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Transcatheter Aortic Valve Implantation vs. Surgical Aortic Valve Replacement In Patients At Low To Intermediate Risk

One Year Outcomes Of The Randomized DEDICATE-DZHK6 Trial

Moritz Seiffert, MD

On behalf of the DEDICATE-DZHK6 investigators

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Disclosures

Within the past 24 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Financial relationship	Company
Speaker‘s Bureau	Amgen, AstraZeneca, BMS/Pfizer, Boston Scientific, Daiichi Sankyo, Edwards Lifesciences, Inari Medical, Medtronic, Siemens Healthineers

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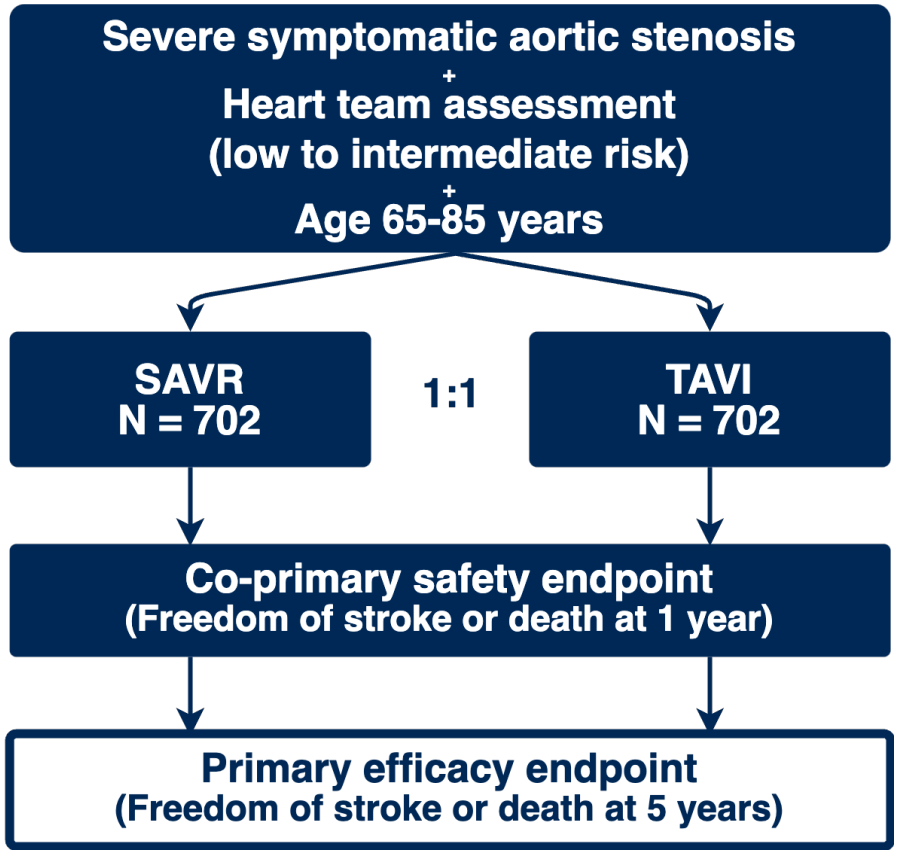
Background

- TAVI has become the preferred treatment for most patients with symptomatic severe aortic-valve stenosis
- Current evidence for young low-risk patients restricted to device-specific and industry-sponsored trials, potentially limiting applicability to routine practice
- In low-risk patients, eligible for TAVI or SAVR and with unrestricted access to contemporary devices, optimal treatment strategy remains unknown

DEDICATE Study Design



- Independent investigator-initiated trial
- Evaluation of treatment strategies
- All contemporary devices allowed
- Procedures and periprocedural management according to local best practice to reflect routine medical care

https://www.clinicaltrials.gov/study/NCT03112980

DEDICATE Study Design

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Main Inclusion Criteria

- ✓ Severe symptomatic aortic stenosis
- ✓ Age: **65-85 years**
- ✓ **Low or intermediate operative risk***
- ✓ Eligible for both **TAVI and SAVR***

*** According to Heart team assessment**

Main Exclusion Criteria

Congenital **bicuspid/unicuspid** or non-calcified aortic valve, endocarditis

Cardiac **reoperation**

Relevant CAD or PCI w/in 1 month

Severe **mitral or tricuspid valve disease**

Severely impaired LV function (**LVEF <20%**)

Stroke/ICB w/in 1 month

Contraindication for **isolated aortic valve procedure**

DEDICATE Enrolling Sites

Universitäres Herz- und Gefäßzentrum Hamburg (190)
Kerckhoff-Klinik Bad Nauheim (151)
Herzzentrum Leipzig – Universität Leipzig (121)
Deutsches Herzzentrum Charité Berlin including Vivantes Berlin (93)
Universitätsklinikum Schleswig-Holstein, Campus Kiel (75)
Universitätsklinikum Heidelberg (73)
Universitäts-Herzzentrum Freiburg-Bad Krozingen (Bad Krozingen) (68)
Herz- und Diabeteszentrum NRW Bad Oeynhausen (65)
Deutsches Herzzentrum München (51)
Universitätsklinikum Schleswig-Holstein, Campus Lübeck (46)
Universitätsklinikum an der TU Dresden (45)
Universitätsklinikum Regensburg (41)
Charité Universitätsmedizin Berlin (Campus Benjamin-Franklin) (36)
Universitätsklinikum Frankfurt (32)
Universitätsklinikum Köln (28)
Universitätsklinikum Münster (27)
Universitätsklinikum Gießen und Marburg (Gießen) (23)
Universitätsklinikum Göttingen (22)
LMU Klinikum der Universität München (21)
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Immanuel Klinikum Bernau Herzzentrum Brandenburg (15)
Robert-Bosch-Krankenhaus Stuttgart (14)
Charité Universitätsmedizin Berlin (Campus Mitte) (13)
Universitätsklinikum Halle (Saale) (13)
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RWTH Aachen (12)
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Universitätsklinikum Ulm (12)
Universitätsklinikum Düsseldorf (9)
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Universitätsklinikum Brandenburg (8)
Universitäts-Herzzentrum Freiburg-Bad Krozingen (Freiburg) (8)
Universitätsmedizin Mainz (5)
BG Universitätsklinikum Bergmannsheil Bochum (4)
Universitätsmedizin Greifswald / Klinikum Karlsburg (2)
Universitätsklinikum Essen (0)

Trial Management, Boards and Committees

Principal Investigators

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Cremer, J (Kiel)

Coordinating Investigator

Seiffert, M (Hamburg, Bochum)

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Choi, YH (Bad Nauheim)

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Trial management

UHZ Hamburg (Hamburg)

Data management

German Center for Cardiovascular Research (DZHK), partner site North

Echocardiographic Corelab

Hagendorff, A (Leipzig)

Funding

German Center for Cardiovascular Research (DZHK)

German Heart Foundation

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Primary Outcome

Composite of death from any cause or stroke within 1 year after randomization

(Co-primary safety endpoint)

- **Primary analysis performed for non-inferiority of TAVI vs. SAVR**
- **Evaluated in intention-to-treat population (ITT), validated in as-treated dataset (AT)**
- **Stratification by STS-PROM score**
- **Events assessed by a blinded event adjudication committee**
- **Definitions according to the Valve Academic Research Consortium (VARC-2)**

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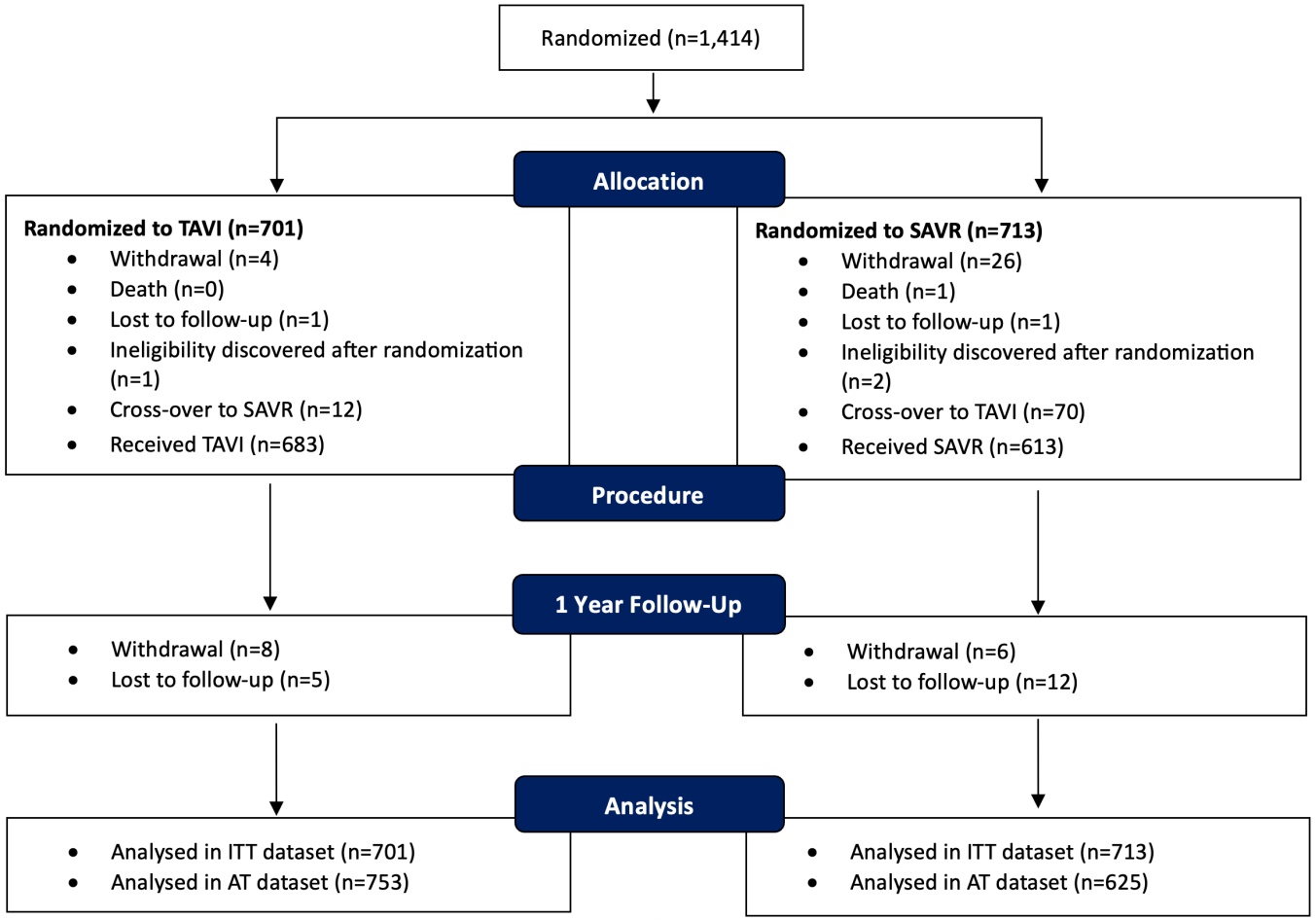
Statistics – Power Considerations

- Assumed event rate, i.e., overall incidence of the primary outcome : 6.2%
- Non-inferiority margin: hazard ratio of 1.14 for TAVI vs. SAVR
  (rejectable absolute between-group difference at 1 year: 1%)
- Sample size: approx. 1,404 patients for a power of 80% to reject the non-inferiority margin at 1 year for alternative hazard ratio of 0.67 when censoring is at 10%

Patient Allocation and Follow-up



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Baseline Patient Characteristics

	TAVI (n=701)	SAVR (n=713)
Age (years)	74.3 ± 4.6	74.6 ± 4.2
Male sex (%)	56.0%	57.3%
BMI (kg/m^2)	28.1 (25.3 - 31.9)	28.1 (25.4 - 31.2)
STS-PROM (%)	1.8 (1.2 - 2.4)	1.9 (1.2 - 2.5)
EuroSCORE II (%)	2.1 ± 1.4	2.1 ± 1.8
NYHA Class III/IV	46.2%	45.6%
LV-EF (%)	57.8 ± 9.8	57.7 ± 9.3
Diabetes mellitus	33.8%	32.8%
Coronary artery disease	34.3%	38.2%

Mean ± SD or median and interquartile range, Intention-to-treat population

Baseline Patient Characteristics (continued)

	TAVI (n=701)	SAVR (n=713)
Peripheral vascular disease	4.9%	6.5%
Cerebrovascular disease	4.0%	4.5%
Previous stroke	6.1%	6.0%
Atrial fibrillation	28.9%	27.4%
COPD	14.5%	16.9%
Pulmonary hypertension	12.1%	10.6%
Permanent pacemaker	5.3%	5.0%
Left bundle branch block	7.8%	7.9%
Right bundle branch block	9.6%	9.5%

Mean ± SD or median and interquartile range, Intention-to-treat population

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Procedural Characteristics

	TAVI (n=752)	SAVR (n=625)
Conscious sedation or Local anesthesia	75.1%	–
Transfemoral access	97.3%	–
Partial sternotomy	–	38.7%
Balloon-expandable THV	61.4%	–
Self-expanding THV	35.1%	–
Stented SAVR	–	77.4%
Sutureless SAVR	–	15.8%
Cerebral embolic protection	5.1%	–

Mean ± SD or median and interquartile range, As-treated population

Procedural Characteristics (continued)

	TAVI (n=752)	SAVR (n=625)
Procedure time (min)	48 (35 - 65)	165 (136 - 201)
Dose-area-product (cGy*cm²)	2,375 (764 - 5,552)	–
Contrast medium (ml)	100 (69 - 140)	–
Extracorporeal circulation (min)	–	88 (72 - 108)
Aortic cross clamp (min)	–	61 (50 - 75)
Concomitant procedures		
CABG	–	1.8%
Ascending aorta repl.	–	1.0%
MV/TVsurgery	–	0.5%
ICU stay (days)	1 (1 - 2)	2 (1 - 4)
Hospital stay (days)	5 (4 - 7)	9 (8 - 12)

Mean ± SD or median and interquartile range, As-treated population

Procedural Complications

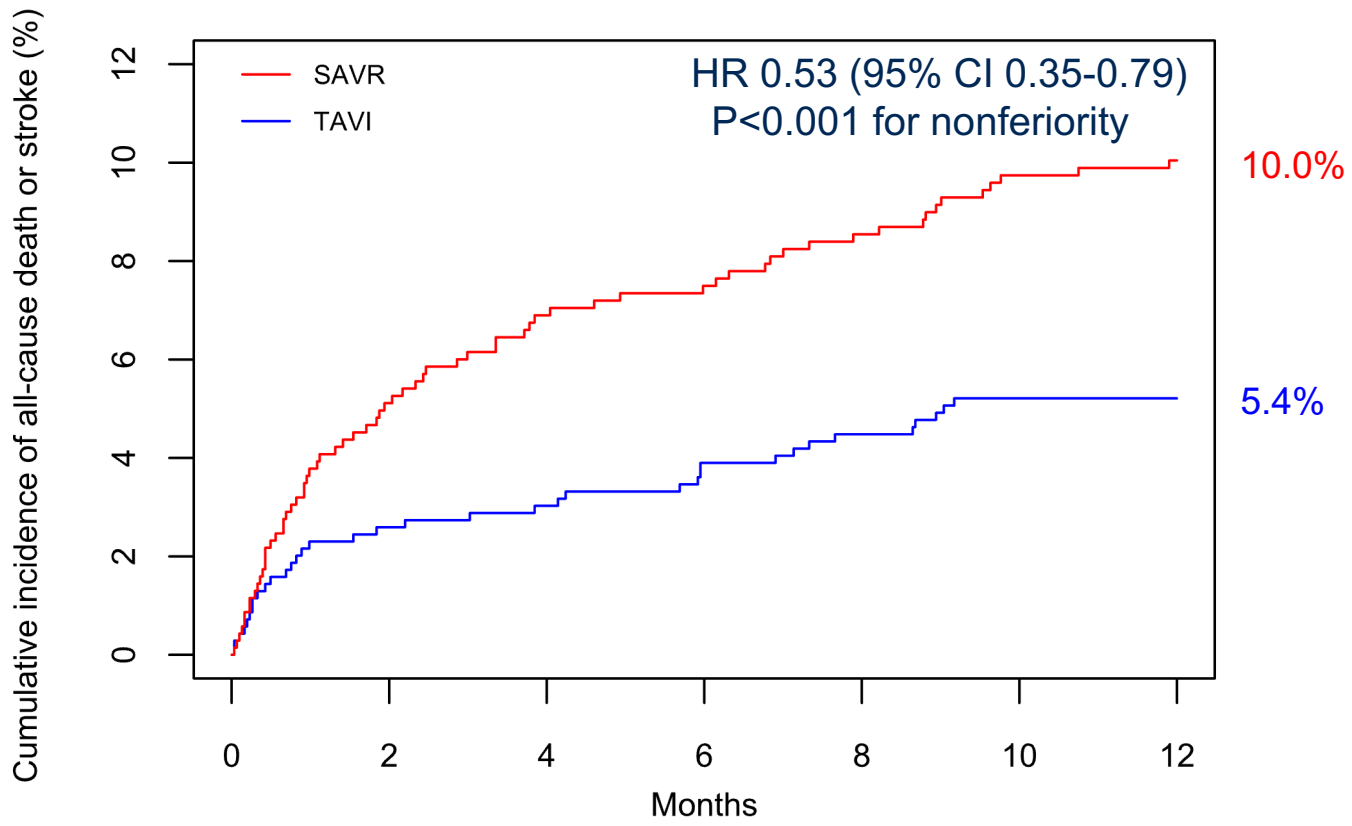
	TAVI (n=752)	SAVR (n=625)
Conversion to open heart surgery *	0.8% (6)	–
Implantation of a 2nd valve prosthesis	0.4% (3)	–
Pericardial tamponade	0.5% (4)	0.5% (3)
Coronary obstruction	0.1% (1)	0.3% (2)
Prosthesis malposition or embolization **	0.8% (6)	–

* Conversion to open-heart surgery due to valve embolization (n=3), wire-induced perforation (n=2) or annulus rupture (n=1).

** Prosthesis malposition or embolization resulted in conversion to open-heart surgery (n=3) or implantation of a 2nd valve prosthesis (n=3).

Mean ± SD or median and interquartile range, As-treated population

Primary Outcome: All-Cause Death or Stroke

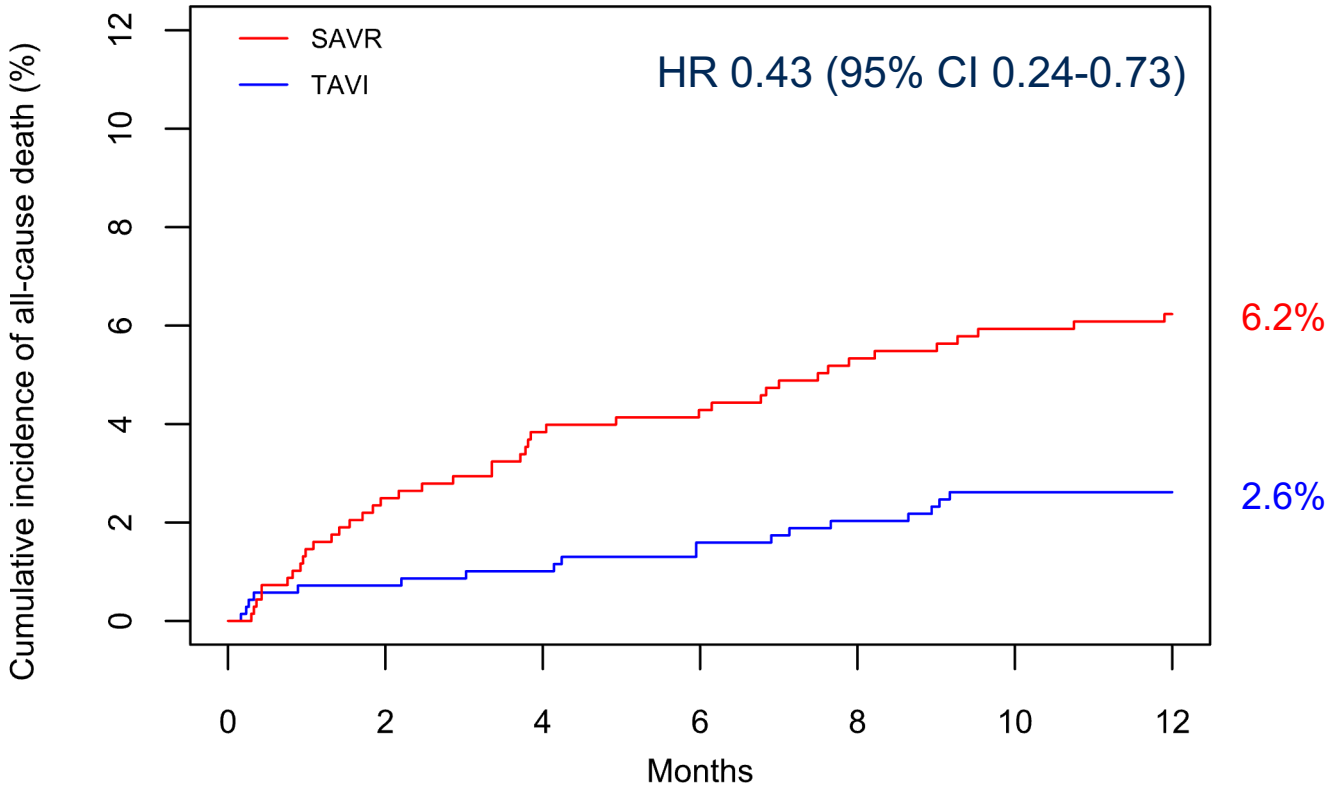


At risk

SAVR	697	658	641	631	625	622	619	615	612	608	602	600	591
TAVI	696	680	674	670	668	666	663	661	656	653	651	651	639

Intention-to-treat population, analysis stratified by STS-PROM score class, Kaplan-Meier estimates.

All-cause Death



At risk

SAVR	697	674	659	652	645	643	640	637	633	632	627	625	616
TAVI	696	691	685	681	680	678	677	675	671	669	667	667	655

Intention-to-treat population, analysis stratified by STS-PROM score class, Kaplan-Meier estimates.

Stroke

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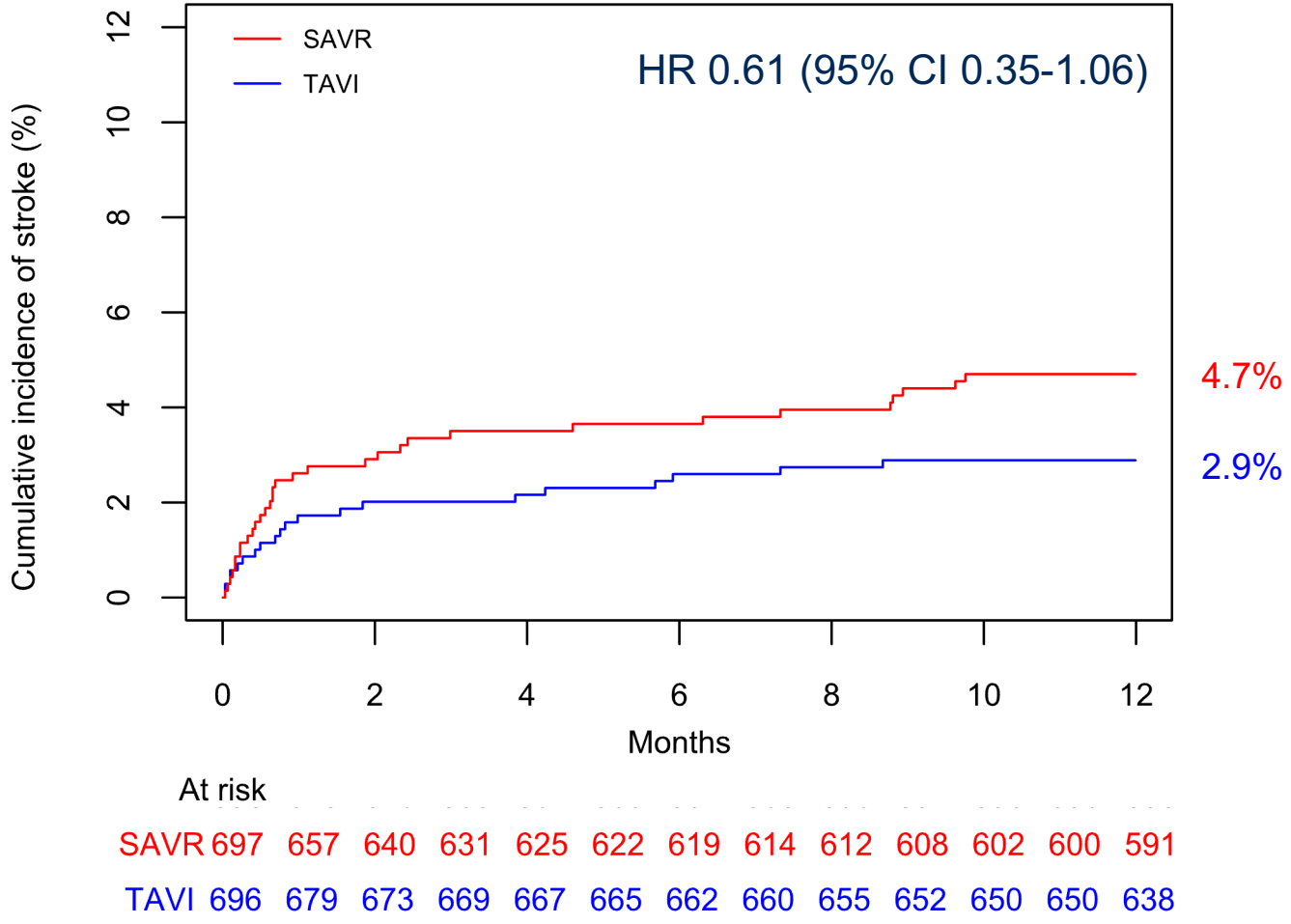

Intention-to-treat population, analysis stratified by STS-PROM score class, Kaplan-Meier estimates.

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Secondary Endpoints

Outcomes at 1 year	TAVI (n=701)	SAVR (n=713)	HR (95% CI)
Disabling stroke	1.3%	3.1%	**0.42 (0.19-0.88)**
Cardiovascular death	2.0%	4.4%	**0.47 (0.24-0.86)**
Vascular access site complication *(minor or major)*	7.9%	0.7%	**10.64 (4.84-28.94)**
Bleeding *(major or life-threatening/disabling)*	4.3%	17.2%	**0.24 (0.16-0.35)**
AKI stage II/III	1.3%	2.5%	0.56 (0.24-1.21)
Myocardial infarction	1.0%	2.1%	0.51 (0.20-1.19)
New-onset atrial fibrillation	12.4%	30.8%	**0.36 (0.28-0.46)**
New-onset LBBB	32.0%	17.5%	**2.03 (1.63-2.54)**
New permanent pacemaker implantation	11.8%	6.7%	**1.81 (1.27-2.61)**

Intention-to-treat population, analysis stratified by STS-PROM score class, Kaplan-Meier estimates.

Secondary Endpoints (continued)

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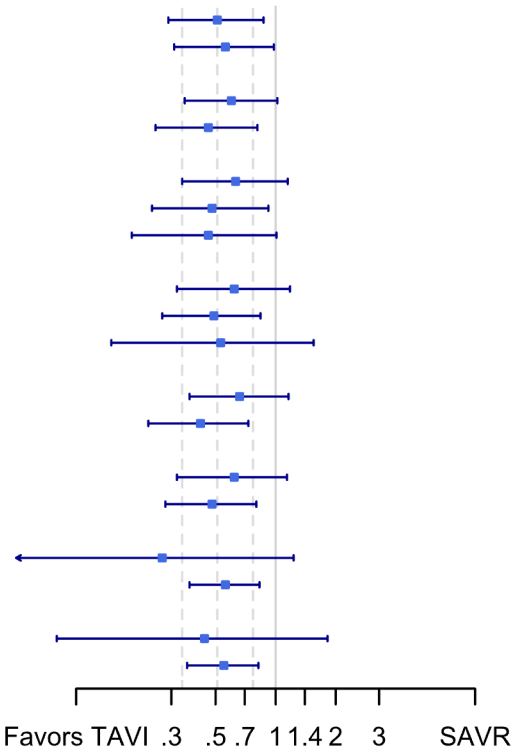
Outcomes at 1 year	TAVI (n=701)	SAVR (n=713)	HR (95% CI)
Prosthetic valve dysfunction	1.6%	0.6%	2.44 (0.87-8.15)
Prosthetic valve endocarditis	0.6%	0.9%	0.66 (0.18-2.19)
Prosthetic valve thrombosis	0.7%	0.3%	2.09 (0.50-11.64)
Aortic-valve reintervention	0.6%	0.3%	1.70 (0.38-9.78)
Rehospitalization (Cardiovascular)	12.2%	13.3%	0.89 (0.66-1.20)

Intention-to-treat population, analysis stratified by STS-PROM score class, Kaplan-Meier estimates.

Subgroup Analyses (Primary Outcome)

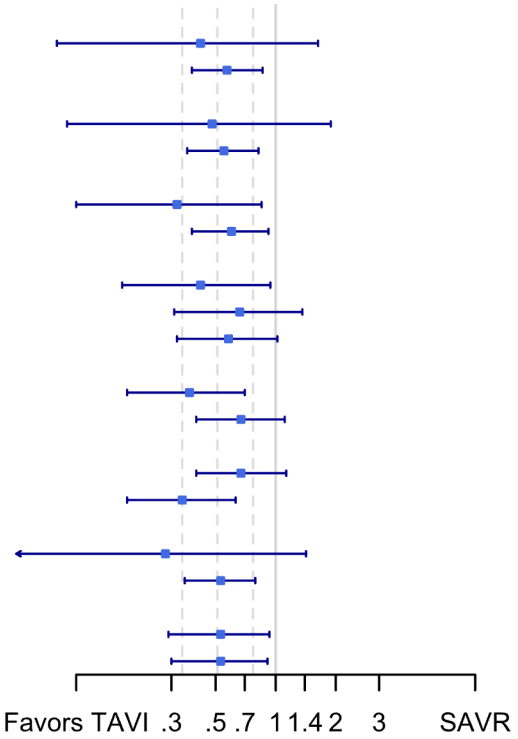
	TAVI n/N	SAVR n/N	HR (95%CI)
Age			
≥ 75 years	19/337	38/354	0.51 (0.29 to 0.87)
< 75 years	18/359	30/345	0.56 (0.31 to 0.98)
Sex			
Male	21/390	35/400	0.60 (0.35 to 1.02)
Female	16/306	33/298	0.46 (0.25 to 0.81)
BMI			
≥ 30 kg/m²	17/255	25/246	0.63 (0.34 to 1.15)
25 to < 30 kg/m²	12/277	26/293	0.48 (0.24 to 0.92)
< 25 kg/m²	8/163	17/159	0.46 (0.19 to 1.01)
STS PROM			
≤ 2 %	15/387	23/378	0.62 (0.32 to 1.18)
> 2 % to ≤ 4 %	18/282	36/284	0.49 (0.27 to 0.84)
> 4 %	4/27	9/35	0.53 (0.15 to 1.55)
NYHA class			
≤ 2	20/374	30/379	0.66 (0.37 to 1.16)
> 2	17/321	38/318	0.42 (0.23 to 0.73)
Coronary artery disease			
Yes	15/238	26/266	0.62 (0.32 to 1.14)
No	22/456	42/431	0.48 (0.28 to 0.80)
Previous myocardial infarction			
Yes	1/36	7/52	0.27 (0.03 to 1.23)
No	36/660	61/645	0.56 (0.37 to 0.83)
Previous stroke			
Yes	2/42	5/42	0.44 (0.08 to 1.82)
No	35/650	62/654	0.55 (0.36 to 0.82)



Intention-to-treat population

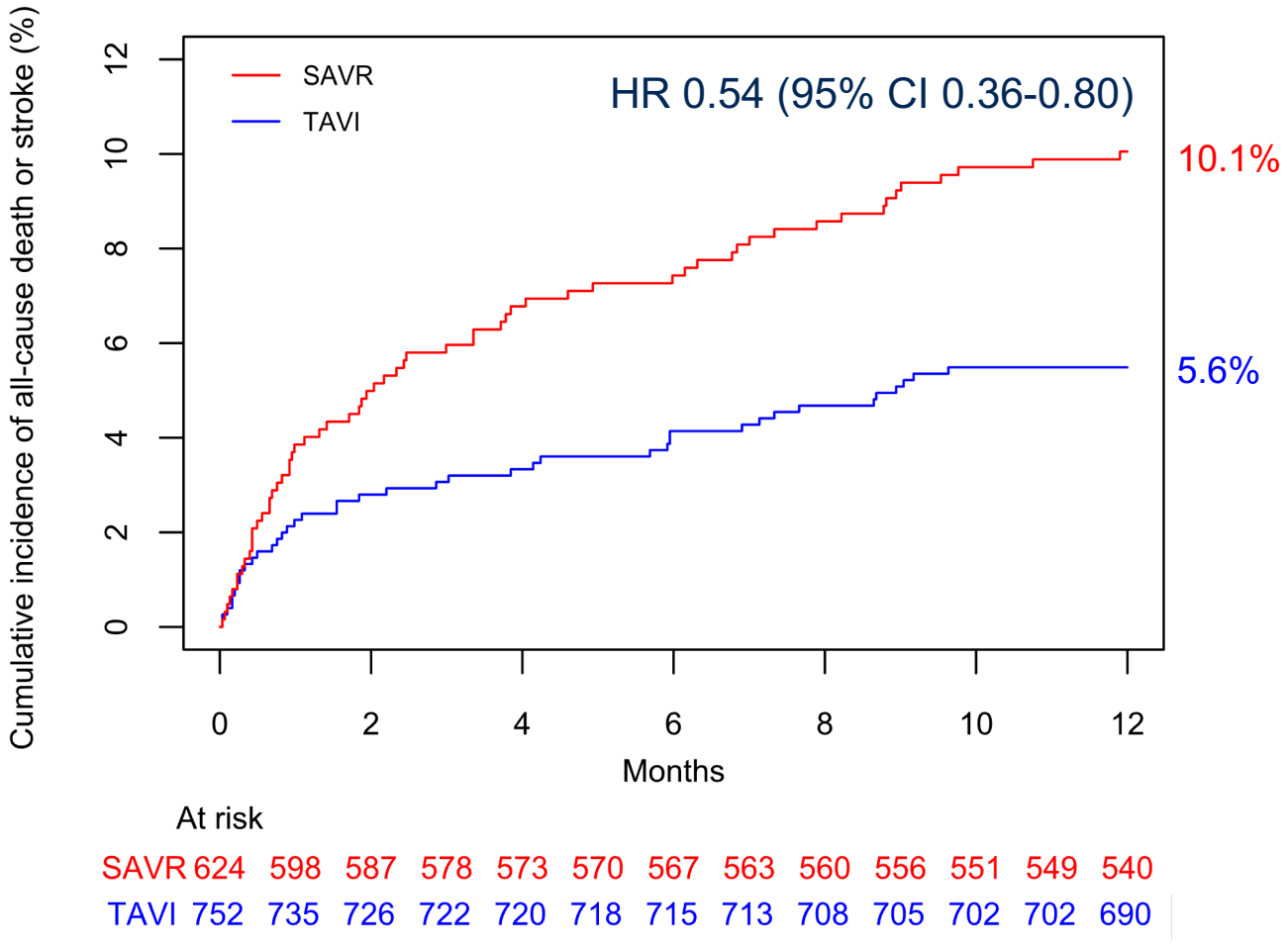
Subgroup Analyses (Primary Outcome) (continued)

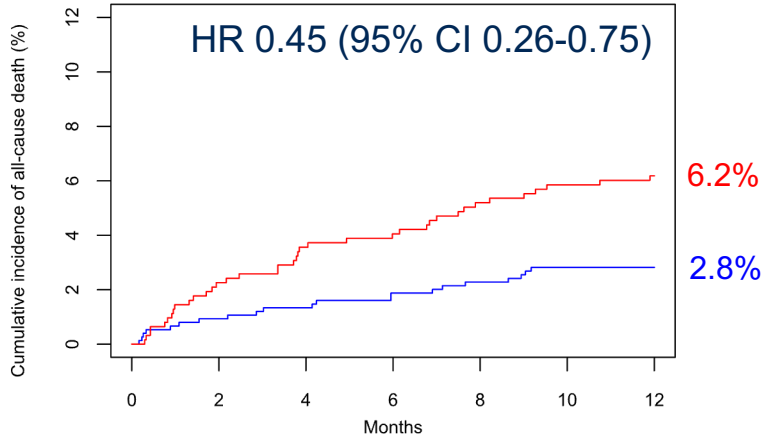
	TAVI n/N	SAVR n/N	HR (95%CI)
Cerebrovascular disease			
Yes	2/27	6/31	0.42 (0.08 to 1.63)
No	35/649	60/662	0.57 (0.38 to 0.86)
Peripheral vascular disease			
Yes	2/34	6/45	0.48 (0.09 to 1.89)
No	35/660	61/652	0.55 (0.36 to 0.82)
COPD			
Yes	4/101	15/118	0.32 (0.10 to 0.85)
No	33/594	52/579	0.60 (0.38 to 0.92)
Left ventricular ejection fraction			
< 55%	7/165	18/179	0.42 (0.17 to 0.94)
≥ 55% to < 60%	11/165	18/181	0.66 (0.31 to 1.36)
≥ 60%	19/336	29/306	0.58 (0.32 to 1.02)
AV mean gradient			
< 40 mmHg	11/243	33/291	0.37 (0.18 to 0.70)
≥ 40 mmHg	26/458	35/422	0.67 (0.40 to 1.11)
GFR			
≥ 60 ml/min/1.73m²	23/469	35/493	0.67 (0.40 to 1.13)
< 60 ml/min/1.73m²	13/210	33/194	0.34 (0.18 to 0.63)
COVID lockdown at admittance			
Yes	1/38	5/40	0.28 (0.03 to 1.42)
No	36/663	63/673	0.53 (0.35 to 0.79)
Randomized			
before March 1, 2020	18/374	32/365	0.53 (0.29 to 0.93)
after March 1, 2020	19/327	36/348	0.53 (0.30 to 0.91)

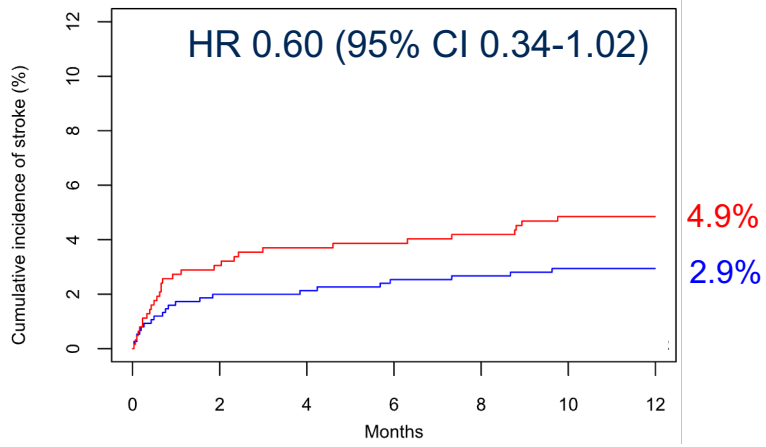


Intention-to-treat population

Primary Outcome and Components (As-Treated)

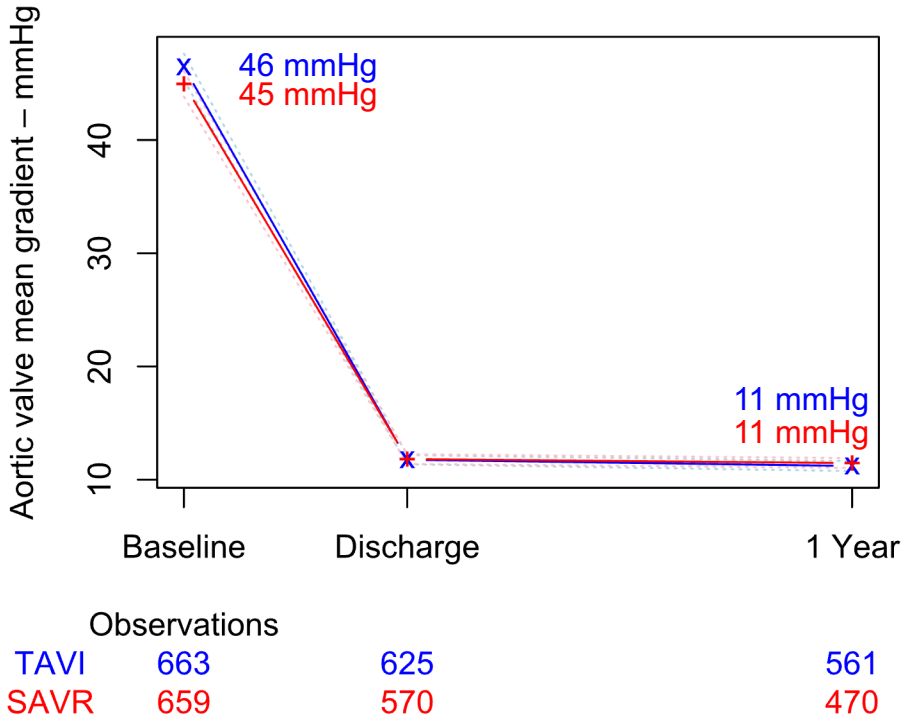




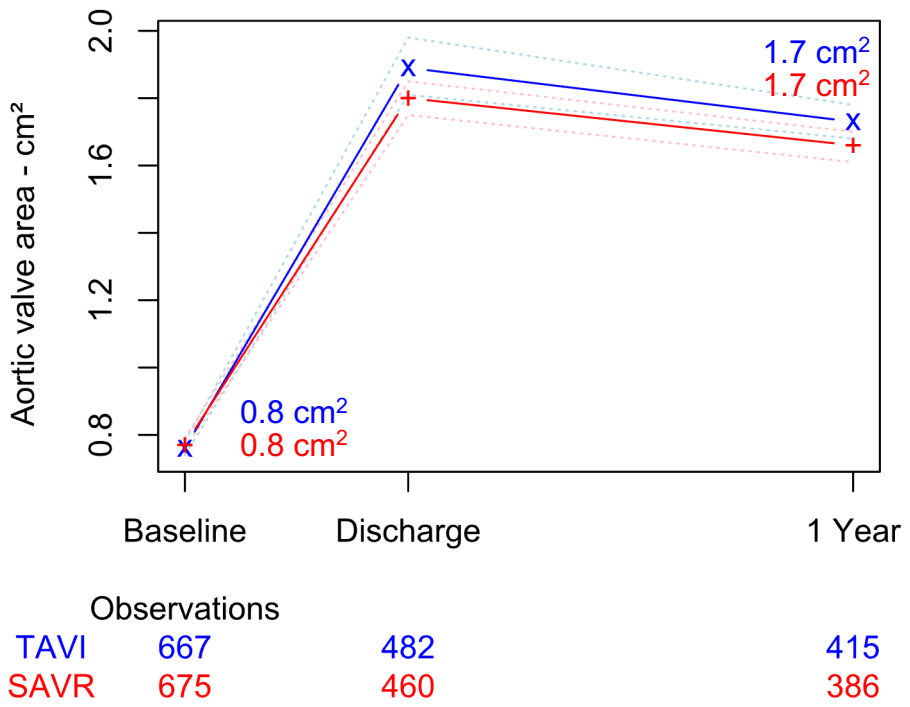


As-treated population, analysis stratified by STS-PROM score class, Kaplan-Meier estimates

Echocardiography Findings



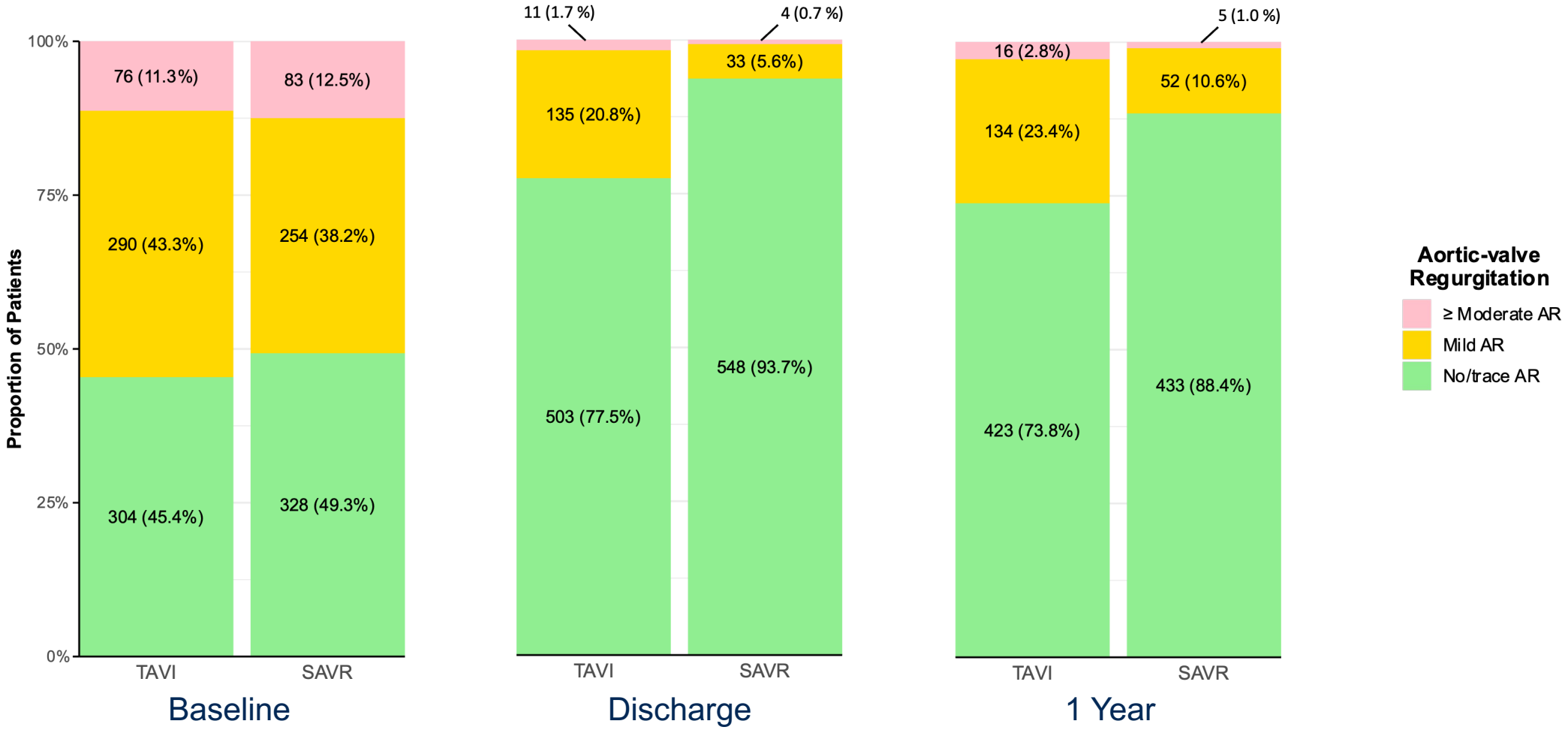
Observations			
TAVI	663	625	561
SAVR	659	570	470



Observations			
TAVI	667	482	415
SAVR	675	460	386

Intention-to-treat population.

Aortic Regurgitation



Intention-to-treat population.

Limitations

- Analyses limited to 1-year follow-up, primary outcome will be re-evaluated at 5-years (Primary efficacy endpoint, tested for non-inferiority and, if significant, for superiority)
- Exclusion of patients with bicuspid AS or concomitant CAD or other VD
- Number of crossovers from SAVR to TAVI – ITT and AT analyses
- Potential impact of the Covid-19 pandemic on outcomes

Conclusion

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Among patients with severe aortic stenosis at low or intermediate surgical risk,

TAVI with prosthesis selection based on operator discretion was noninferior to

SAVR with respect to the risk of death from any cause or stroke at 1 year.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter or Surgical Treatment of Aortic-Valve Stenosis

S. Blankenberg, M. Seiffert, R. Vonthein, H. Baumgartner, S. Bleiziffer, M.A. Borger, C. Yeong-Hoon, P. Clemmensen, J. Cremer, M. Czerny, N. Diercks, I. Eitel, S. Ensminger, D. Frank, N. Frey, A. Hagendorff, C. Hagl, C. Hamm, U. Kappert, M. Karck, W.-K. Kim, I.R. König, M. Krane, U. Landmesser, A. Linke, L.S. Maier, S. Massberg, F.-J. Neumann, H. Reichenspurner, T.K. Rudolph, C. Schmid, H. Thiele, R. Twerenbold, T. Walther, D. Westermann, E. Xhepa, A. Ziegler, and V. Falk, for the DEDICATE-DZHK6 Trial Investigators*

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