Highlights Session 4. Valve Session (July 7, 2020)

TAVR Long-Term Durability: *Is it a concern for late catch-up in PARTNER 3?*

Martin B. Leon, MD

Columbia University/NYP Hospital

Cardiovascular Research Foundation

New York City

10 mins

Disclosures - Martin B. Leon, MD

TCTAP & AP Valves 2020 Online; July 7, 2020

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

Financial Relationship	Company
• Research Support	Abbott, Boston Scientific, Edwards Lifesciences, Medtronic
• Consulting Activities*	Abbott, Boston Scientific, Edwards Lifesciences, Gore, Medtronic
• Equity	Ancora, Claret (BSC), Conveyor, Valve Medical

*Medical or scientific advisory boards (no direct physician payments)

Highlights Session 4. Valve Session (July 7, 2020)

TAVR Long-Term Durability: *Is it a concern for late catch-up in PARTNER 3?*

YES… TAVR long-term durability is always a concern!

10 mins

TAVR Long-Term Durability

Lecture Agenda

Clinical Catch-up

Structural Valve Deterioration

TAVR Long-Term Durability

Clinical Catch-up

- In earlier TAVR vs. Surgery RCTs with at least 5 years follow-up, in patients at high or intermediate-risk profiles, including either balloon-expandable or self-expanding valves, there are no indications of late clinical catch-up favoring Surgery.

Five-year Outcomes from the PARTNER 2A Trial: Transcatheter vs. Surgical Aortic Valve Replacement in Intermediate-Risk Patients

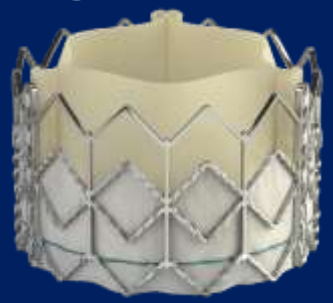
Vinod H. Thourani, MD
on behalf of The PARTNER Trial Investigators

TCT | San Francisco | September 28, 2019

THE PARTNER II TRIAL

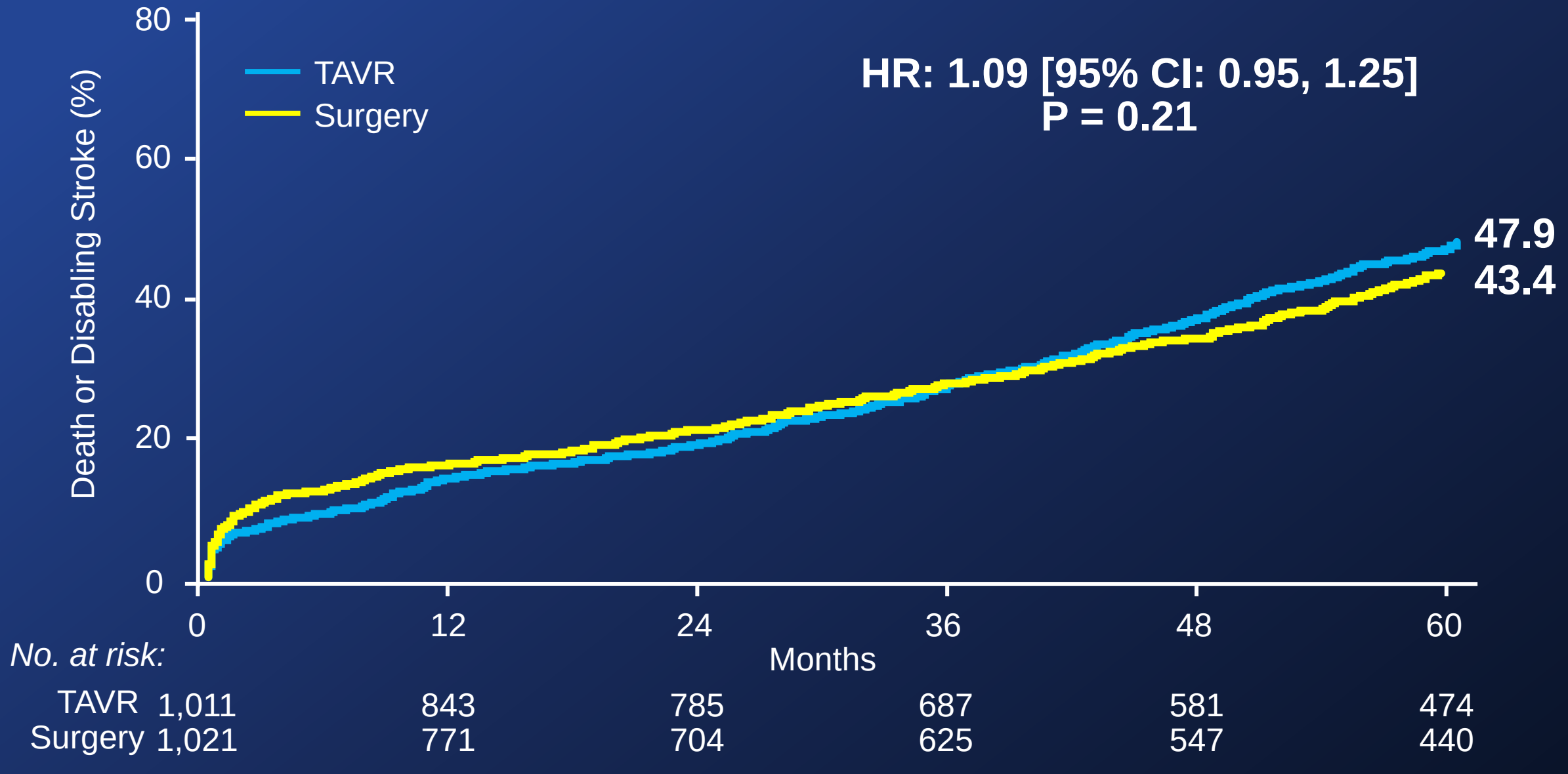
PARTNER SAPIEN Platforms
Device Evolution

THE PARTNER II TRIAL

	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility			
Available Valve Sizes	 23 mm 26 mm	 23 mm 26 mm 29 mm* *First Implant Oct 30, 2012	 20 mm 23 mm 26 mm 29 mm

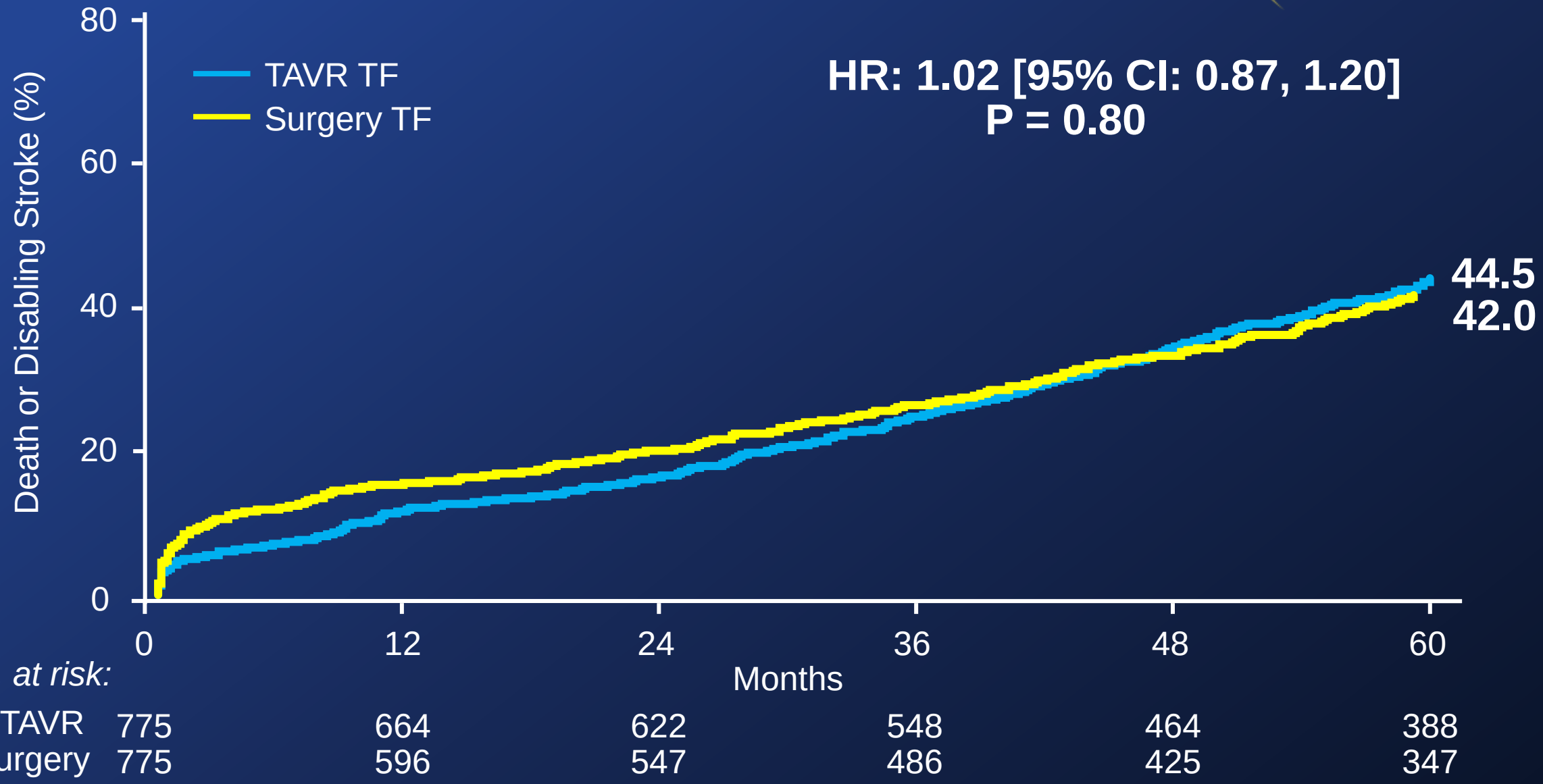
Primary Endpoint
ITT Population

THE PARTNER II TRIAL



Primary Endpoint
Transfemoral Cohort

THE PARTNER II TRIAL



TAVR Long-Term Durability

Clinical Catch-up

- In earlier TAVR vs. Surgery RCTs with at least 5 years follow-up, in patients at high or intermediate-risk profiles, including either balloon-expandable or self-expanding valves, there are no indications of late clinical catch-up favoring Surgery.
- The most recent (TVT 2020) propensity-matched analysis of Sapien 3 vs. Surgery in intermediate-risk patients with 5-year follow-up, also showed no late catch-up.

SAPIEN 3 Transcatheter Aortic Valve Replacement Compared with Surgery in Intermediate-risk Patients: A Propensity-Matched Analysis of 5-year Outcomes

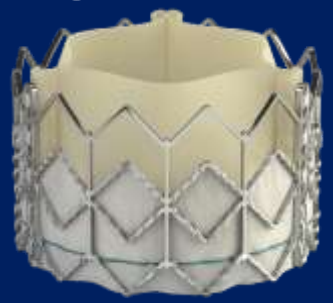
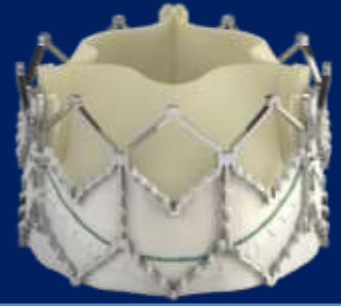
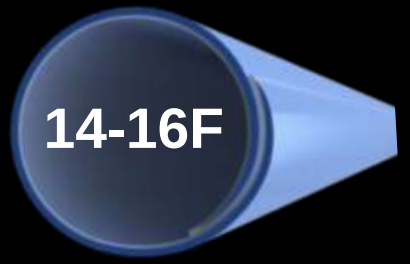
Susheel K. Kodali, MD
on behalf of The PARTNER Trial Investigators

TVT | June 21, 2020

THE PARTNER II TRIAL

PARTNER SAPIEN Platforms
Device Evolution

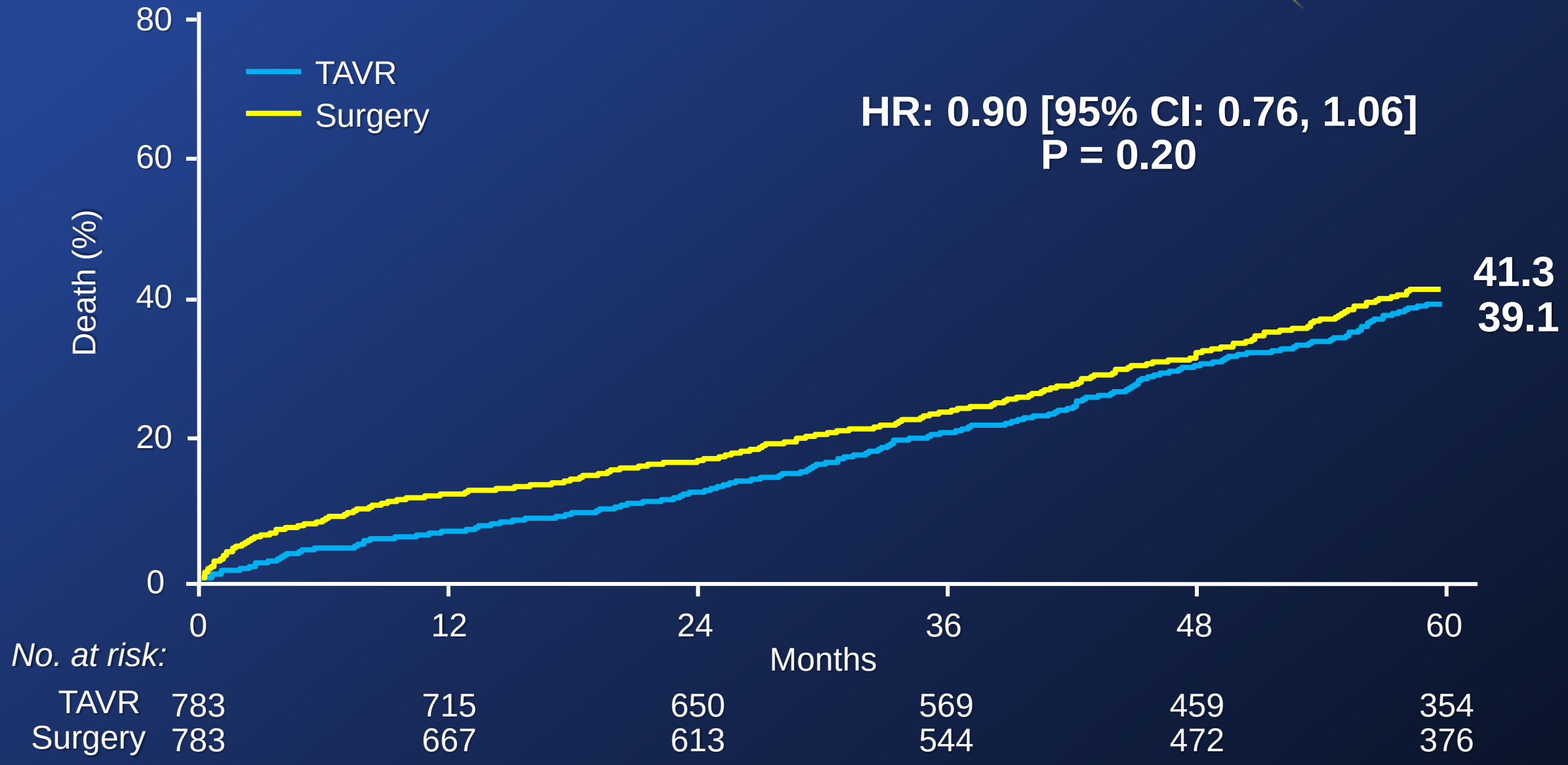
THE PARTNER II TRIAL

	SAPIEN	SAPIEN XT	SAPIEN 3
Valve Technology			
Sheath Compatibility	 22-24F	 16-20F	 14-16F
Available Valve Sizes	 23 mm, 26 mm	 23 mm, 26 mm, 29 mm*	 20 mm, 23 mm, 26 mm, 29 mm

*First Implant Oct 30, 2012

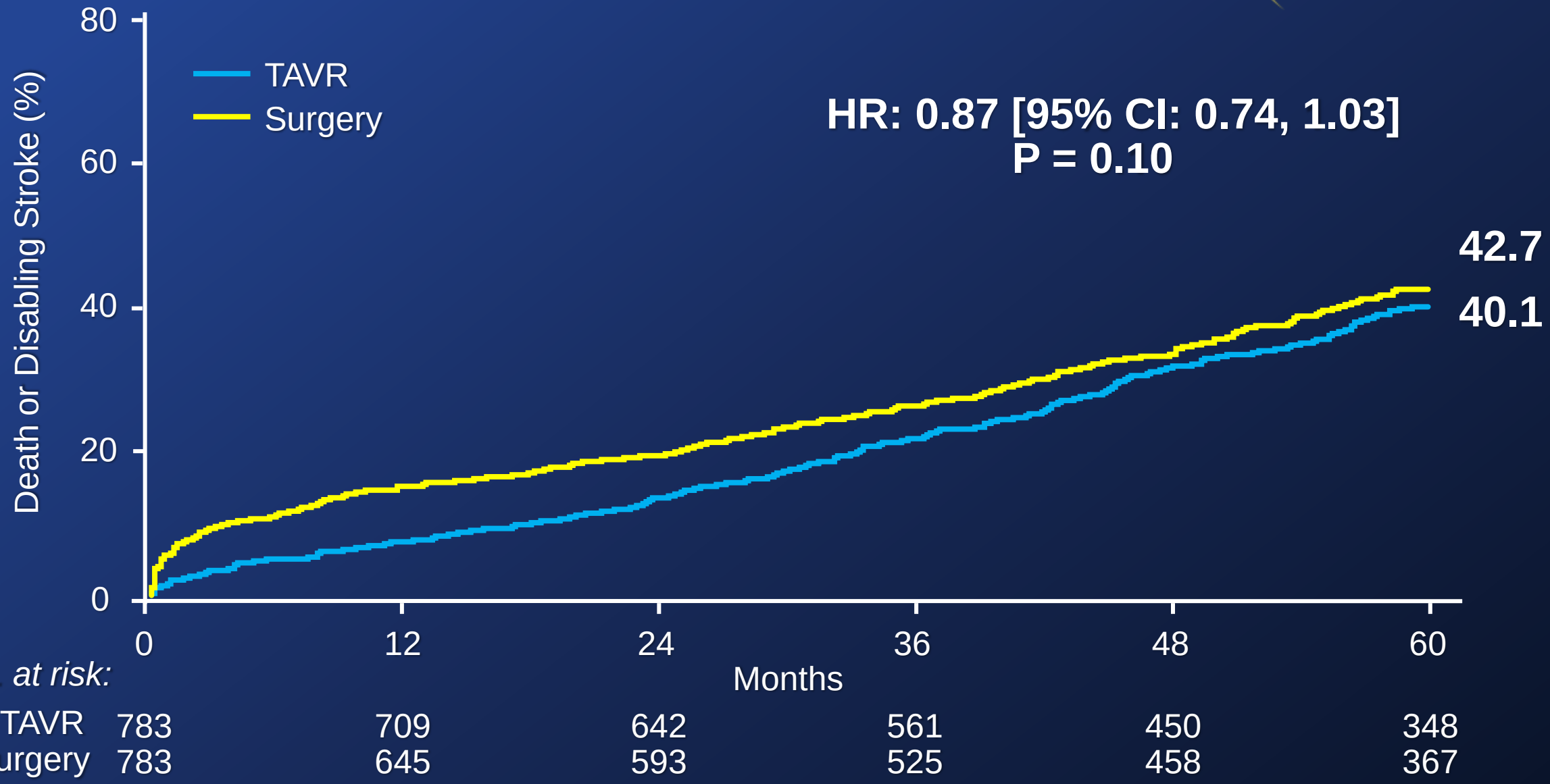
All-Cause Death
Matched Cohort

THE PARTNER II TRIAL



Death or Disabling Stroke
Matched Cohort

THE PARTNER II TRIAL



TAVR Long-Term Durability

Clinical Catch-up

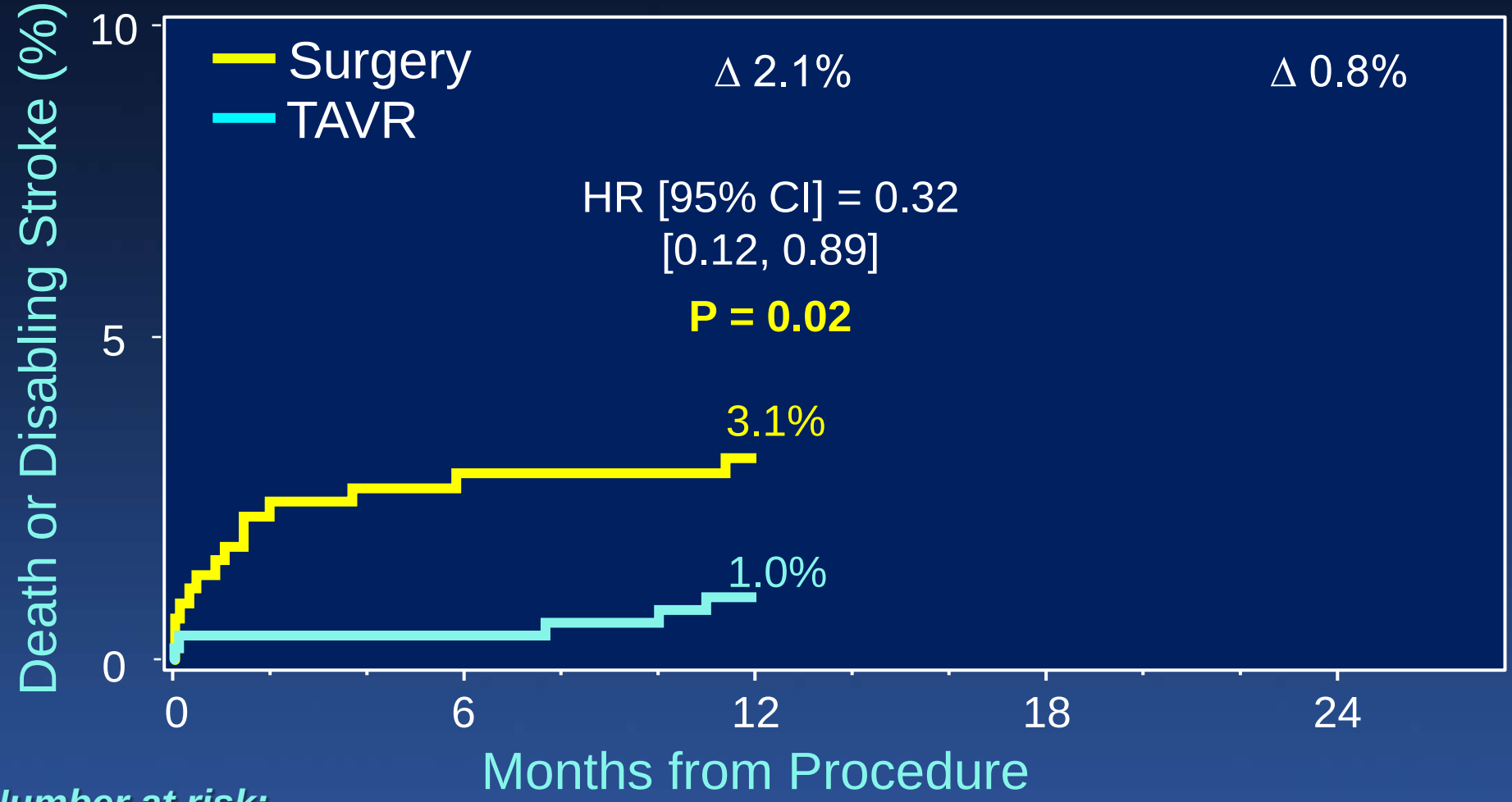
- In earlier TAVR vs. Surgery RCTs with at least 5 years follow-up, in patients at high or intermediate-risk profiles, including either balloon-expandable or self-expanding valves, there are no indications of late clinical catch-up favoring Surgery.
- The most recent (TVT 2020) propensity-matched analysis of Sapien 3 vs. Surgery in intermediate-risk patients with 5-year follow-up, also showed no late catch-up.
- The recent (ACC 2020) 2-year follow-up from PARTNER 3 (Sapien 3 vs. Surgery in low-risk patients) indicated narrowing of death/stroke endpoints (still favoring TAVR) and increased TAVR valve thrombosis between 1 and 2 years.

THE PARTNER 3 TRIAL

Two-year Clinical and Echocardiographic Outcomes from the PARTNER 3 Low-risk Randomized Trial

Michael J. Mack, MD &
Martin B. Leon, MD
on behalf of the PARTNER 3 Trial Investigators

Death or Disabling Stroke



Number at risk:

Surgery	**454**	**430**	**423**	**406**	**395**
TAVR	**496**	**493**	**489**	**475**	**463**

Valve Thrombosis to 2 Years

Outcomes	TAVR (N=496)	Surgery (N=454)	P-value
Valve Thrombosis	2.6% (13)	0.7% (3)	0.02
Mean Gradient > 20mmHg and ↑ > 10mmHg	53.8% (7)	0% (0)	
Mean Gradient > 20mmHg and ↑ < 10mmHg	30.7% (4)	100.0% (3)	
↑ transvalvular AR (mild) with no change in mean gradient	7.7% (1)	0% (0)	
CT findings with no change in hemodynamics	7.7% (1)	0% (0)	

CEC adjudicated valve thrombosis per VARC 2 (all patients received anticoagulation). Valve thrombosis events are Kaplan-Meier estimate [% (no. of subjects with event)] and P-value is based on Log-Rank test; all other event rates are incidence [% (no. of subjects with event)]

TAVR Long-Term Durability

Structural Valve Deterioration

- Earlier definitions of valve durability focused on ‘soft’ clinical endpoints (re-operation or presumed valve-related death) which clearly underestimated the true frequency of structural valve deterioration (SVD).
- Recently, standardized definitions have been developed focusing on prosthesis-centered and patient-centered outcomes, using serial echocardiography and longitudinal follow-up, to report valve durability and accounting for competing risk (e.g. EAPCI/ESC/EACTS and VARC 3).

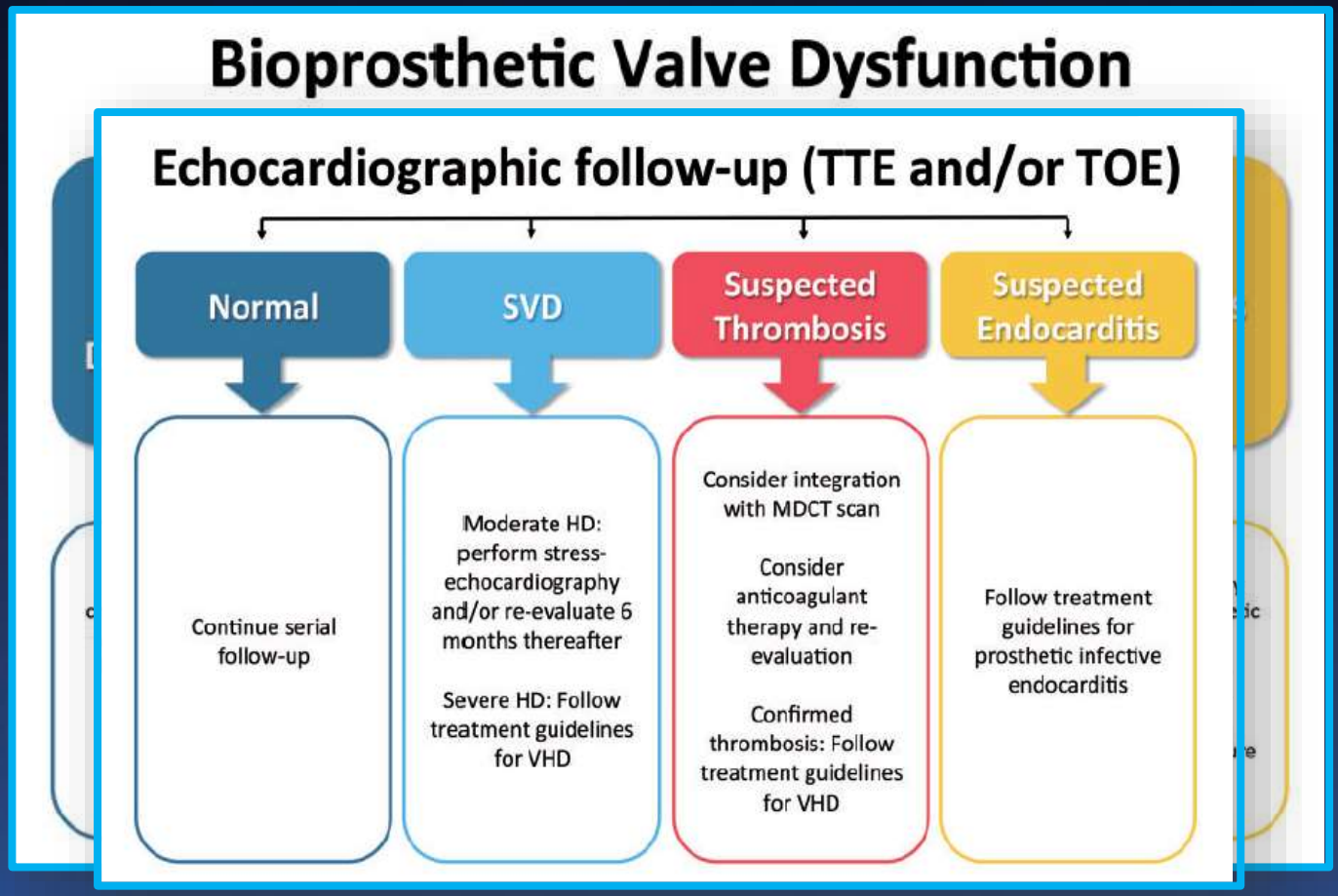
TAVR Long-Term Durability

EAPCI/ESC/EACTS Definitions

SPECIAL ARTICLE

Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Davide Capodanno[1*†], Anna S. Petronio[2†], Bernard Prendergast[3], Helene Eltchaninoff[4], Alec Vahanian[5], Thomas Modine[6], Patrizio Lancellotti[7], Lars Sondergaard[8], Peter F. Ludman[9], Corrado Tamburino[1], Nicolo Piazza[10], Jane Hancock[3], Julinda Mehilli[11], Robert A. Byrne[12], Andreas Baumbach[13], Arie Pieter Kappetein[14], Stephan Windecker[15], Jeroen Bax[16], and Michael Haude[17]



Capodanno D et al. Europ Heart J 2017

TAVR Long-Term Durability

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- Earlier definitions of valve durability focused on ‘soft’ clinical endpoints (re-operation or presumed valve-related death) which clearly underestimated the true frequency of structural valve deterioration (SVD).
- Recently, standardized definitions have been developed focusing on prosthesis-centered and patient-centered outcomes, using serial echocardiography and longitudinal follow-up to report valve durability and accounting for competing risk (e.g. EAPCI/ESC/EACTS and VARC 3).
- Applying standardized definitions for SVD and bioprosthetic valve failure, recent analyses of Sapien 3 vs. Surgery through 5 years follow-up in various patient groups have shown no important differences.

Incidence, Predictors, and Outcome of Structural Valve Deterioration in Transcatheter versus Surgical Aortic Valve Replacement: 5 Year Follow-up from the PARTNER 2 Trials – Intermediate risk

Philippe Pibarot, DMV, PhD & Rebecca Hahn, MD
on behalf of The PARTNER Trial Investigators

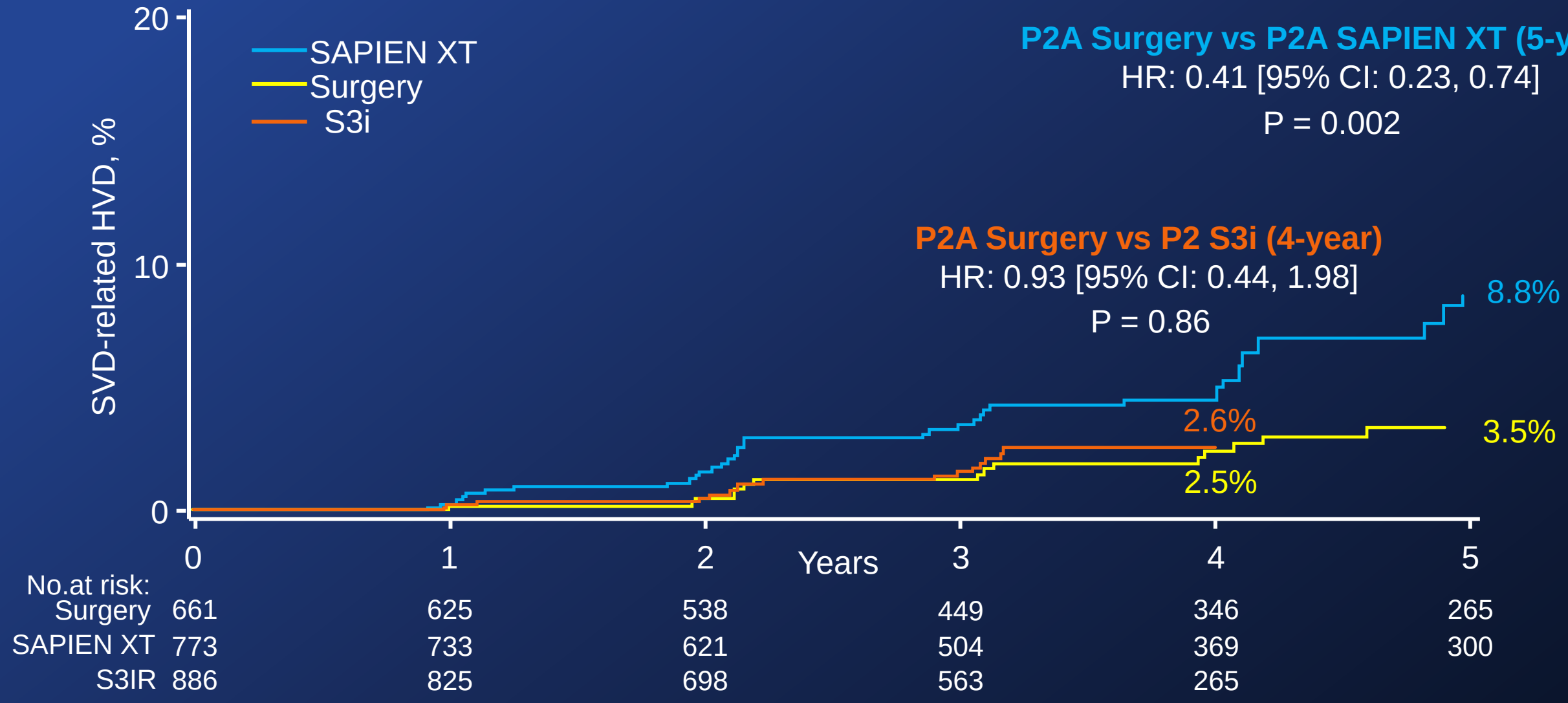
London Valves | London | November 18, 2019

THE PARTNER II TRIAL

SVD-related HVD

P2A Surgery, P2A SAPIEN XT, & P2 S3i

THE PARTNER II TRIAL



P2A Surgery vs P2A SAPIEN XT (5-year)

HR: 0.41 [95% CI: 0.23, 0.74]

P = 0.002

P2A Surgery vs P2 S3i (4-year)

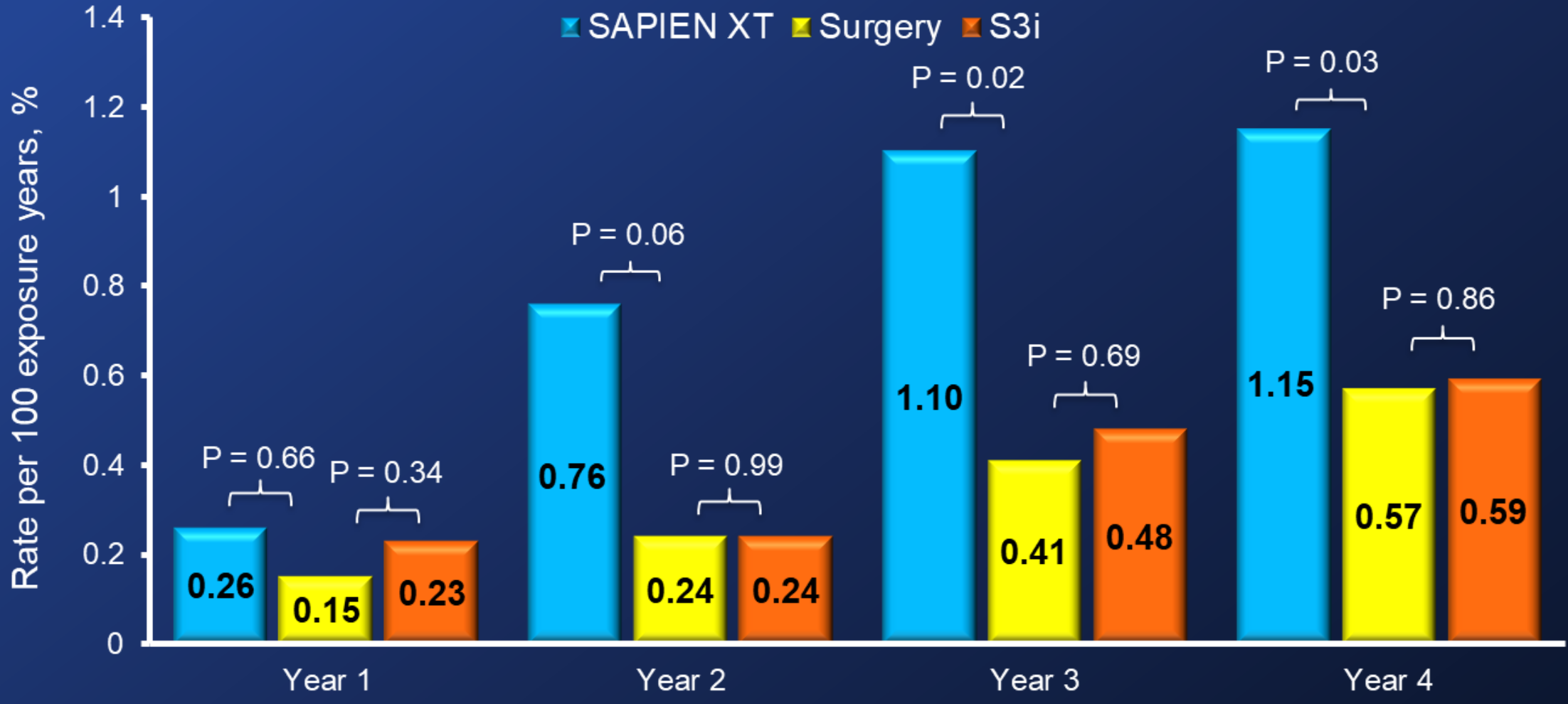
HR: 0.93 [95% CI: 0.44, 1.98]

P = 0.86

SVD-related HVD

P2A Surgery, P2A SAPIEN XT, & P2 S3i

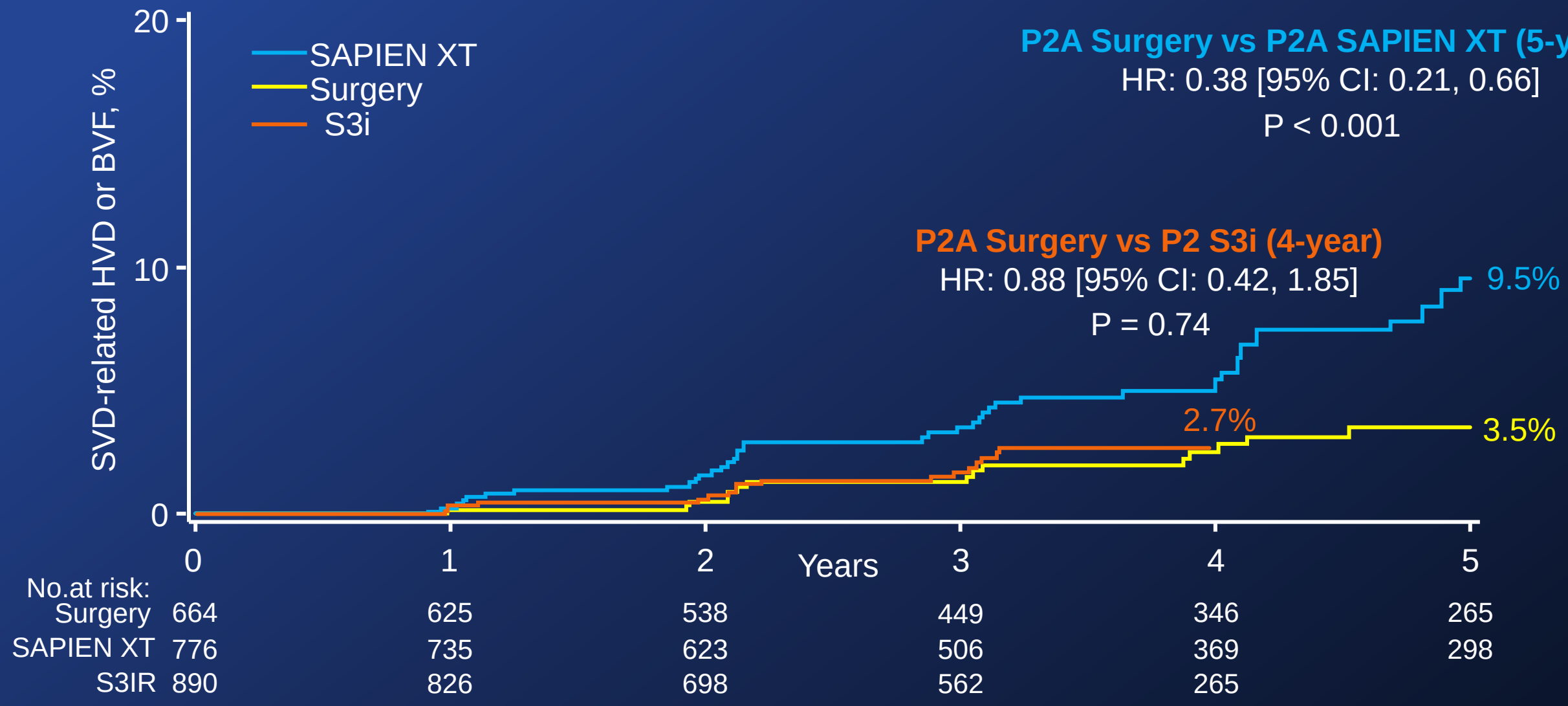
THE PARTNER II TRIAL



SVD-related HVD or BVF (Overall SVD)

P2A Surgery, P2A SAPIEN XT, & P2 S3i

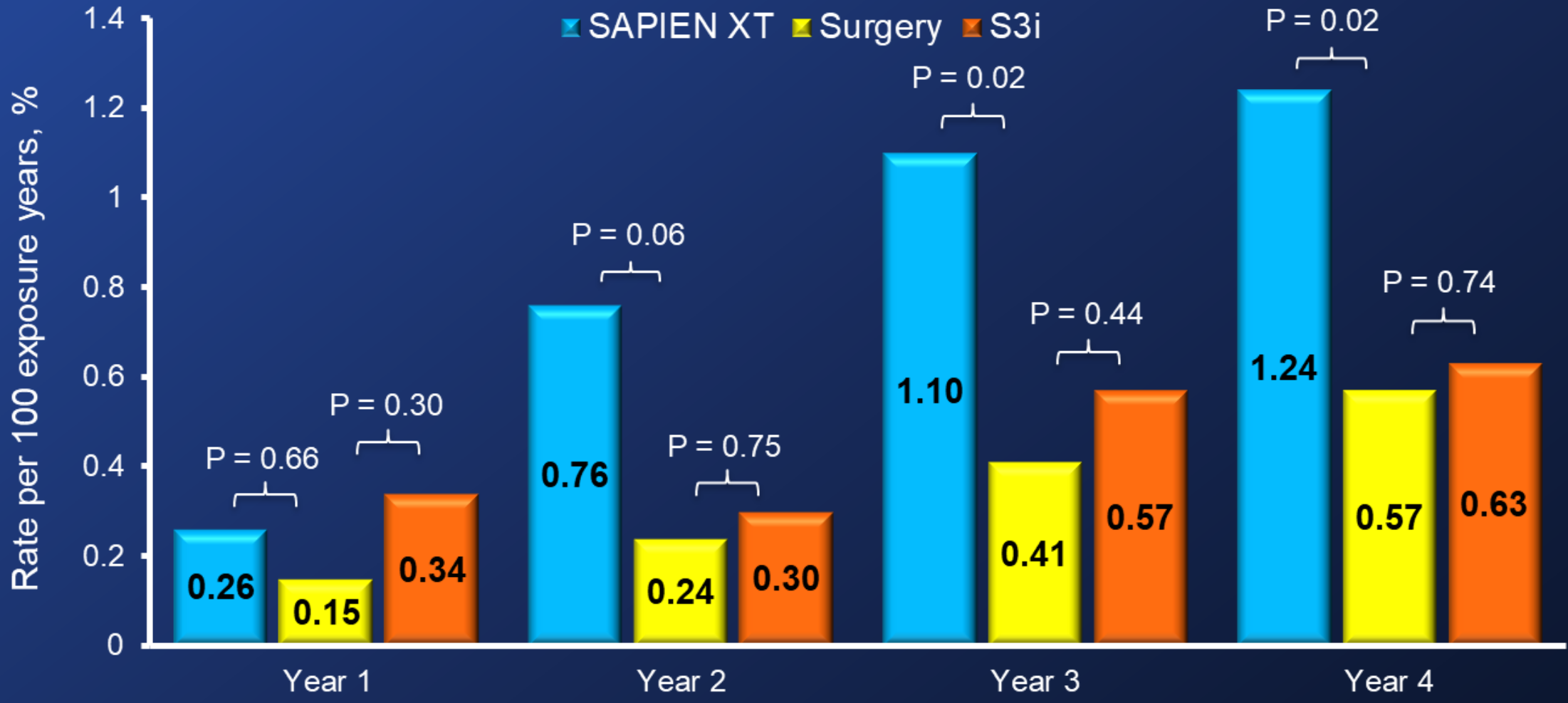
THE PARTNER II TRIAL



SVD-related HVD or BVF (Overall SVD)

P2A Surgery, P2A SAPIEN XT, & P2 S3i

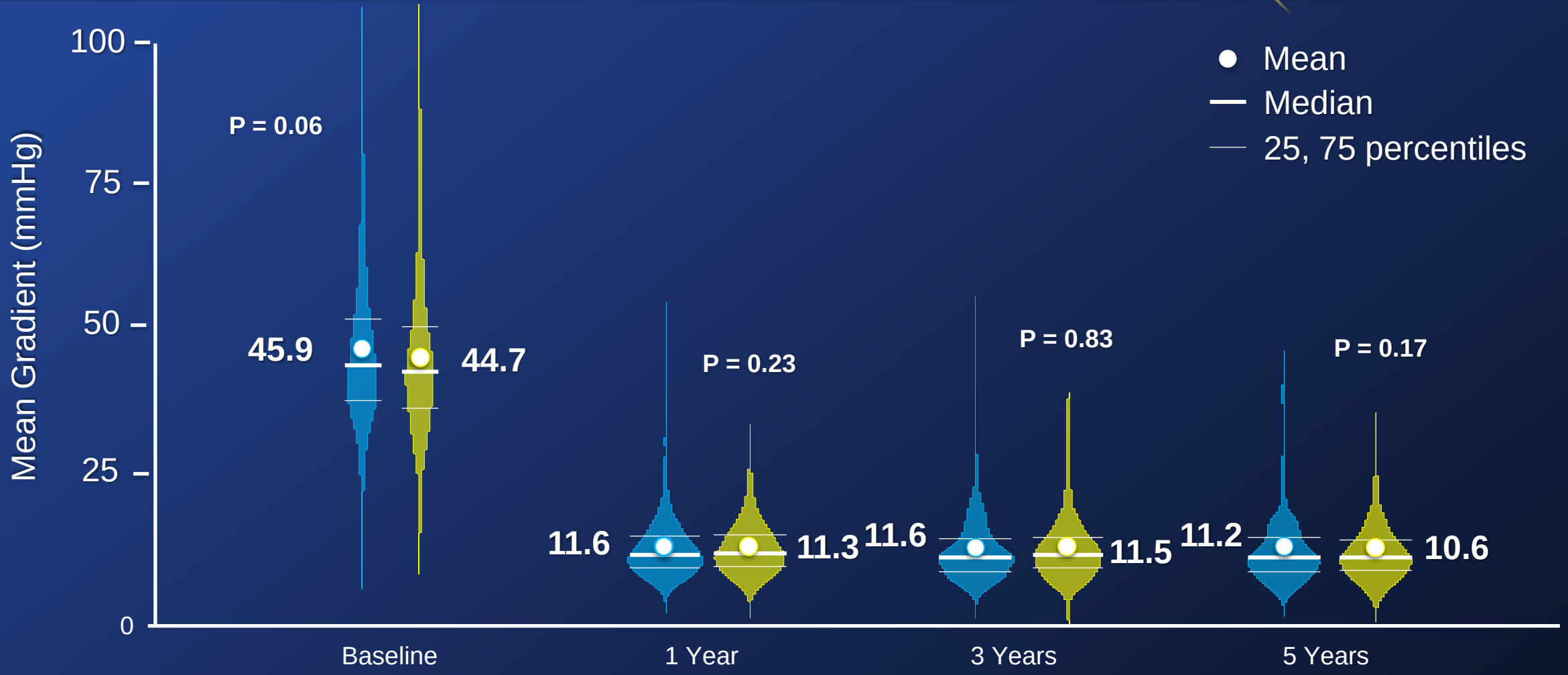
THE PARTNER II TRIAL



Mean Aortic Valve Gradient

P2A Matched Cohort

THE PARTNER II TRIAL



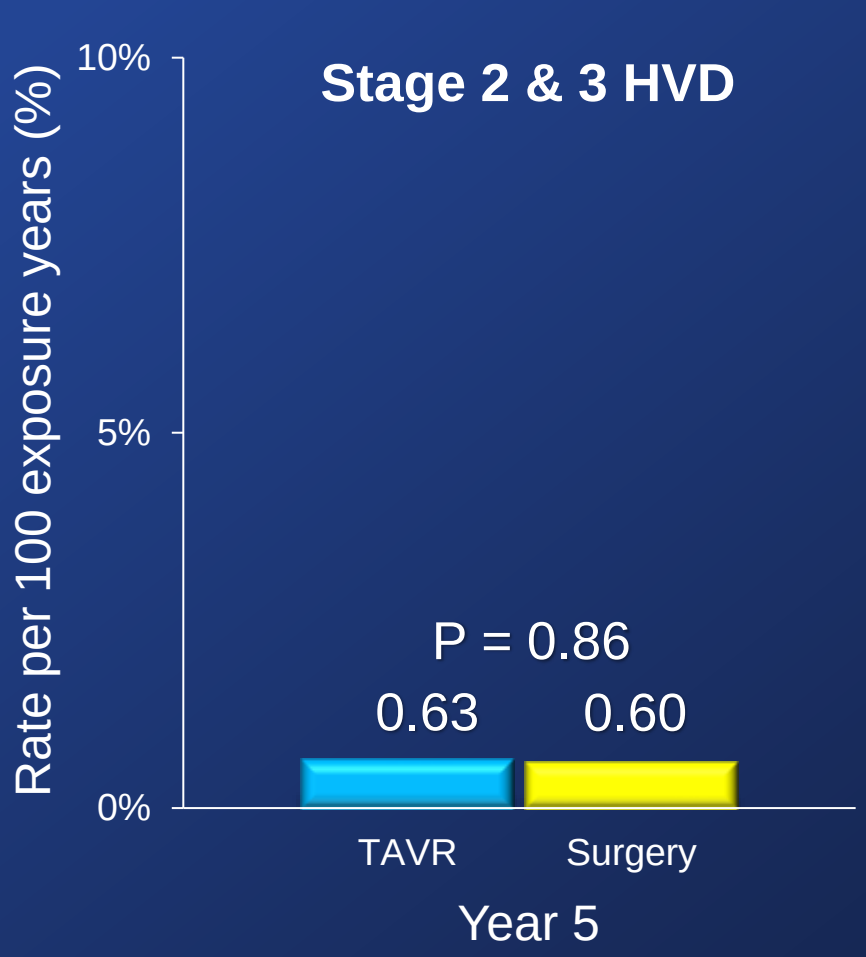
No. of Echos:

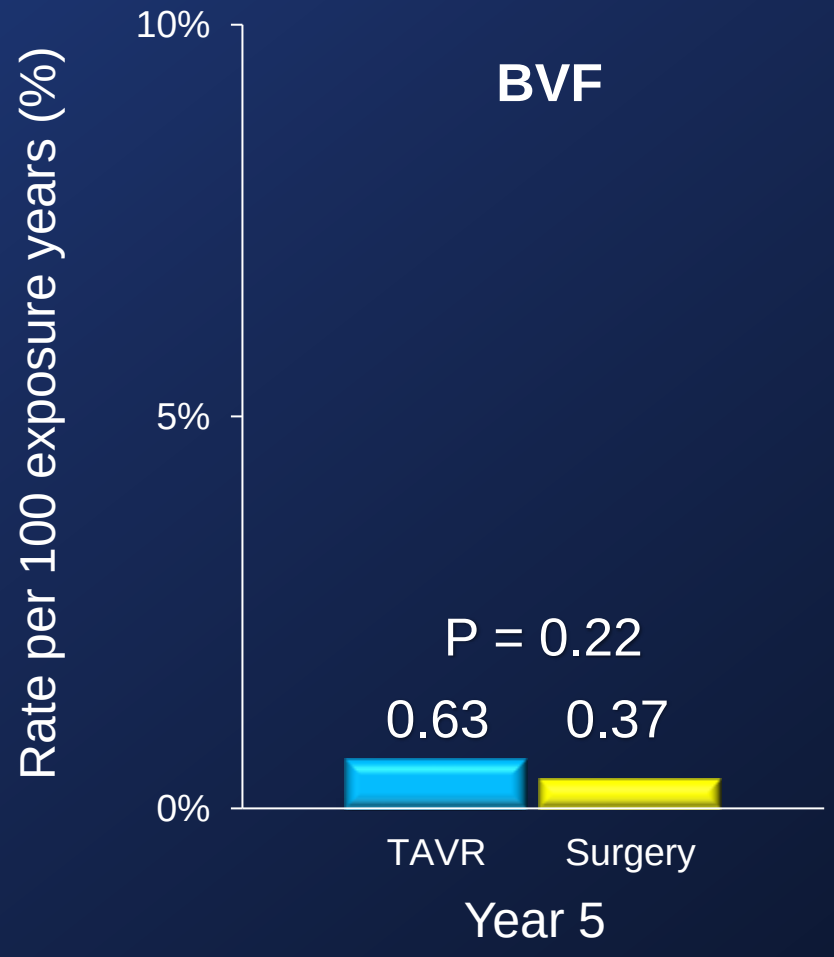
	Baseline	1 Year	3 Years	5 Years
TAVR	769	648	457	277
Surgery	767	535	384	248

Core lab adjudicated

Hemodynamic Valve Deterioration & Bioprosthetic Valve Failure

THE PARTNER II TRIAL

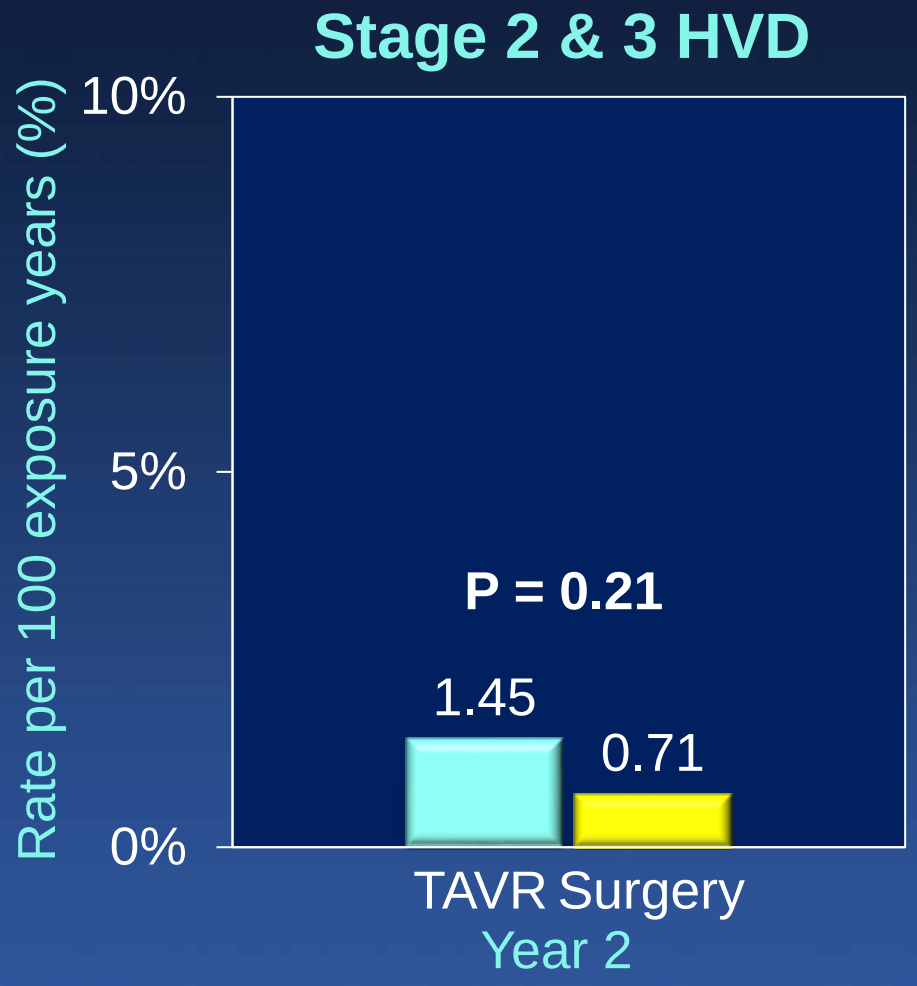


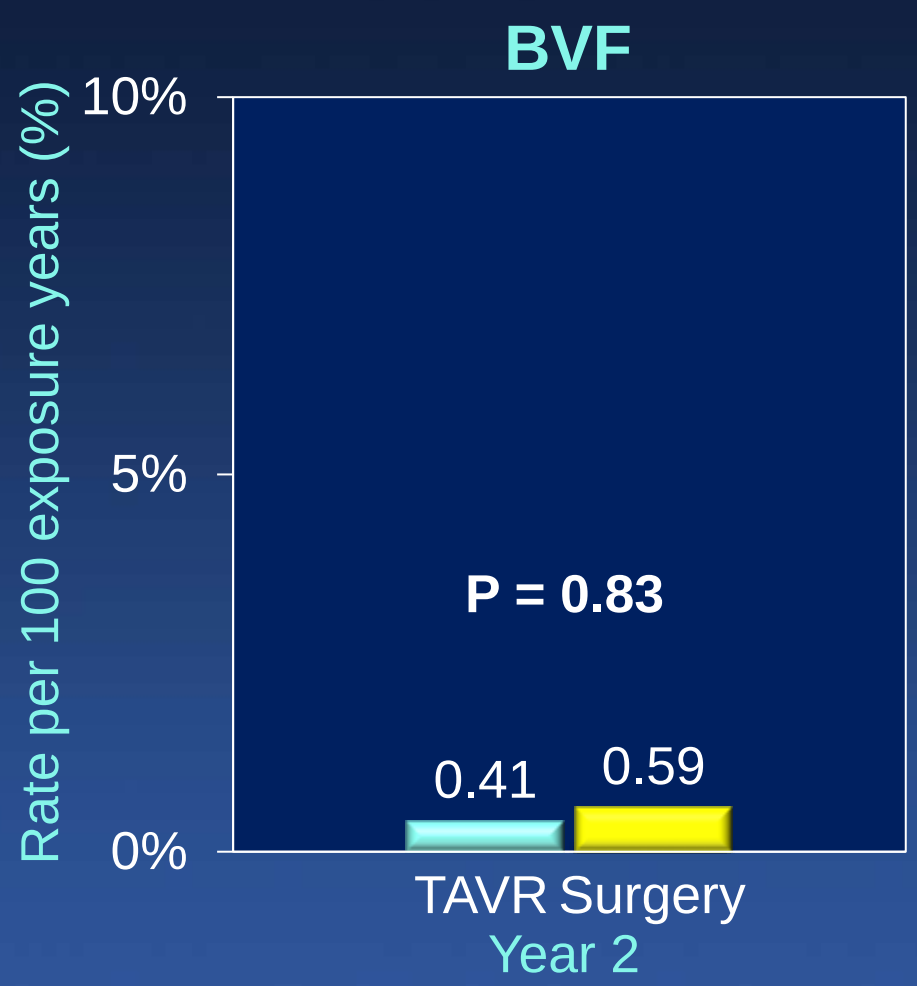


Stage 2 & 3 HVD: +Δ mean gradient ≥ 10 mmHg and -Δ AVA ≥ 0.3 cm^2 or ≥ 25%, -Δ DVI ≥ 0.1 or ≥ 20%, AND/OR ≥ 1 grade Δ transvalvular AR with final grade ≥ moderate

BVF: Re-intervention or death related to valve dysfunction OR Severe (Stage 3) SVD-related HVD

Hemodynamic Valve Deterioration & Bioprosthetic Valve Failure (VARC 3/EACTS-EAPCI) through 2 years





TAVR Long-Term Durability

Final thoughts…

- There is NO EVIDENCE of important clinical ‘catch-up’ favoring surgery through 5 years follow-up with Sapien 3 TAVR!
- Using standardized definitions and serial echos, there is also NO EVIDENCE of increased SVD or BVF associated with Sapien 3 TAVR compared to surgery (5 yrs intermediate-risk and 2 yrs low-risk)
- Nevertheless, late (> 10 yrs) follow-up is not available and even mid-term (> 1 yr) follow-up in low-risk patients is very limited. PLEASE STAY TUNED, as it will require at least another 5 years follow-up to have sufficient data to make meaningful inferences re: Sapien 3 durability!