Results of Self-Expandable CoreValve Studies

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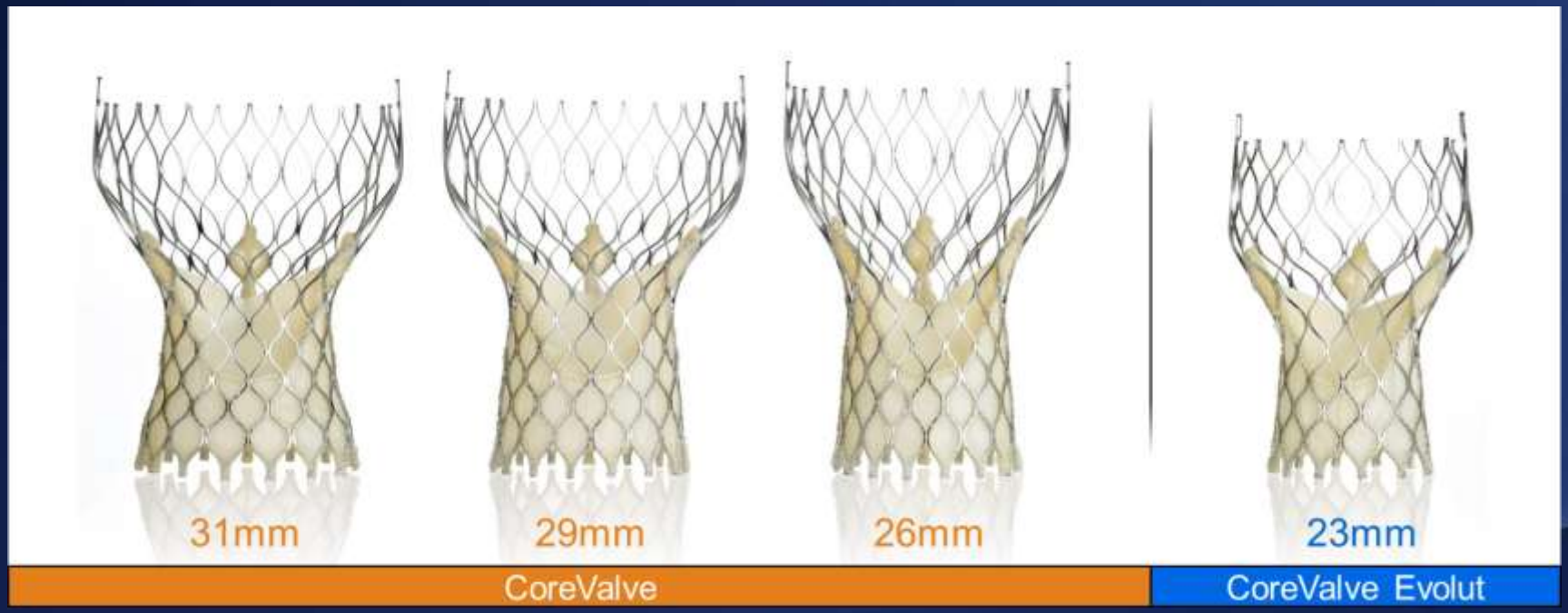
Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF Sadra Medical: E, C, SB, AB Direct Flow: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Biosensors: E, SB, C, AB Cordis: AB Abbott Vascular: AB Capella: SB, C, AB Valtech: E, SB, Claret: SB

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'

The Medtronic CoreValve System

- Implanted in more than **55,000** patients in more than **60** countries worldwide.
  - Self-expanding nitinol frame
  - Tri-leaflet porcine pericardial tissue valve with supra-annular function
  - Four sizes (23, 26, 29, and 31 mm) to fit aortic annuli ranging from 18 to 29 mm
  - 18-Fr delivery catheter for all valve sizes
  - Delivery from a transfemoral, subclavian, or direct aortic approach



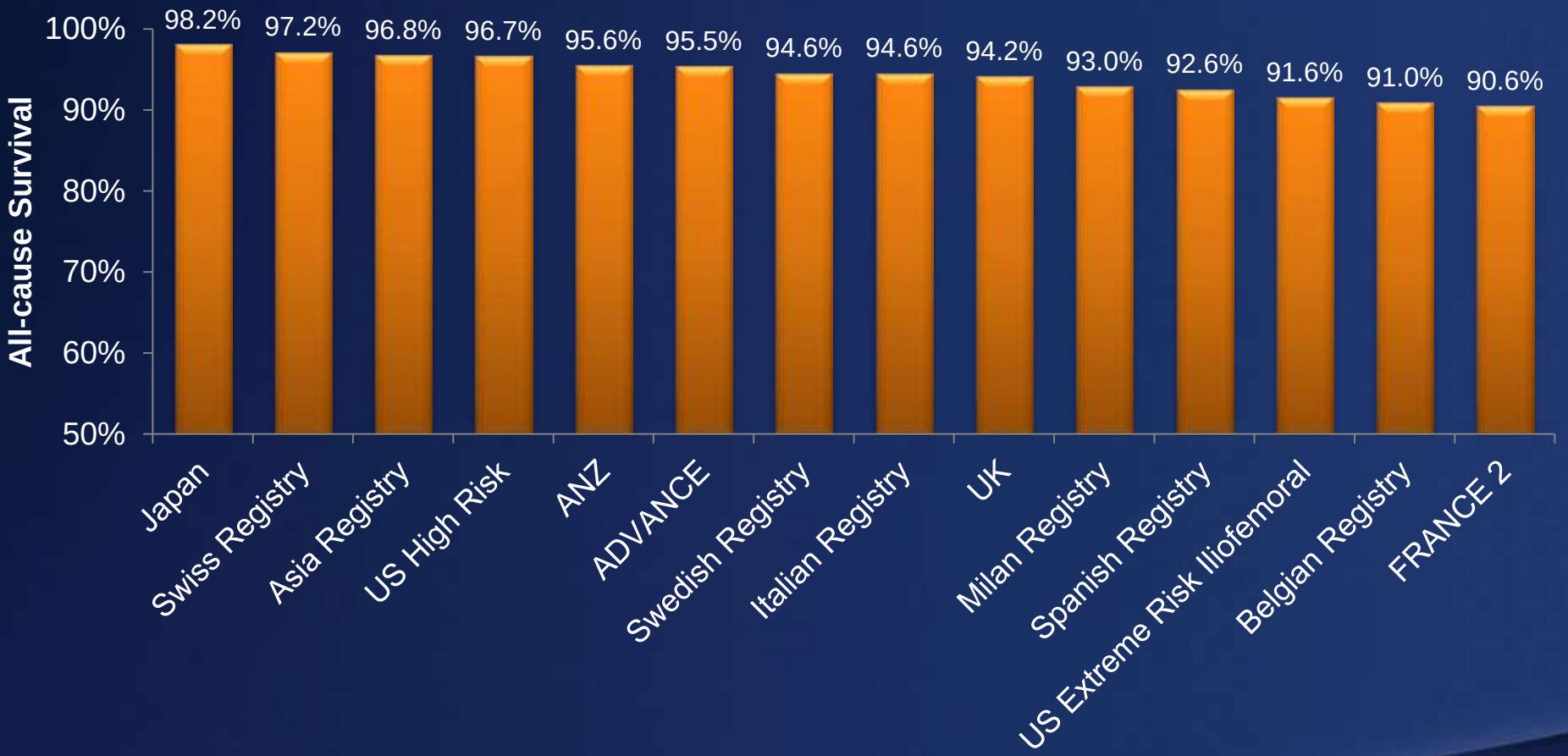
CoreValve® System Clinical Experience

National CoreValve Registries

Study	CoreValve Study Size	Number of Centers	Reported Data
FRANCE 2 Registry	1298	34	1 year
Italian Registry	1334	14	3 year
Israel Registry	867	10	3 year
UK Registry	1932	31	2 years
Belgian Registry	408	12	3 year
Brazilian Registry	360	18	5 years
Spanish Registry	108	3	6 months
Milan Registry	89	1	1 year
Asia Registry	285	14	30 days
Ibero-American Registry	1220	43	2 years
Swedish Registry	311	7	1 year
GARY	3627	74	1 year
German TAVI Registry	1071	27	30 days
Swiss TAVI Registry	336	8	30 days
TOTAL:	**>13,000**	**296**	

Global CoreValve Experience

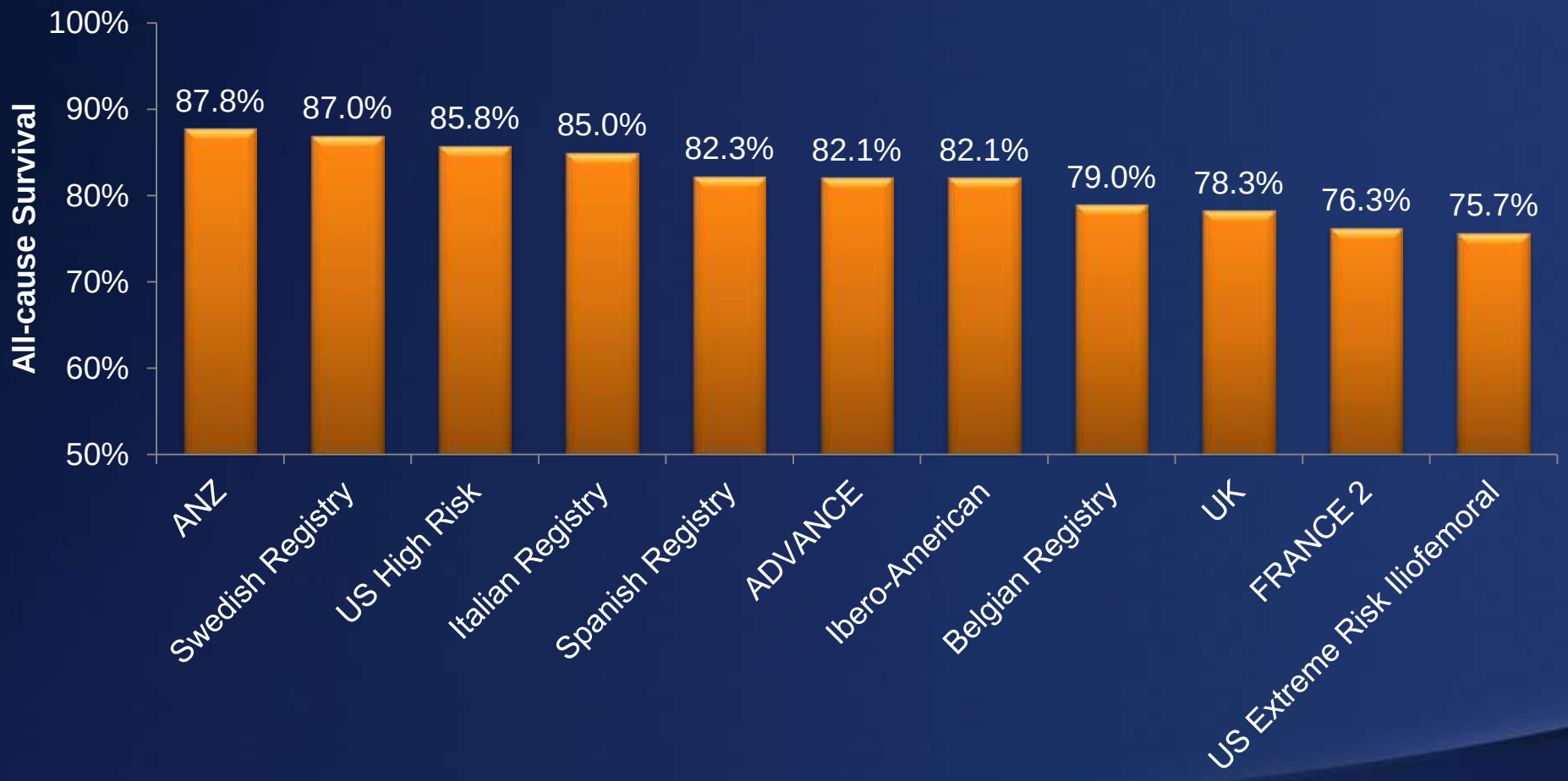
- 30-day survival in national registries and Medtronic sponsored studies
  (independent studies, not head-to-head comparisons)



[1]Sawa, et al., *Circ J* 2014; epub; [2]Wenaweser, et al., *EuroIntervention* 2014; epub; [3]Chiam, et al., presented at ACC 2014; [4]Adams, et al., *N Engl J Med* 2014; epub; [5]Meredith, et al., presented at CSANZ 2013; [6]Linke, et. al. *Eur Heart J* 2014; epub; [7]Rueck, et al., presented at London Valves 2012; [8]Tamburino, et al., *Circulation* 2011; 123: 299-308; [9]Moat, et al. *J Am Coll Cardiol* 2011; 58(20): 2130-38; [10]Godino, et al., *J Am Coll Cardiol Intv* 2010; 3: 1110-21; [11]Avanzas, et al., *Rev Esp Cardiol* 2010; 63(2): 141-8; [12]Popma, et al., *J Am Coll Cardiol* 2014; epub; [13]Bosmans, et al., *ICVTS* 2011; 12: 762-7; [14]Gilard, et al. *N Engl J Med* 2012; 366: 1705-15

Global CoreValve Experience

- 1-year survival in national registries and Medtronic sponsored studies
  (independent studies, not head-to-head comparisons)



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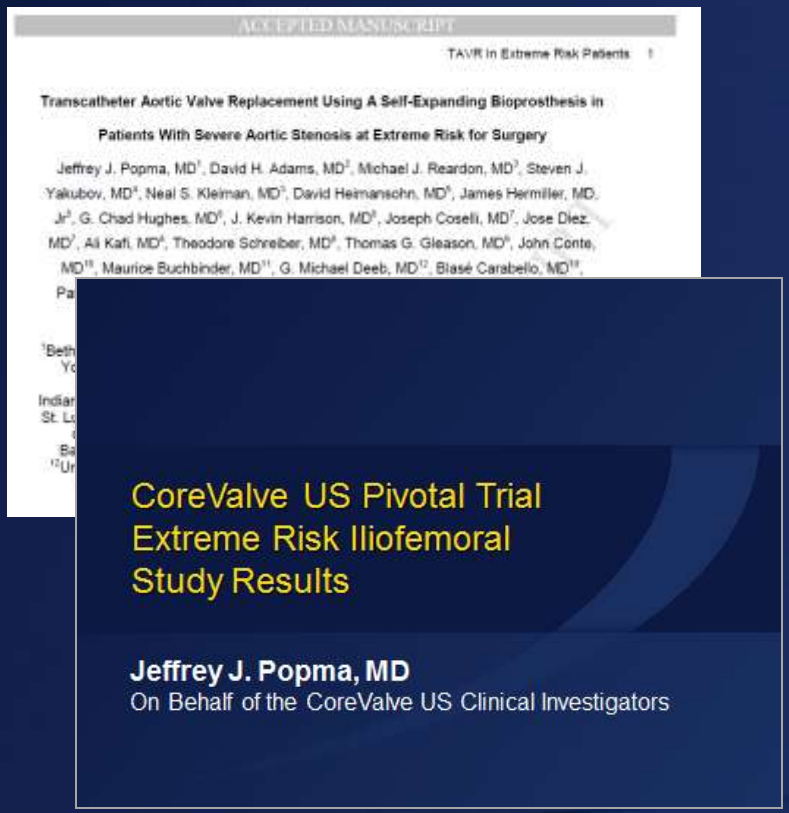
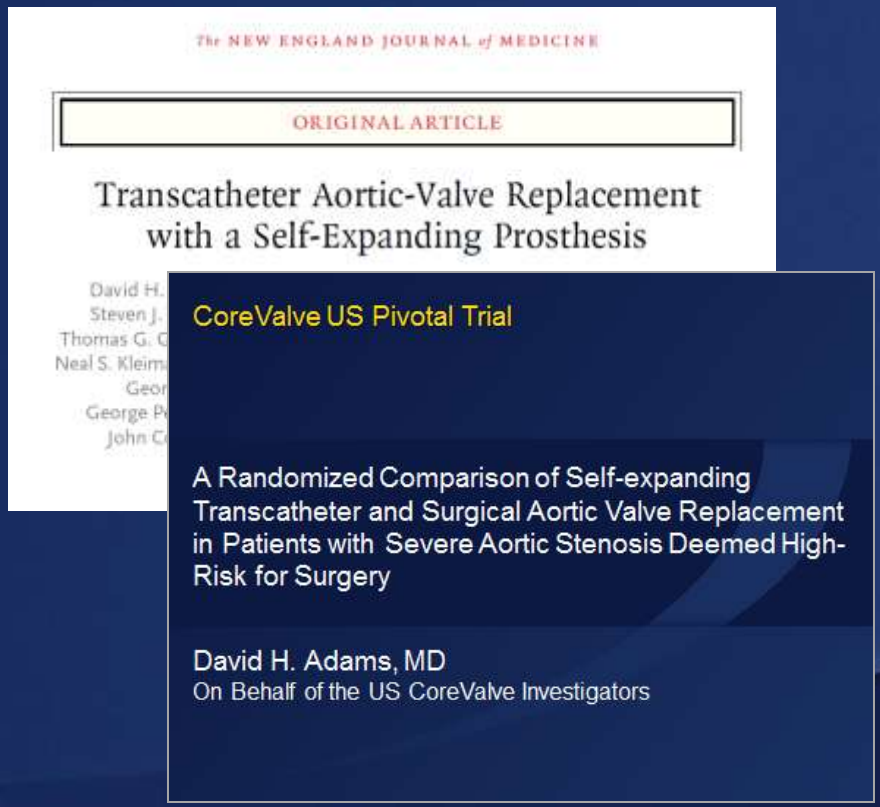
Recent Clinical Evidence

- One year outcomes from the CoreValve US Pivotal Trial Extreme Risk and High Risk studies have been recently reported at TCT 2013 and ACC 2014 and published in JACC and NEJM





Recent Clinical Evidence

- Additionally, one year outcomes from the CoreValve ADVANCE Study were published in European Heart Journal

European Heart Journal Advance Access published March 28, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu162

FASTTRACK CLINICAL RESEARCH
Tavi

Treatment of aortic stenosis with a self-expanding transcatheter valve: the International Multi-centre ADVANCE Study

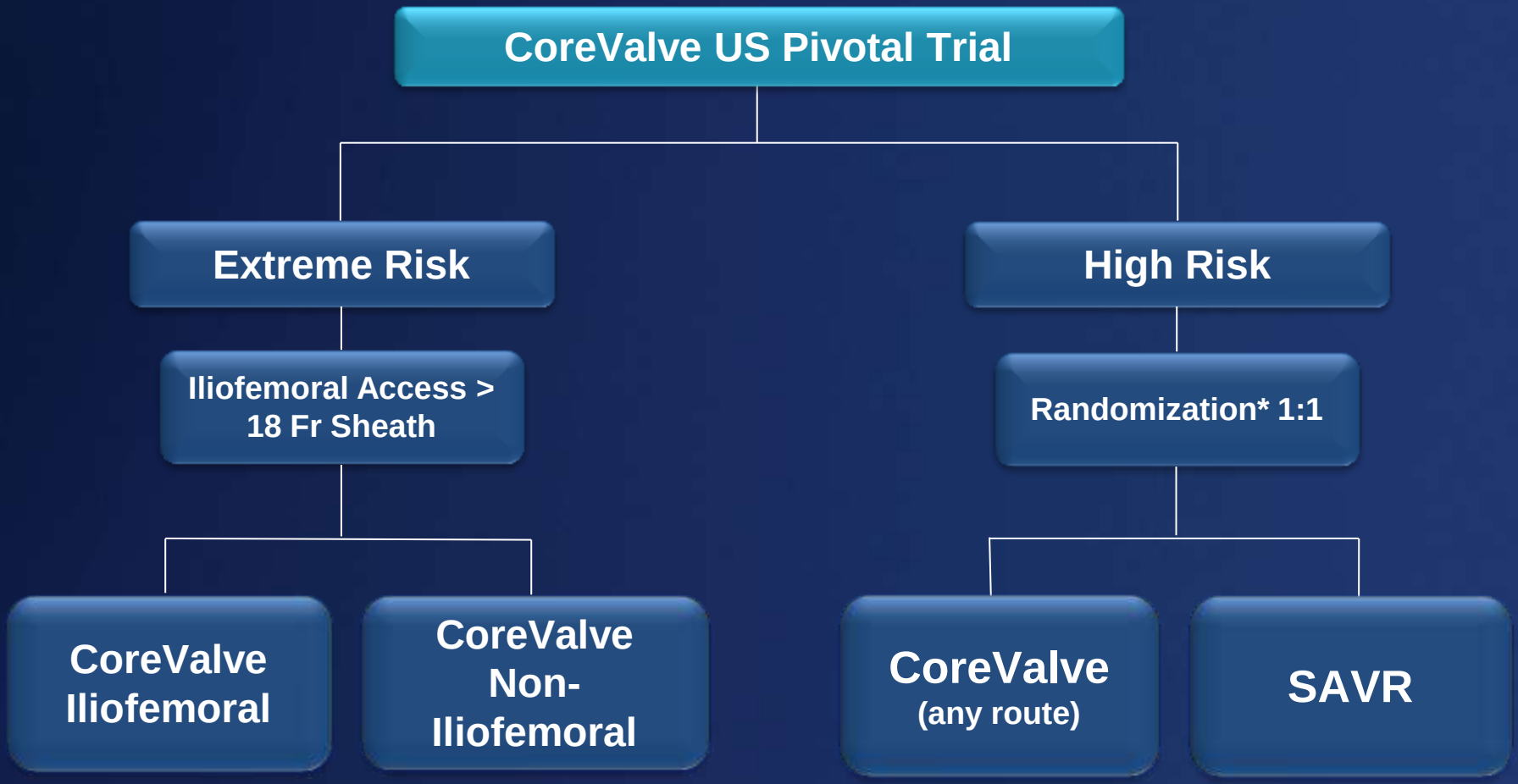
Axel Linke[1]*, Peter Wenaweser[3], Ulrich Gerckens[4], Corrado Tamburino[5], Johan Bosmans[6], Sabine Bleiziffer[7], Daniel Blackman[8], Ulrich Schäfer[9], Ralf Müller[10], Horst Sievert[11], Lars Søndergaard[12], Silvio Klugmann[13], Rainer Hoffmann[14], Didier Tchétché[15], Antonio Colombo[16], Victor M. Legrand[17], Francesco Bedogni[18], Pascal lePrince[19], Gerhard Schuler[1], Domenico Mazzitelli[7], Christos Eftychiou[8], Christian Frerker[9], Peter Boekstegers[10], Stephan Windecker[3], Friedrich-Wilhelm Mohr[2], Felix Woitek[1], Rüdiger Lange[7], Robert Bauernschmitt[20], and Stephen Brecker[21], For the ADVANCE study Investigators

CoreValve ADVANCE Study

ADVANCE Study | Summary and Conclusions

- Medtronic CoreValve ADVANCE is one of the largest “real world” TAVI trials performed in multiple experienced centres.
- 1-year outcomes demonstrate
  - low stroke rates at 1-year
  - low rates of AR and PVL at 1-year
  - mild AR with the same low mortality rate as those patients with no AR
  - improved valve performance
- 2-year patient survival rates continues to remain high

Pivotal Trial Design



* Randomization stratified by intended access site

CoreValve US Pivotal Trial
Extreme Risk

Extreme Risk | Baseline Demographics

Characteristic	N=489
Age, years	83.2 ± 8.7
Men, %	47.9
STS Predicted Risk of Mortality, %	10.3 ± 5.5
Logistic EuroSCORE, %	22.6 ± 17.1
New York Heart Association (NYHA)	
NYHA Class III/IV, %	91.8
Diabetes Mellitus, %	41.5
Insulin Requiring Diabetes, %	18.4
Prior Stroke, %	13.7
Modified Rankin 0 or 1, %	70.7
Modified Rankin > 1, %	29.3

Extreme Risk | Baseline Co-Morbidities

Co-Morbidity Assessment	N=489
Any Chronic Lung Disease (STS Criteria), %	58.8
Moderate, %	15.3
Severe*, %	23.5
Home Oxygen, %	29.9
FEV1 ≤ 1000 cc, %	23.7
Diffusion Capacity < 50%, %	22.3
Charlson Co-Morbidity Score**, %	5.3 ± 2.3
Moderate (3, 4), %	32.9
Severe (≥ 5), %	58.7

*STS Criteria: Severe = FEV1 < 50% predicted and/or RA pO_2 < 60 or pCO_2 > 50

**Charlson Score: = 1 MI, CHF, PVD, CVD, dementia, chronic lung disease, connective tissue disease, ulcer, mild liver disease, DM; = 2 hemiplegia, mod-severe kidney disease, diabetes with end organ damage, leukemia, lymphoma; = 3 moderate or severe liver disease; = 6 metastatic solid tumor, AIDS

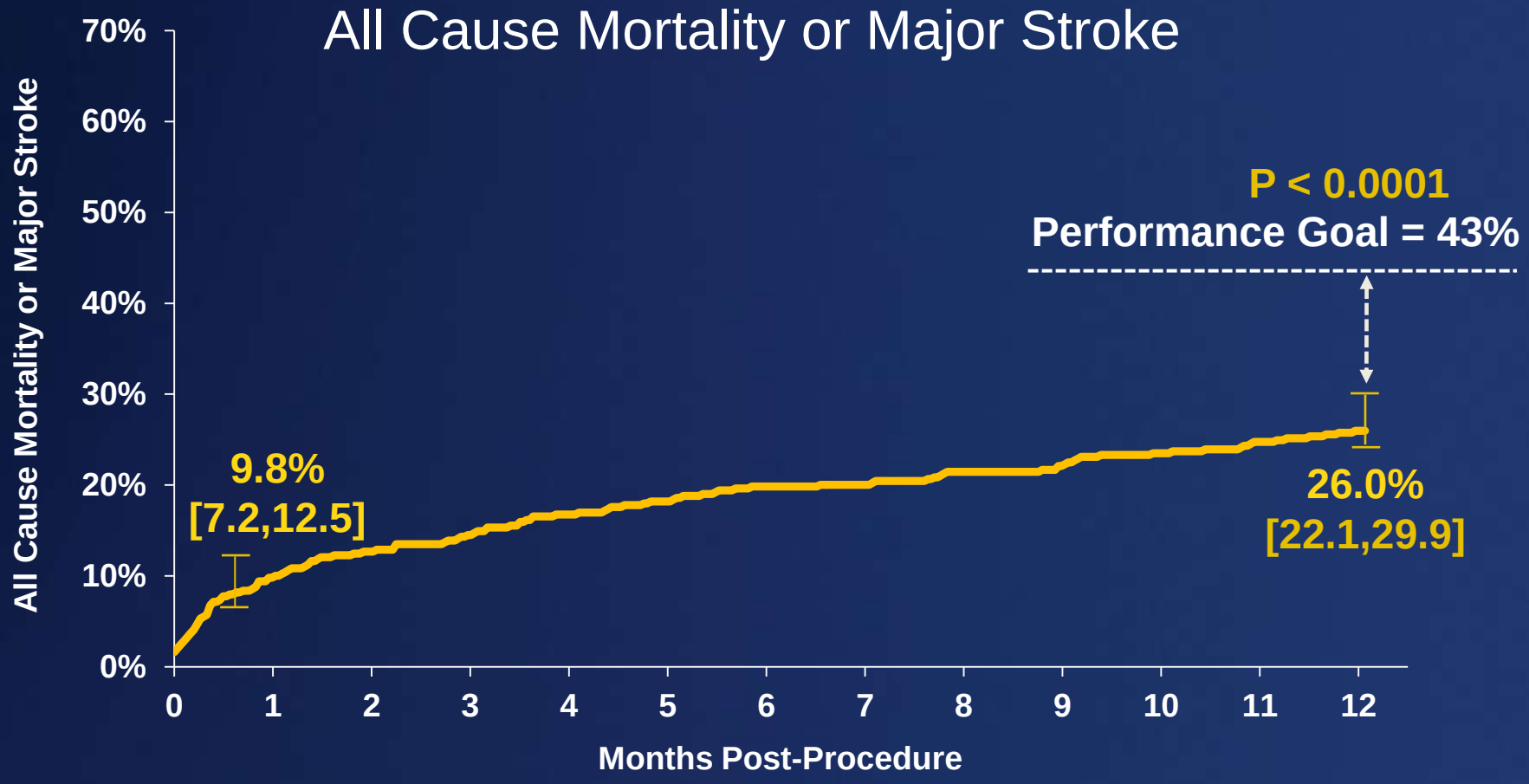
Extreme Risk | Baseline Frailty Assessment

Frailty Characteristic	N=489
Anemia With Prior Transfusion, %	22.8
BMI < 21 kg/m^2, %	8.6
Albumin < 3.3 g/dL, %	18.2
Unplanned Weight Loss > 10 pounds, %	12.5
Falls in Past 6 Months, %	18.0
5 Meter Gait Speed > 6 secs, %	84.2
Grip Strength < Threshold, %	67.7

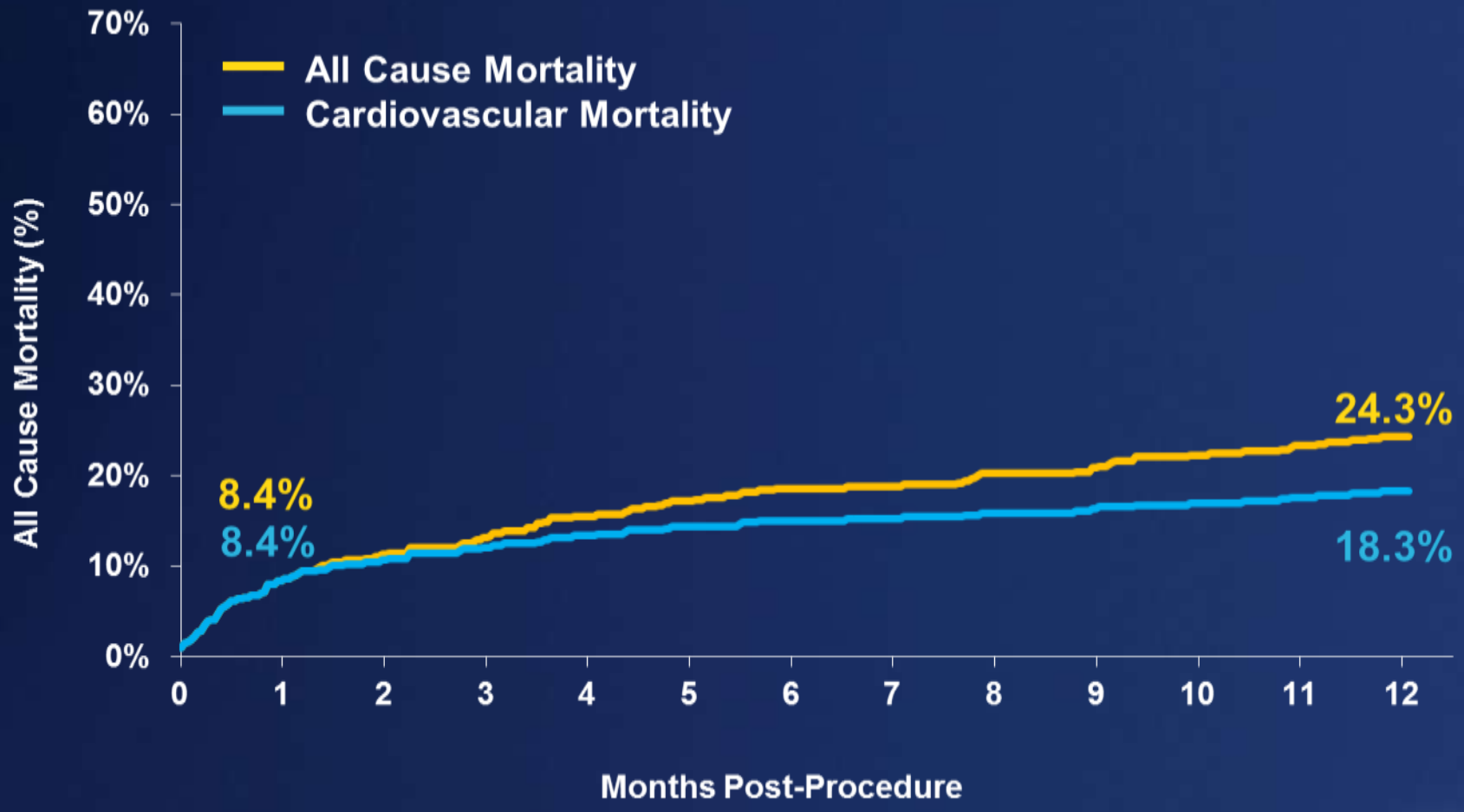
Extreme Risk | Baseline Disabilities Assessment

Disability Factors	N=489
Assisted Living, %	27.6
Katz Score (Index of ADLs), %	
≥ 1 ADLs Deficits, %	28.0
≥ 2 ADLs Deficits, %	20.7
≥ 3 ADLs Deficits, %	13.9
Mini-Mental Score (MMSE Score 0–30)	26.0 ± 3.1
Dementia (Based on MMSE)	
None (≥ 25), %	72.1
Mild (21–24), %	23.0
Moderate or Severe (< 20), %	4.9
Wheelchair Bound, %	16.6

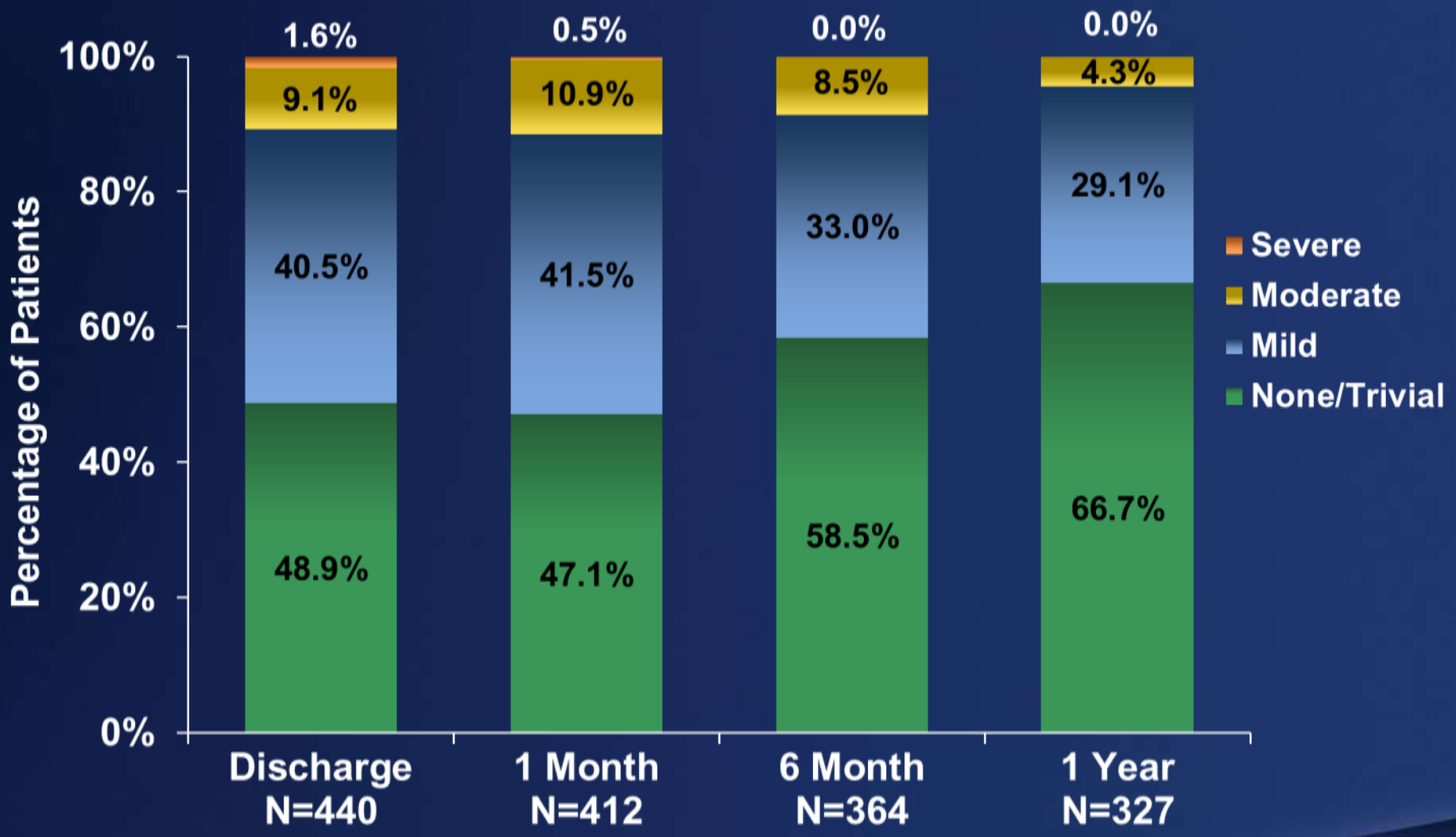
Extreme Risk | Primary Endpoint



Extreme Risk | 1 Year Mortality

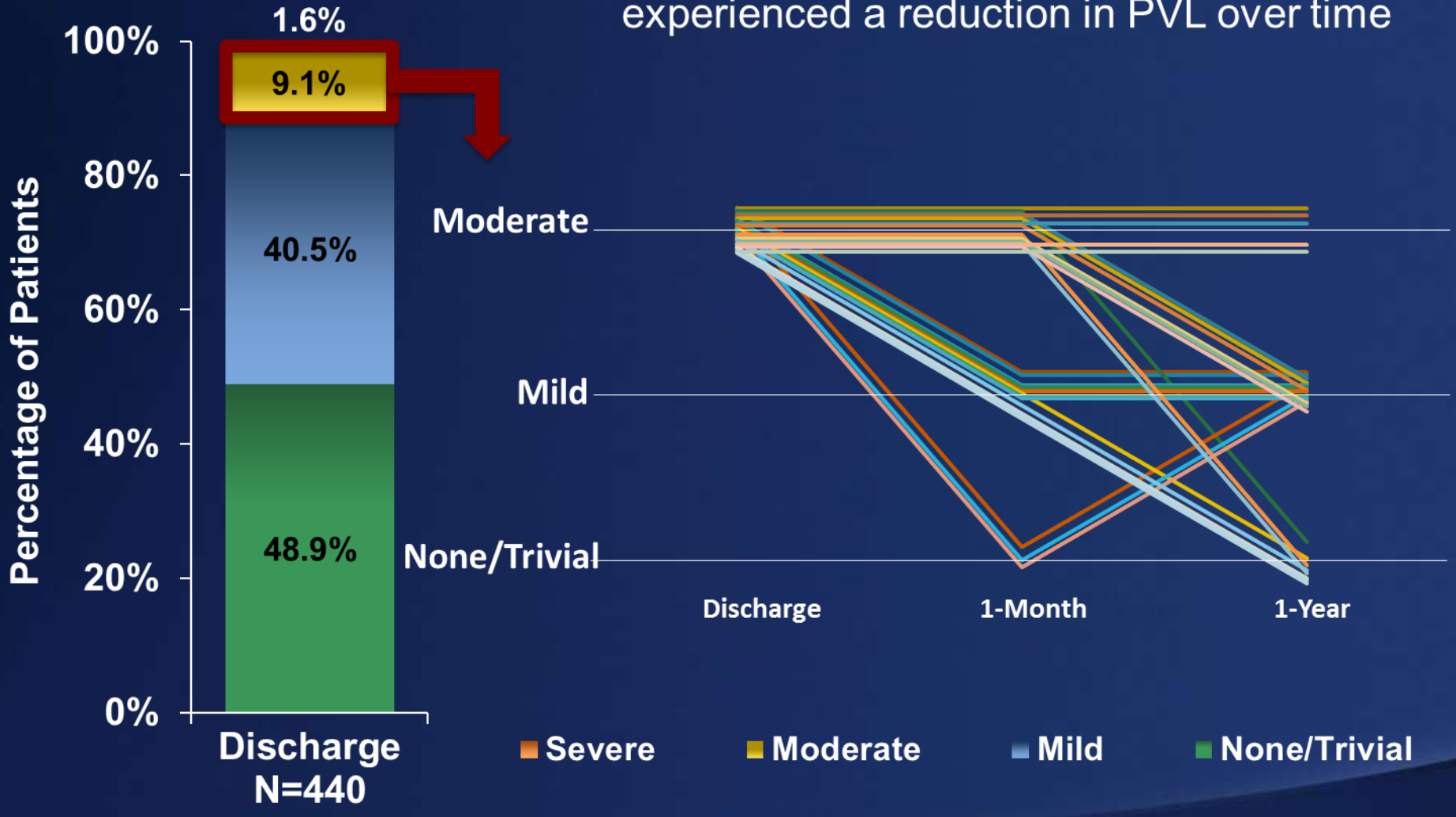


Extreme Risk | Paravalvular Regurgitation



Extreme Risk | Paravalvular Regurgitation

83% of patients with moderate PVL at discharge who survived to one year experienced a reduction in PVL over time



CoreValve US Pivotal Trial
High Risk

High Risk | Baseline Demographics

Characteristic	TAVR N=390	SAVR N=357
Age, years	83.1 ± 7.1	83.2 ± 6.4
Men, %	53.1	52.4
STS Predicted Risk of Mortality, %	7.3 ± 3.0	7.5 ± 3.4
Logistic EuroSCORE, %	17.7 ± 13.1	18.6 ± 13.0
NYHA Class III/IV, %	85.6	86.8
Prior Coronary-artery Bypass Surgery	29.5	31.1
Diabetes Mellitus, %	34.9*	45.4*
Insulin Requiring Diabetes, %	11.0	13.2
Prior Stroke, %	12.6	14.0
Modified Rankin 0 or 1, %	74.5	87.2
Modified Rankin > 1, %	25.5	12.8
STS Severe Chronic Lung Disease, %	13.3	9.0

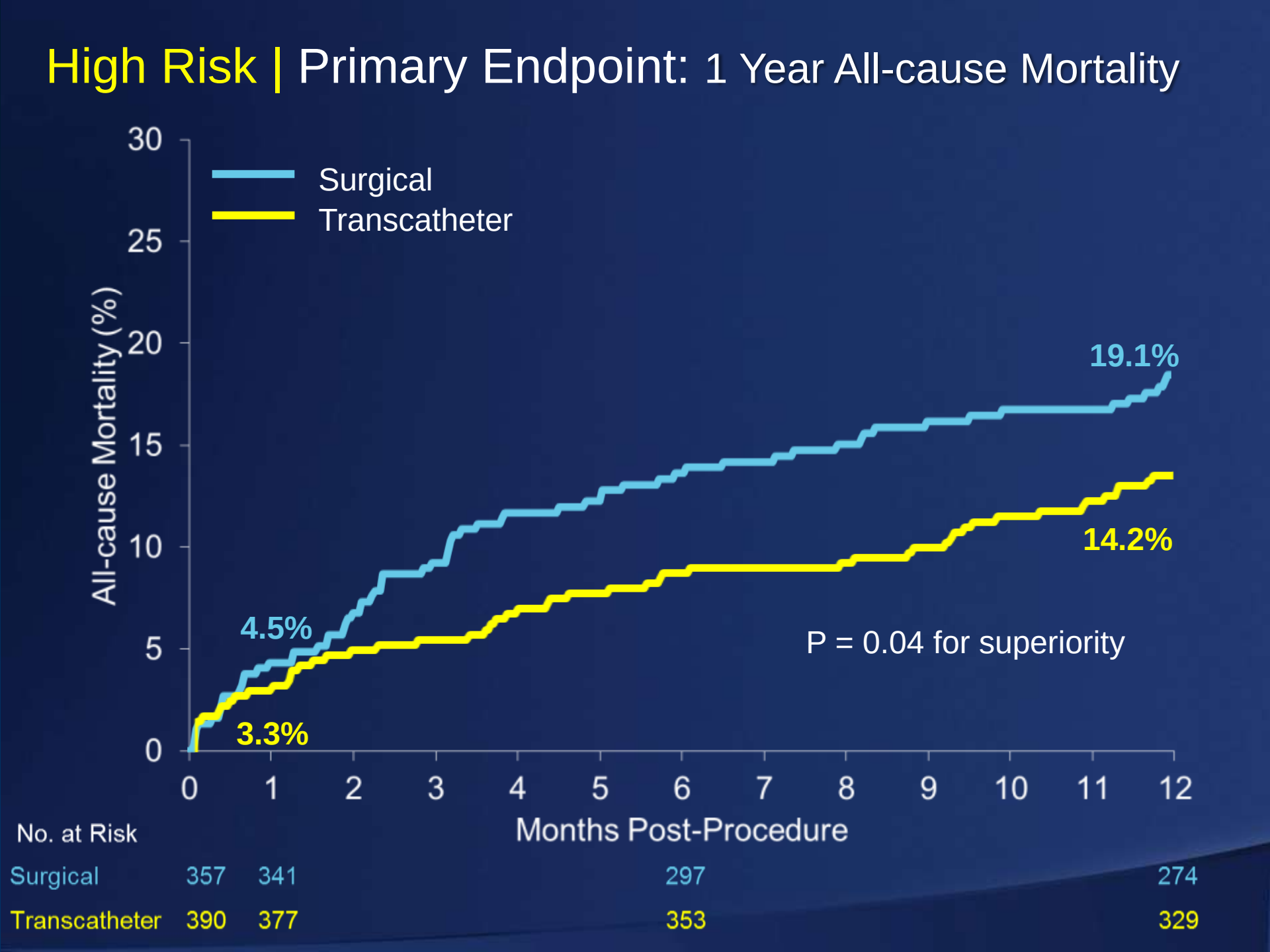
*P < 0.01

High Risk | Non-STS Co-Morbidity, Frailty, Disability

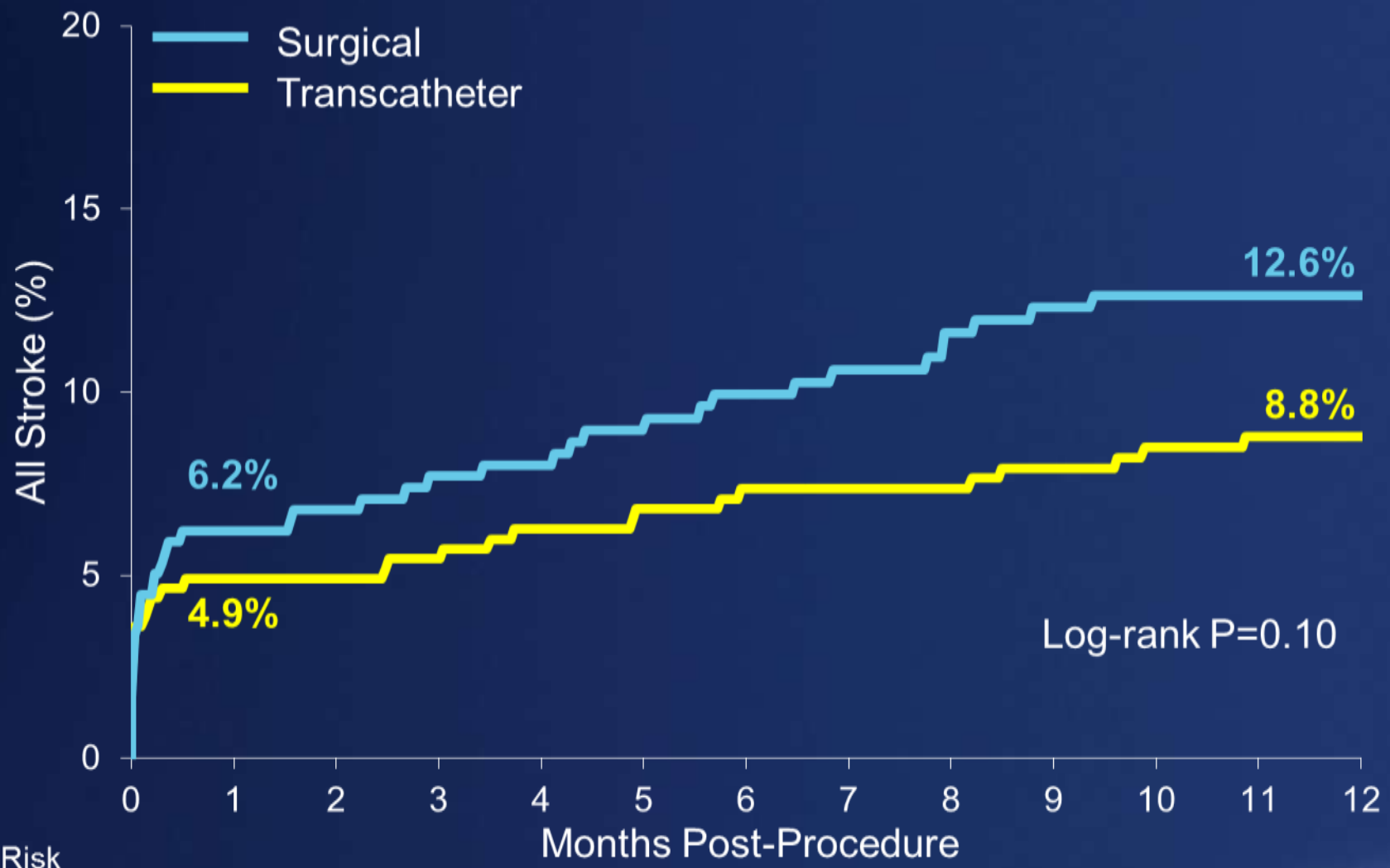
Assessment	TAVR N=390	SAVR N=357
Home Oxygen, %	12.9	11.5
Liver Cirrhosis, %	2.6	2.0
Anemia With Prior Transfusion, %	18.2	15.9
Severe (> 5) Charlson Co-Morbidity*, %	54.1	57.9
Falls in Past 6 Months, %	18.5	18.2
5 Meter Gait Speed > 6 secs, %	79.3	80.4
Assisted Living, %	9.7	10.9
Katz ≥ 1 ADLs Deficits, %	10.5	12.3

*Charlson Score: = 1 MI, CHF, PVD, CVD, dementia, chronic lung disease, connective tissue disease, ulcer, mild liver disease, DM; = 2 hemiplegia, mod-severe kidney disease, diabetes with end organ damage, leukemia, lymphoma; = 3 moderate or severe liver disease; = 6 metastatic solid tumor, AIDS

High Risk | Primary Endpoint: 1 Year All-cause Mortality



High Risk | All Stroke



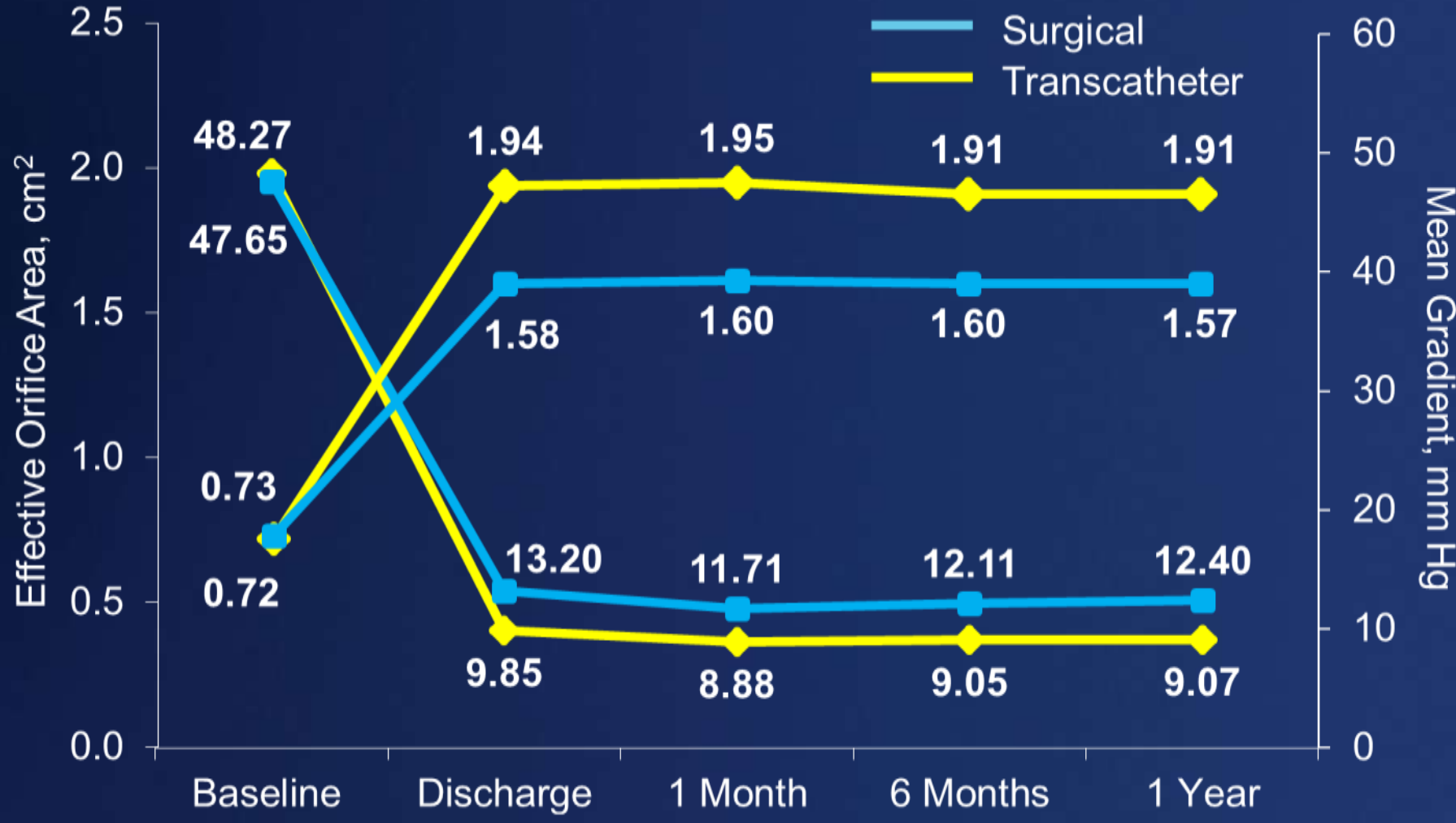
No. at Risk				
Surgical	357	322	274	249
Transcatheter	390	363	334	314

High Risk | Other Endpoints

Events*	1 Month			1 Year		
	TAVR	SAVR	P Value	TAVR	SAVR	P Value
Vascular complications (major), %	5.9	1.7	0.003	6.2	2.0	0.004
Pacemaker implant, %	19.8	7.1	<0.001	22.3	11.3	<0.001
Bleeding (life threatening or disabling),%	13.6	35.0	<0.001	16.6	38.4	<0.001
New onset or worsening atrial fibrillation, %	11.7	30.5	<0.001	15.9	32.7	<0.001
Acute kidney injury, %	6.0	15.1	<0.001	6.0	15.1	<0.001

* Percentages reported are Kaplan-Meier estimates and log-rank P values

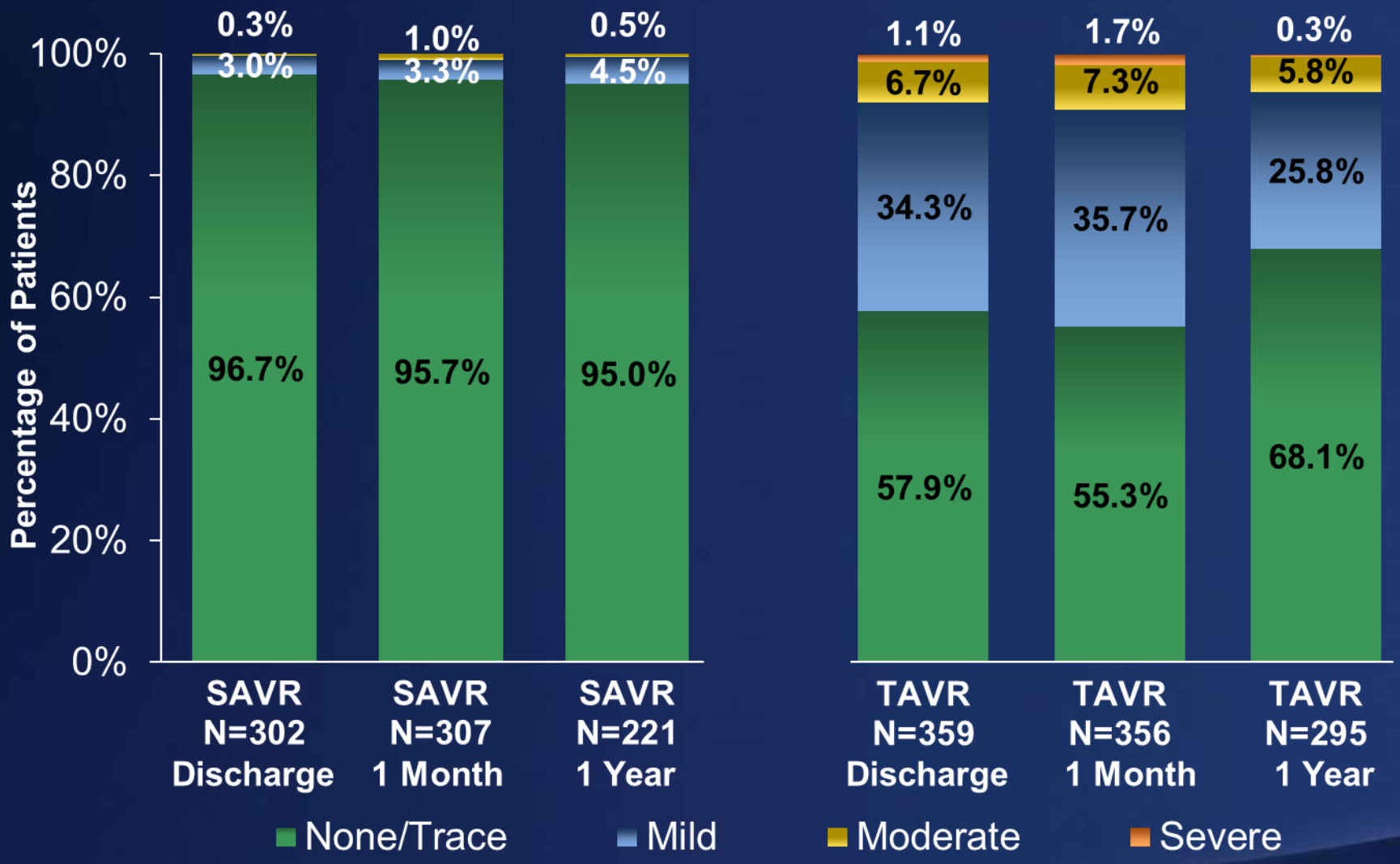
High Risk | Echocardiographic Findings



Post implant, there were significant differences ($P < 0.001$) between TAVR and SAVR at each time point for both EOA and mean gradient.

High Risk | Paravalvular Regurgitation

76.2% TAVR patient with moderate/severe at discharge had improved PVL by 1 Year



There was significantly lower PVL with SAVR over TAVR at each time point (P<0.001)

Summary CoreValve US Pivotal Trial Extreme and High Risk

CoreValve US Pivotal Trial | Conclusions

- Both the Extreme and High Risk studies showed constant performance of the CoreValve prosthesis
  - improved and stable valve function through one year
  - low rates of major stroke at 1 month and one year
  - low rates of moderate/severe aortic regurgitation that improved over time

CoreValve US Pivotal Trial | Conclusions

- The results from the US CoreValve Pivotal Trial support the safety and efficacy of the CoreValve prosthesis in patients
  - who are deemed unsuitable for surgical aortic valve replacement and,
  - who are at increased surgical risk

- Survival at 1 year was superior surgical valve replacement in patients that underwent transcatheter replacement with CoreValve prosthesis

Thank you very much for Your Attention!