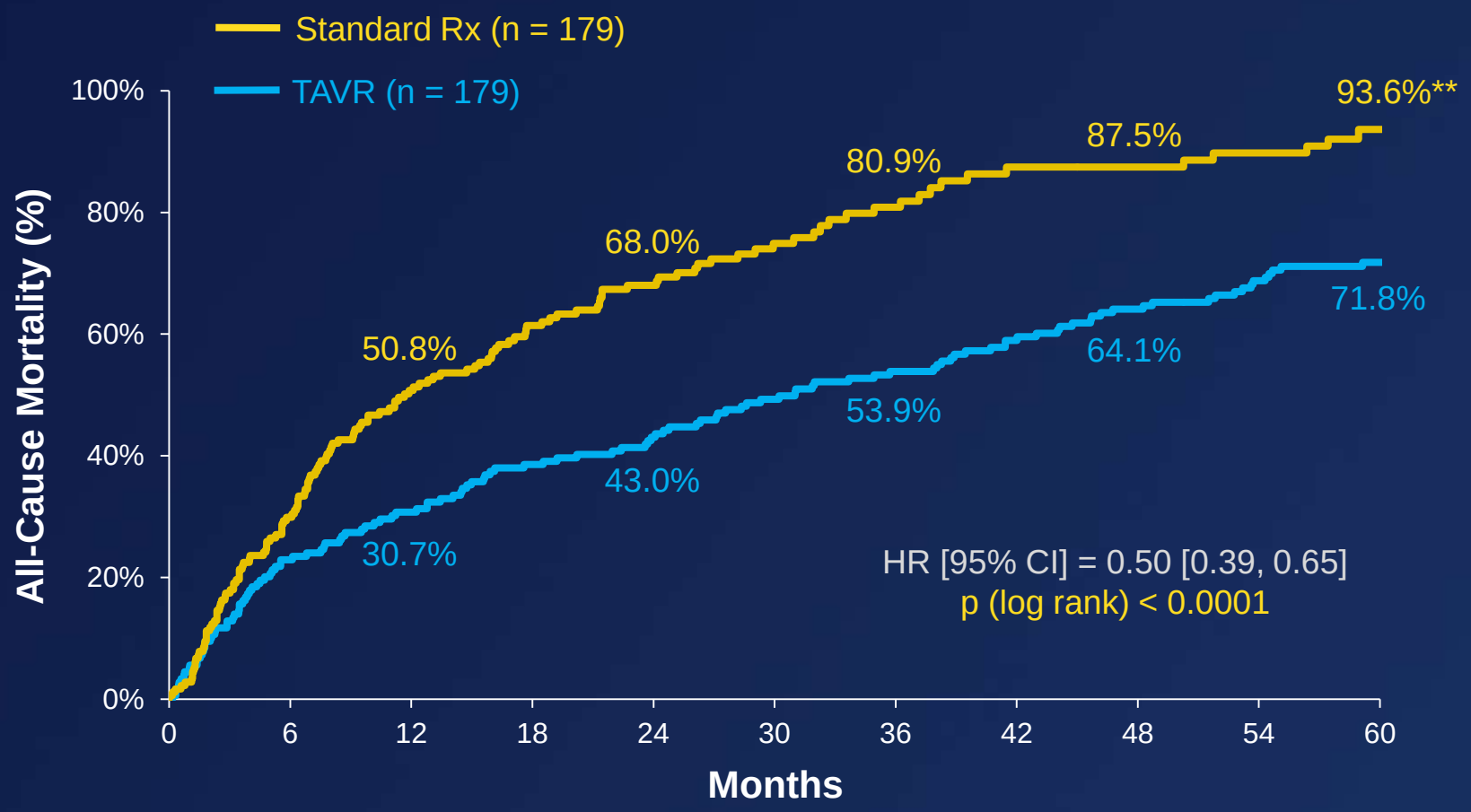
ORIGINAL ARTICLE

Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement

Susheel K. Kodali, M.D., Mathew R. Williams, M.D., Craig R. Smith, M.D., Lars G. Svensson, M.D., Ph.D., John G. Webb, M.D., Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Todd M. Dewey, M.D., Vinod H. Thourani, M.D., Augusto D. Pichard, M.D., Michael Fischbein, M.D., Wilson Y. Szeto, M.D., Scott Lim, M.D., Kevin L. Greason, M.D., Paul S. Teirstein, M.D., S. Chris Malaisrie, M.D., Pamela S. Douglas, M.D., Rebecca T. Hahn, M.D., Brian Whisenant, M.D., Alan Zajarias, M.D., Duolao Wang, Ph.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

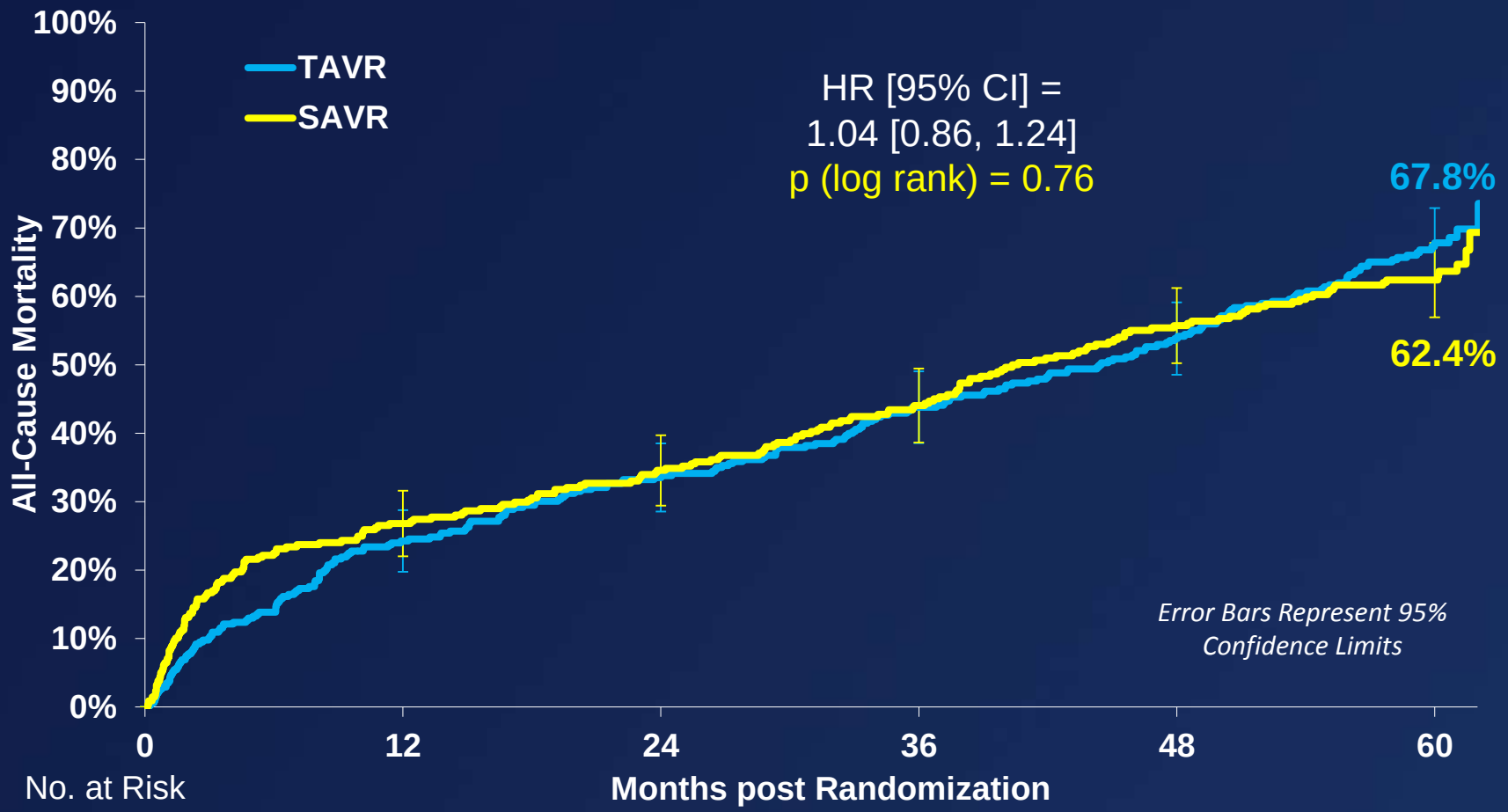
All-Cause Mortality (ITT) Inoperable Pts

All Patients



All-Cause Mortality (ITT) (Extreme Risk)

All Patients



CoreValve High-Risk U.S. Pivotal Trial (1 and 2-Yr Follow-up)

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. ■, NO. ■, 2015

ISSN 0735-1097/$36.00
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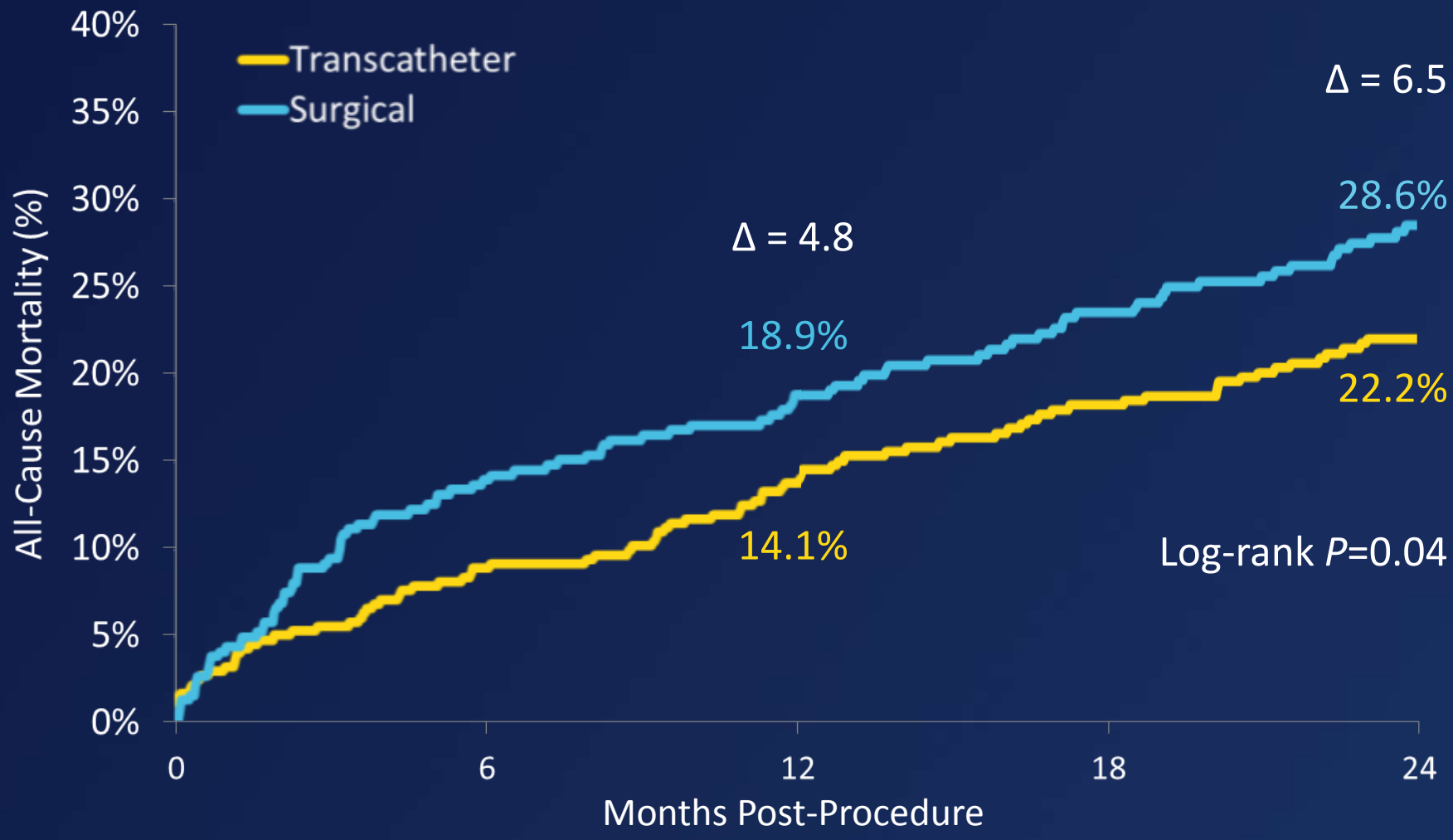
2-Year Outcomes in Patients Undergoing Surgical or Self-Expanding Transcatheter Aortic Valve Replacement

Michael J. Reardon, MD,* David H. Adams, MD,† Neal S. Kleiman, MD,* Steven J. Yakubov, MD,‡
Joseph S. Coselli, MD,§ G. Michael Deeb, MD,‖ Thomas G. Gleason, MD,¶ Joon Sup Lee, MD,¶
James B. Hermiller, Jr, MD,# Stan Chetcuti, MD,‖ John Heiser, MD,** William Merhi, MD,** George L. Zorn III, MD,††
Peter Tadros, MD,†† Newell Robinson, MD,‡‡ George Petrossian, MD,‡‡ G. Chad Hughes, MD,§§
J. Kevin Harrison, MD,§§ Brijeshwar Maini, MD,‖‖ Mubashir Mumtaz, MD,‖‖ John V. Conte, MD,¶¶
Jon R. Resar, MD,¶¶ Vicken Aharonian, MD,## Thomas Pfeffer, MD,## Jae K. Oh, MD,*** Hongyan Qiao, PhD,†††
Jeffrey J. Popma, MD‡‡‡

All-Cause Mortality (Core Valve High Risk)

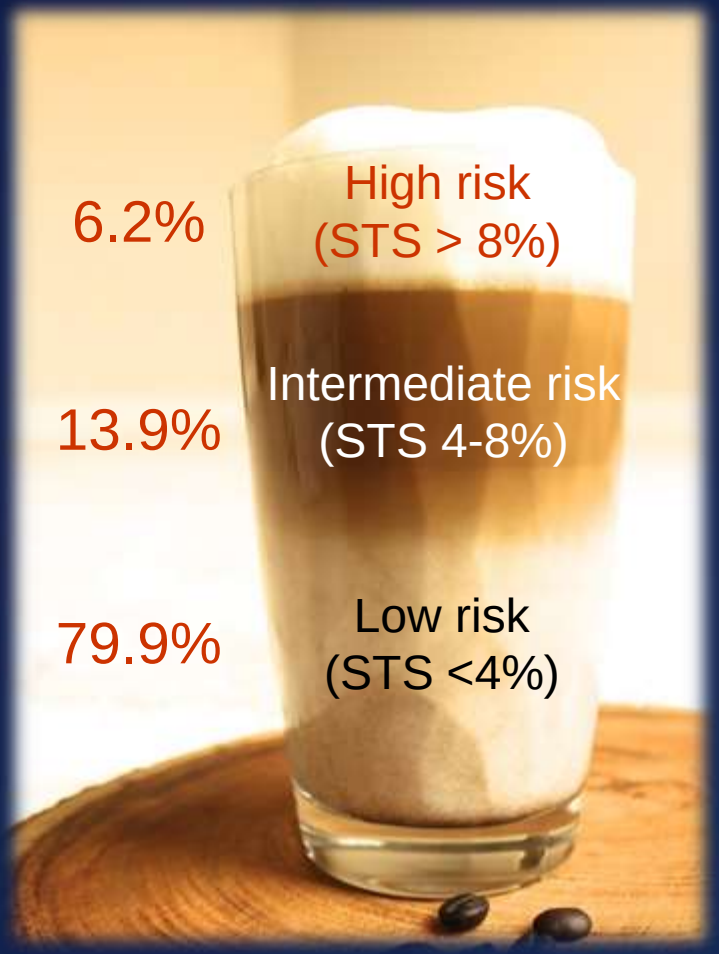


Echocardiographic Findings

TAVR had significantly better valve performance over SAVR at all follow-up visits (*P*<0.001)

The Low-Risk Journey

STS database 2002-2010 (141,905 pts)



PARTNER 2A, S3i
SURTAVI, UK TAVI

The PARTNER 2A and S3i Trial

The NEJM and Lancet On-line

The NEW ENGLAND JOURNAL of MEDICINE

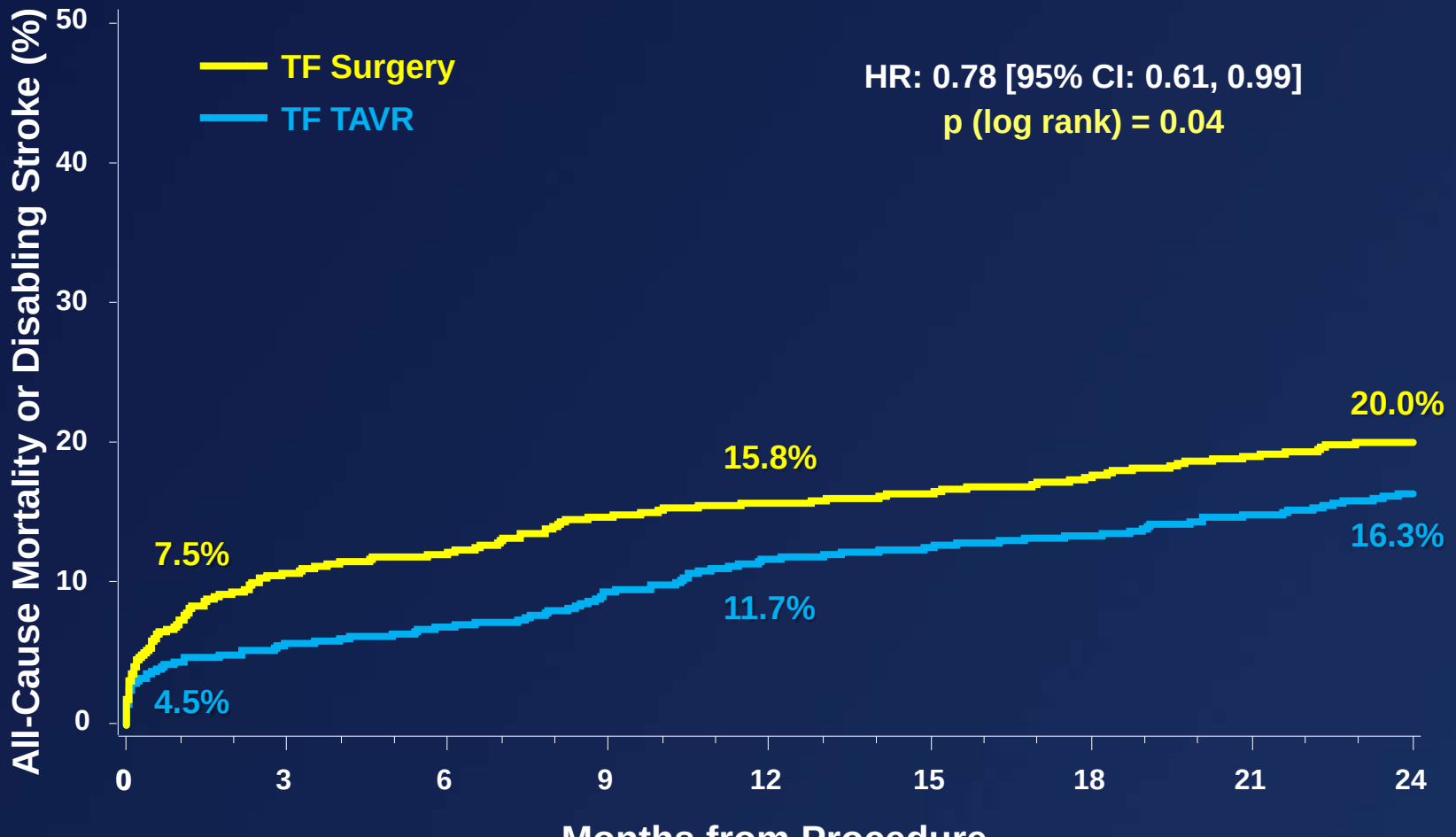
ORIGINAL ARTICLE

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

Vinod H Thourani, Susheel Kodali, Raj R Makkar, Howard C Herrmann, Mathew Williams, Vasilis Babaliaros, Richard Smalling, Scott Lim, S Chris Malaisrie, Samir Kapadia, Wilson Y Szeto, Kevin L Greason, Dean Kereiakes, Gorav Ailawadi, Brian K Whisenant, Chandan Devireddy, Jonathon Leipsic, Rebecca T Hahn, Philippe Pibarot, Neil J Weissman, Wael A Jaber, David J Cohen, Rakesh Suri, E Murat Tuzcu, Lars G Svensson, John G Webb, Jeffrey W Moses, Michael J Mack, D Craig Miller, Craig R Smith, Maria C Alu, Rupa Parvataneni, Ralph B D'Agostino Jr, Martin B Leon

Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

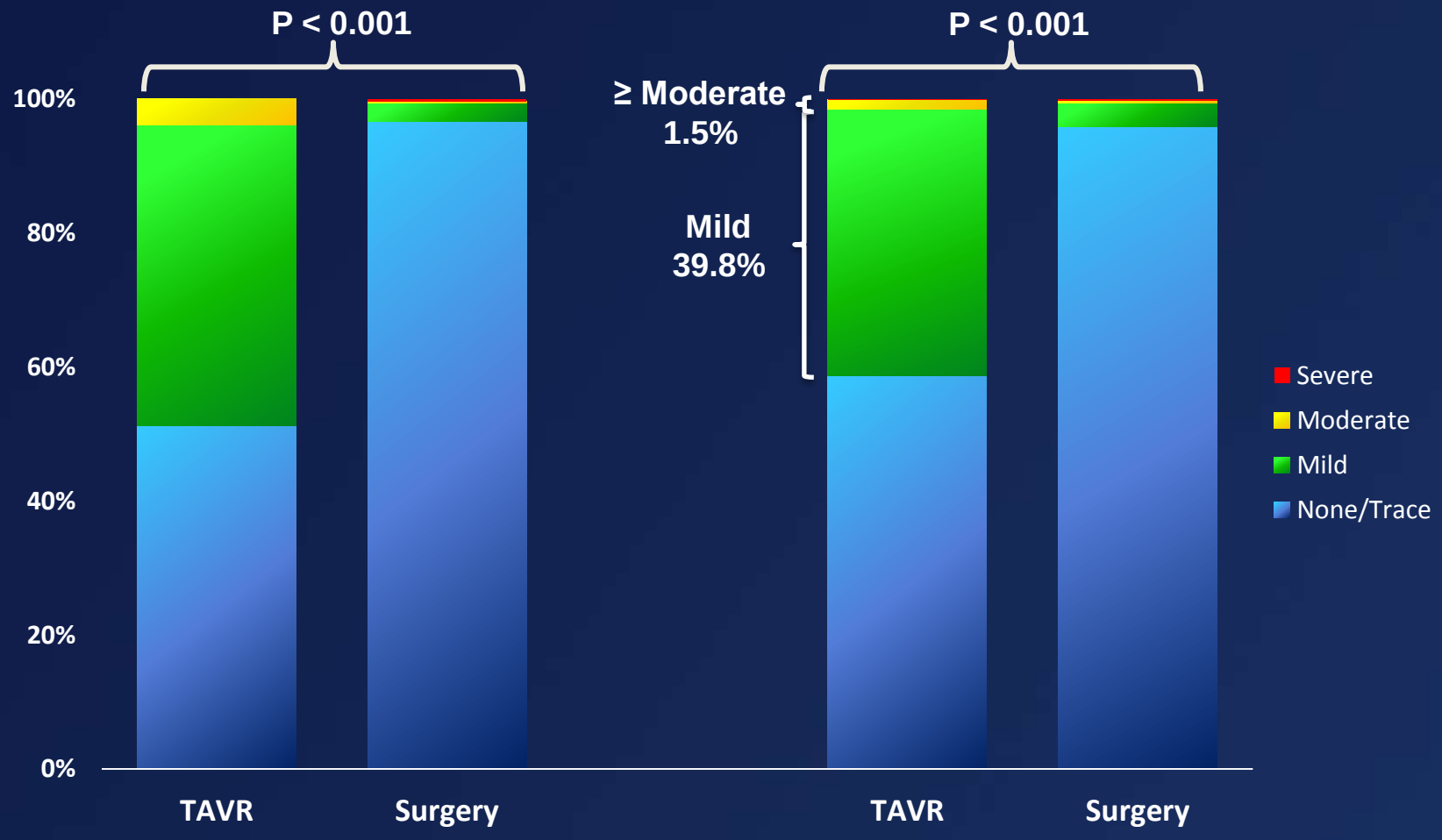
TF Primary Endpoint (AT)
All-Cause Mortality or Disabling Stroke



Number at risk:									
TF Surgery	722	636	624	600	591	573	565	555	537
TF TAVR	762	717	708	685	663	652	644	634	612

Paravalvular Regurgitation

3-Class Grading Scheme (VI)

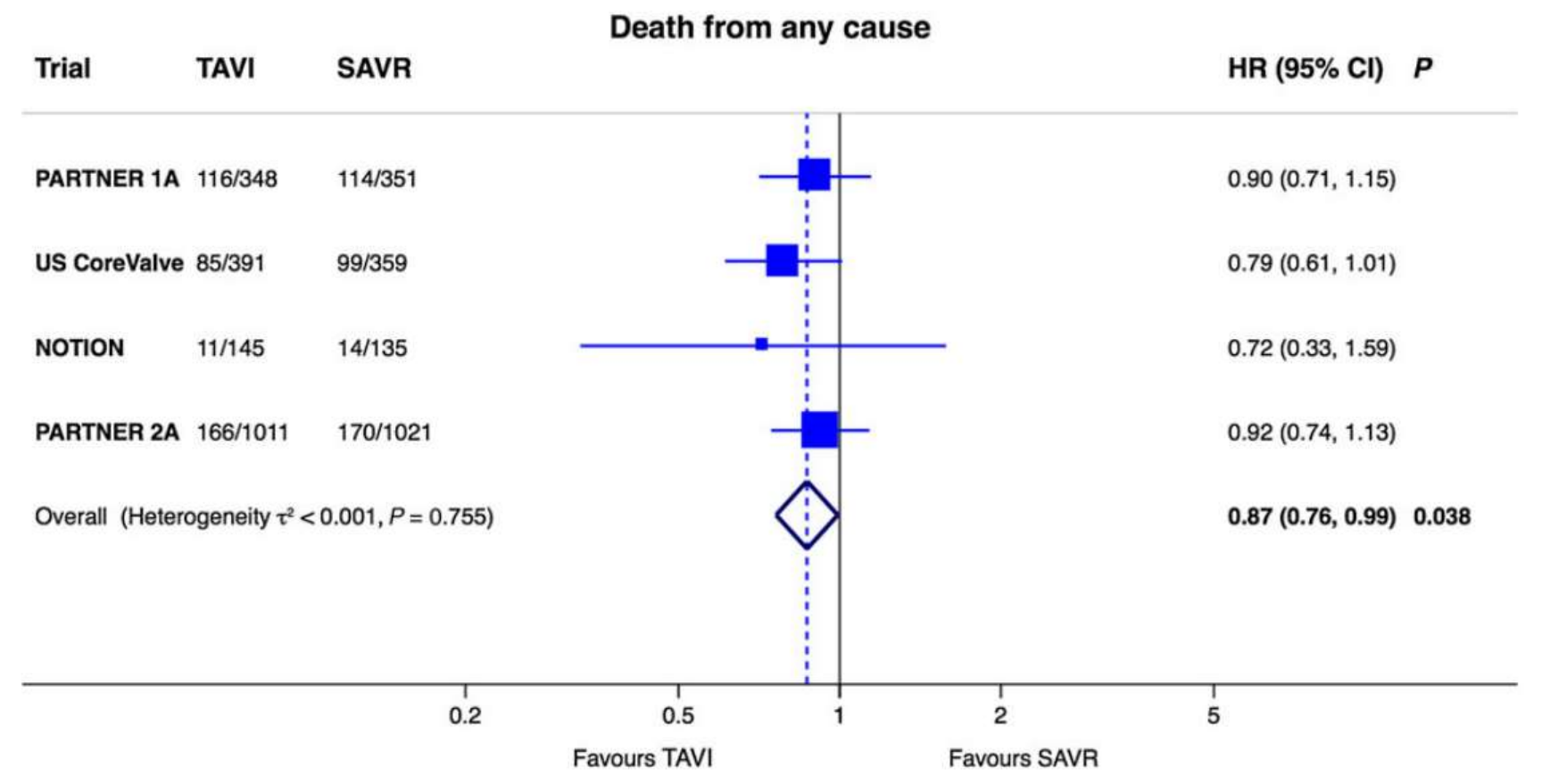


No. of echos	30 Days	1 Year
P2A Surgery	755	610
S3i TAVR	992	875

TAVR vs. SAVR

Meta-Analysis

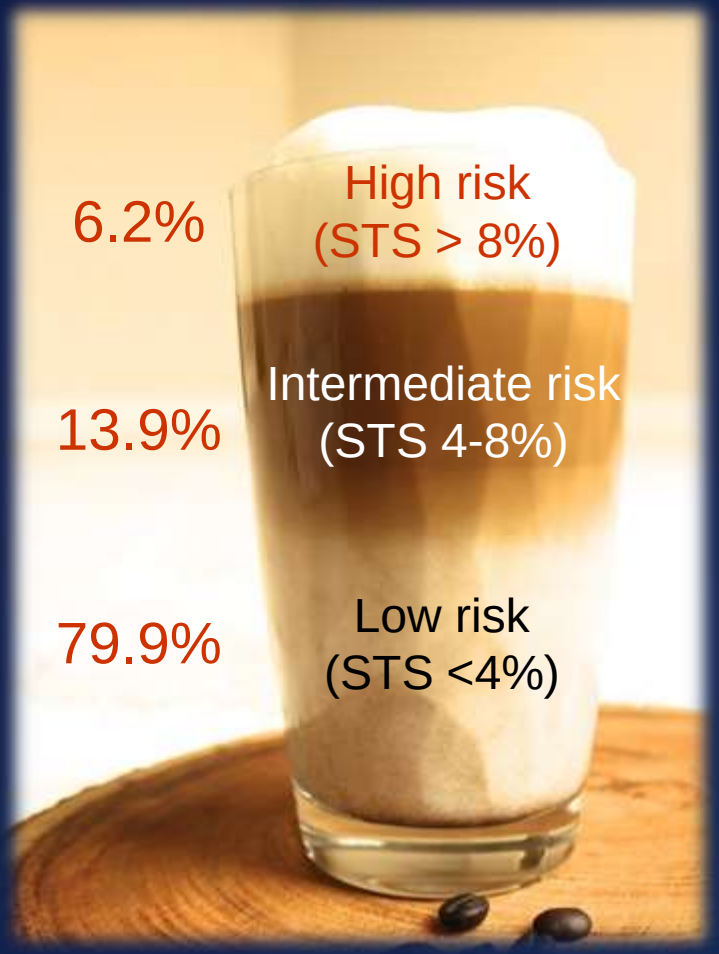
- Putting it all together in a meta-analysis, TAVR when compared to SAVR provides a statistically significant, *13% relative risk reduction of death* from any cause
- This is a class effect, independent of valve type



[1]Siontis, et al., *Eur Hear J* 2016; doi:10.1093/eurheartj/ehw225

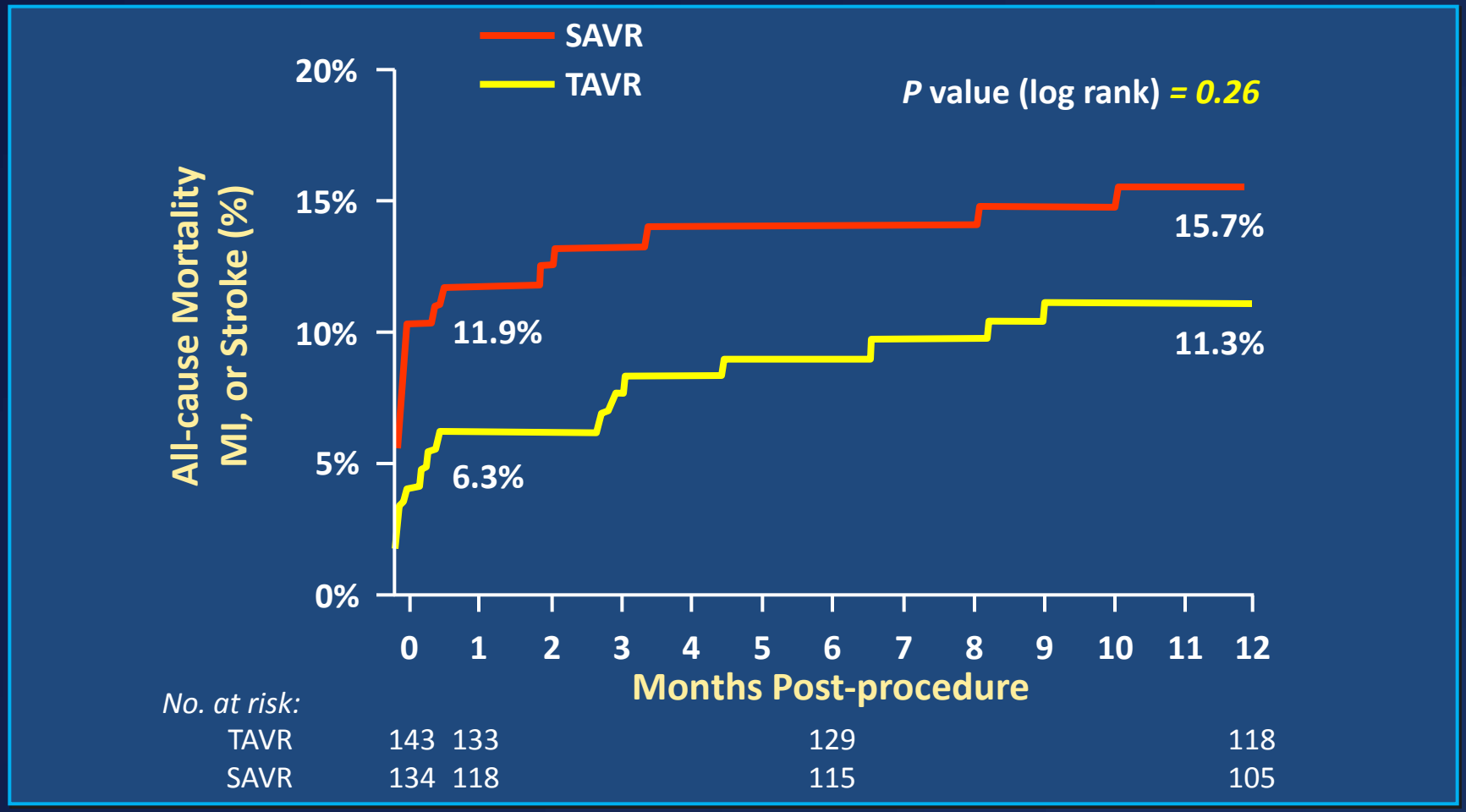
The Low-Risk Journey

STS database 2002-2010 (141,905 pts)



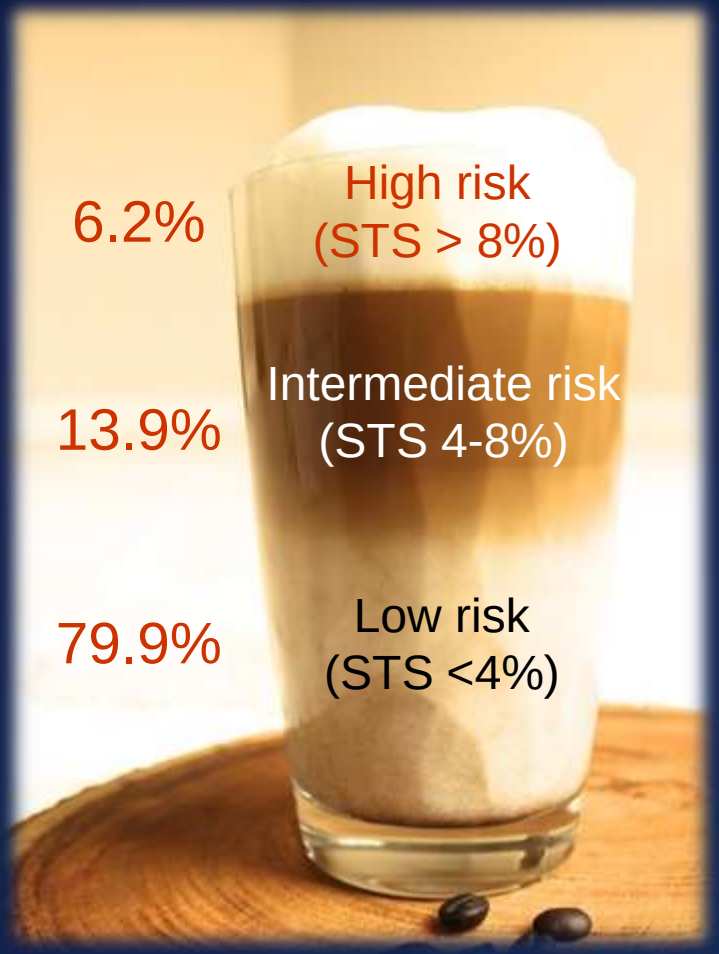
NOTION All Comers,
PARTNER 3 LR, CoreValve LR

NOTION: Death (all-cause), Stroke or MI at 1 Year (as-treated)



The Low-Risk Journey

STS database 2002-2010 (141,905 pts)



The Evidence for TAVR is Definitive, Progressive & Unprecedented!

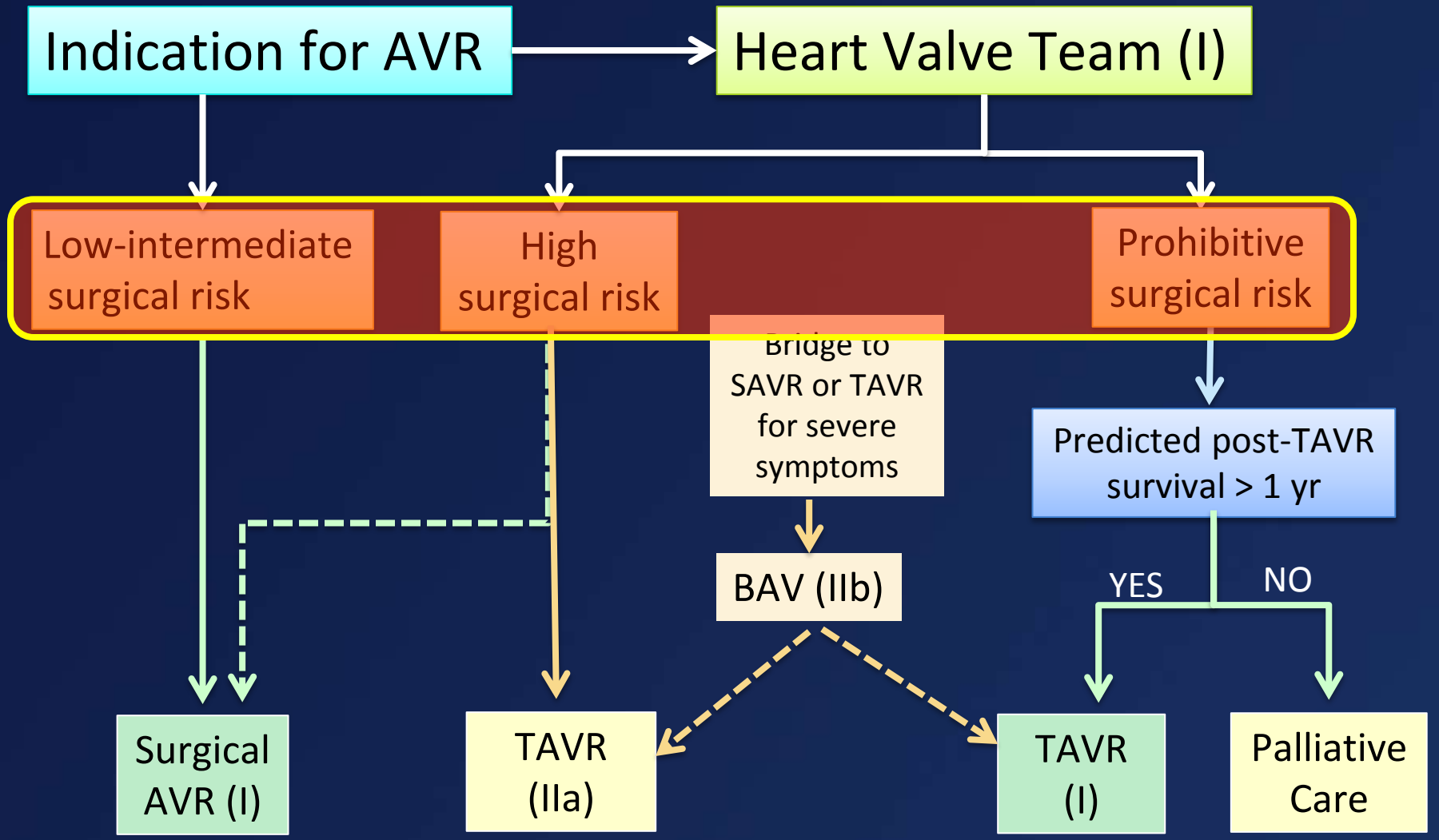
TAVR Journey - 2016

- **The Low-Risk Journey**

  Risk stratification for TAVR, especially based upon surgical risk scores, is imprecise, heavily biased, and mainly served a regulatory purpose to control clinical expansion of TAVR and to encourage a disciplined commitment to evidence-based risk-cohort studies!

2014 ACC/AHA Valve Guidelines

CHOICE of Intervention for AS



ACC/AHA 2014 Risk Assessment (with MHT*)

Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

	Low Risk (ALL criteria)	Intermediate Risk (any 1)	High Risk (any 1 criteria)	Prohibitive Risk (any 1 criteria)
STS PROM*	<4% **AND**	4% to 8% **OR**	>8% **OR**	Predicted risk with surgery of death or major morbidity (all-cause) >50% at 1 y **OR**
Frailty	**None** **AND**	1 index (mild) **OR**	2 or more indices (moderate-severe) **OR**	
Major organ system compromise not to be improved postop	None **AND**	1 organ system **OR**	No more than 2 organ systems **OR**	3 or more organ systems **OR**
Procedure-specific impediment	None	Possible procedure-specific impediment	Possible procedure-specific impediment	Severe procedure-specific impediment

** Multi-disciplinary Heart Team*

The Low-Risk Journey

Imagery of TAVR Risk Strata

AS Patient Population Requiring Treatment

The Low-Risk Journey

Imagery of TAVR Risk Strata

AS Patient Population Requiring Treatment

TAVR Journey - 2016

- **The Low-Risk Journey**

  Realization of TAVR (society guidelines and reimbursement) for essentially ALL patients (including low-risk) with AS requiring treatment, will still require…

  - completion of the low-risk RCTs
  - meaningful TAVR risk scores
  - management of valve durability issues

TAVR Journey - 2016

The Durability Controversy

TAVR Journey - 2016

- **The Durability Controversy**

  Until there is long-term (>10 years) reliable clinical and echo data on normal-risk patients treated with "modern era" transcatheter bioprosthetic valves, there will always be concerns regarding "durability"!

PARTNER 5-year FU in Lancet (March, 2015)

5-year outcomes of transcatheter aortic valve replacement compared with standard treatment for patients with inoperable aortic stenosis (PARTNER 1): a randomised controlled trial

Samir R Kapadia, Martin B Leon, Raj R Makkar, E Murat Tuzcu, Lars G Svensson, Susheel Kodali, John G Webb, Michael J Mack, Pamela S Douglas, Vinod H Thourani, Vasilis C Babaliaros, Howard C Herrmann, Wilson Y Szeto, Augusto D Pichard, Mathew R Williams, Gregory P Fontana, D Craig Miller, William N Anderson, Jodi J Akin, Michael J Davidson†, Craig R Smith, for the PARTNER trial investigators*

5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial

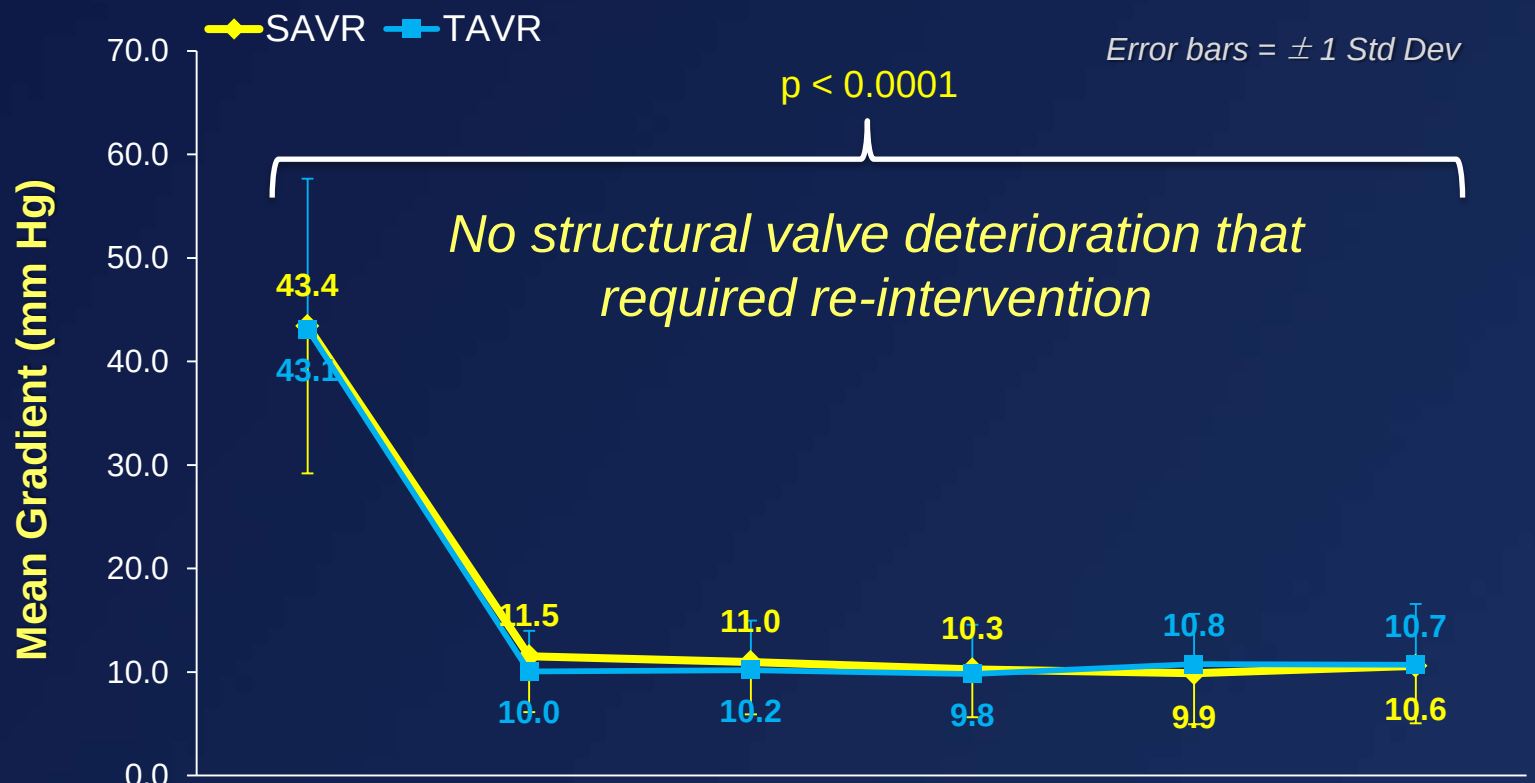
Michael J Mack, Martin B Leon, Craig R Smith, D Craig Miller, Jeffrey W Moses, E Murat Tuzcu, John G Webb, Pamela S Douglas, William N Anderson, Eugene H Blackstone, Susheel K Kodali, Raj R Makkar, Gregory P Fontana, Samir Kapadia, Joseph Bavaria, Rebecca T Hahn, Vinod H Thourani, Vasilis Babaliaros, Augusto Pichard, Howard C Herrmann, David L Brown, Mathew Williams, Jodi Akin, Michael J Davidson†, Lars G Svensson, for the PARTNER 1 trial investigators*

Mean Gradient & Valve Area (AT)

P1B - All Patients

Aortic Valve Mean Area (AT)

P1A - All Patients



	Baseline	1 Year	2 Year	3 Year	4 Year	5 Year
TAVR	310	219	156	106	79	56
SAVR	299	158	123	86	61	48

TAVR Journey - 2016

Proposing New Guidelines

TAVR Journey - 2016

- **Proposing New Guidelines**

  The current TAVR guidelines (ESC and AHA/ACC) are already anachronistic and don't reflect clinical practice!

2014 ACC/AHA Valve Guidelines

TIMING of Intervention (AVR) for AS

Recommendations	COR	LOE	References
AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B	(10,57–59)
AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF <50%	I	B	(60,61)
AVR is indicated for patient surgery		B	(62,63)
AVR is reasonable for asym velocity ≥5.0 m/s) and l		B	(64,65)
AVR is reasonable in asymp tolerance or an exercise		B	(27,38)
AVR is reasonable in sympt LVEF (stage D2) with a l velocity ≥4.0 m/s (or me any dobutamine dose		B	(66–68)
AVR is reasonable in sympt D3) who are normotensiv data support valve obstru		C	N/A
AVR is reasonable for patien undergoing other cardiac		C	N/A
AVR may be considered for as omatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C	N/A

Indications, although "reasonable", are not supported by evidence-based medicine clinical trials!

Summary: 8 class I or IIa indications for AVR; LOE either B or C; no RCTs, supported by few small studies (100's pts) or N/A; *not based on age or risk stratification*

TAVR Journey - 2016

- **Proposing New Guidelines**

  Therefore, until the guidelines are updated, we should consider introducing "clinical" guidelines to help the practicing TAVR community, based upon…

  - ALL available clinical trial evidence
  - global trends and accepted clinical practices
  - important "secondary" endpoints which better indicate the impact/value of TAVR

TAVR Clinical Use in 2016
(evidence + common sense)

CLASS I

Benefit >>> Risk

SHOULD be performed

Class Ia (of course!)

- Cannot have surgery (= inoperable, extreme risk, prohibitive risk)
  - ✓ esp. technical reasons (e.g. hostile chest, chest RT, etc.)
  - ✓ beware futility (e.g. wheelchair-bound, ultra-frail, extreme co-morbidities)
- "Very" high-risk for surgery
  - ✓ e.g. severe COPD, chronic liver disease, dementia, severe PH

TAVR Clinical Use in 2016
(evidence + common sense)

CLASS I

Benefit >>> Risk

SHOULD be performed

Class Ib (enough already!)

- ≥ 90 years old
- All other high-risk patients
- Aortic valve-in-valve (high-risk)
- Special considerations
  - ✓ low EF (esp. <30%)
  - ✓ CKD on dialysis
  - ✓ small annulus (esp. in women)
  - ✓ low flow-low gradient AS

TAVR Clinical Use in 2016
(evidence + common sense)

CLASS IIa

Benefit >> Risk

IT IS REASONABLE to perform

Class IIa (strong preference!)

- Intermediate-risk patients (esp. TF)
- ≥ 80 years old
- Aortic valve-in-valve (normal risk)
- Severe *asymptomatic* AS (PV > 5 m/s)
- Concomitant disease
  - ✓ previous CABG
  - ✓ CKD not requiring dialysis
  - ✓ CAD – non-complex
  - ✓ RH failure

TAVR Clinical Use in 2016
(evidence + common sense)

CLASS IIb

Benefit ≥ Risk

MAY BE CONSIDERED to perform

Class IIb (on the fence = need more evidence; proceed with caution)

- Low-risk patients (except as above)
  - ✓ ? bicuspid aortic valve disease
  - ✓ < 65 years old (the durability issue)
- High "anatomic" risk for TAVR
  - ✓ extreme calcification (esp. LVOT) and high risk of rupture or CA occlusion
  - ✓ marked horizontal aorta

TAVR Clinical Use in 2016
(evidence + common sense)

CLASS III

No Benefit
OR Harm

SHOULD NOT
be performed

Class III (stay away!)

- Concomitant CV lesions requiring surgery (e.g. aortopathies, complex CAD, other valve lesions)
- Poor candidates for TAVR due to technical or anatomic reasons
  - ✓ annulus size too small/large
  - ✓ LV thrombus or endocarditis

TAVR Journey - 2016

Are We There Yet?

The ultimate role of TAVR is yet to be determined. But we can foresee a future time when the use of TAVR will be an objective risk-benefit assessment based upon clinical, anatomic, and evidence-based factors, thus ensuring optimal care for all patients with Aortic Stenosis!