JACC: CARDIOVASCULAR INTERVENTIONS VOL. 18, NO. 12, 2025

PUBLISHED BY ELSEVIER

ORIGINAL RESEARCH

STRUCTURAL

Transcatheter Aortic Valve Replacement With Intra-Annular Self-Expanding or Balloon-Expandable Valves

The Multicenter International NAVULTRA Registry

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ABSTRACT

BACKGROUND No comparative data exist with the self-expanding Navitor (NAV) and the balloon-expandable SAPIEN 3 Ultra (ULTRA) transcatheter heart valves (THVs).

OBJECTIVES This study sought to investigate the 1-year outcomes of transcatheter aortic valve replacement using the intra-annular NAV and the ULTRA THVs.

METHODS The NAVULTRA (Navitor and SAPIEN 3 Ultra) registry included consecutive patients who underwent transfemoral transcatheter aortic valve replacement at 16 centers with NAV or ULTRA between November 2018 and April 2024. Propensity score matching was used for adjustment. The primary outcomes of interest were all-cause death and the composite of all-cause death, disabling stroke, and hospitalization for heart failure at 1 year.

RESULTS The overall study cohort included 3,878 patients treated with NAV (n = 1,746) or ULTRA (n = 2,176). The propensity score–matched population resulted in 1,363 pairs. At 1 year, the rate of death from any cause was 9.7% with NAV and 9.9% with ULTRA (adjusted $P = 0.585$). Similarly, there were no significant differences in primary composite outcome (13.6% in the NAV group and 12.6% in the ULTRA group; adjusted $P = 0.218$). The rate of new permanent pacemaker implantation (20.6% vs 10.6%; adjusted $P < 0.01$) and heart failure rehospitalization (4.6% vs 2.8%; adjusted $P < 0.05$) was higher in NAV group. At 1 year, the use of NAV was associated with higher rates of mild paravalvular leak (OR: 1.53; 95% CI: 1.01 to 2.33; adjusted $P < 0.05$) but lower mean transprosthetic gradients compared with ULTRA (mean change: −3.90, 95% CI: −4.47 to −3.34; adjusted $P < 0.01$).

CONCLUSIONS Both intra-annular THVs were associated with similar 1-year clinical outcomes; however, differences were observed in secondary clinical endpoints and valve hemodynamic performance.
(JACC Cardiovasc Interv. 2025;18:1557–1568) © 2025 by the American College of Cardiology Foundation.

ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2025.03.015

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 18, NO. 12, 2025
JUNE 23, 2025:1557–1568

ABBREVIATIONS AND ACRONYMS

BE = balloon-expandable

HF = heart failure

LVOT = left ventricular outflow tract

NAV = Navitor

PPI = permanent pacemaker implantation

PS = propensity score

PVL = paravalvular leak

SE = self-expanding

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

ULTRA = SAPIEN 3 Ultra

VARC-3 = Valve Academic Research Consortium-3

Transcatheter aortic valve implantation (TAVR) is an established treatment for patients with severe symptomatic aortic stenosis across different surgical risk profiles.[1] Over the past several years, technological advancements and increased operator experience have led to considerable improvements in both procedural and clinical outcomes.[2] Intra-annular self-expanding (SE) and balloon-expandable (BE) valves are implanted in clinical practice. New iterations of these transcatheter heart valves (THVs) have recently become available: the SE Navitor (NAV) (Abbott) and the BE SAPIEN 3 Ultra (ULTRA) (Edwards Lifesciences). Both THVs have demonstrated highly promising results compared with their predecessors.[3-5] However, to date, no direct comparison has been made between these 2 prostheses.

The aim of this study was to compare the clinical and echocardiographic outcomes at 30 days and 1 year of the NAV vs the ULTRA THVs in a propensity score (PS)-matched population.

METHODS

STUDY POPULATION. The NAVULTRA registry is an international, multicenter, observational, physician-led study that included consecutive patients with symptomatic severe aortic stenosis who underwent transfemoral TAVR using the SE NAV and BE ULTRA THVs at 16 high-volume centers across Europe and the United States. Patients who underwent TAVR using approaches other than transfemoral access (nontransfemoral TAVR) were not included. For the purposes of the present analysis, patients with a previous surgical aortic valve replacement (valve-in-valve) were excluded (**Figure 1**). The study was approved by the local ethics committee of the coordinating institution and was performed in accordance with the Declaration of Helsinki.

Both manufacturers of the NAV THV and the ULTRA had no role in data collection, analysis, or manuscript drafting and did not provide any financial support for the study.

DEVICE DESCRIPTION. The NAV THV is a self-expanding valve with intra-annular bovine leaflets and large-frame stent to preserve coronary access in case of future interventions. The new iteration compared with its predecessor, the Portico (Abbott), has a key innovation, which consists of an outer cuff designed to reduce the paravalvular leak (PVL) risk by close integration to the native valve. The NAV THV is currently available in 4 sizes: 23 mm, 25 mm, 27 mm, and 29 mm. The NAV is approved for treating patients with symptomatic severe aortic stenosis who are considered at high surgical risk.

The ULTRA THV has a cobalt-chromium alloy frame and bovine tissue leaflet design. The key difference, compared with its predecessor, SAPIEN 3, is the textured polyethylene terephthalate outer skirt of

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received October 26, 2024; revised manuscript received March 3, 2025, accepted March 7, 2025.

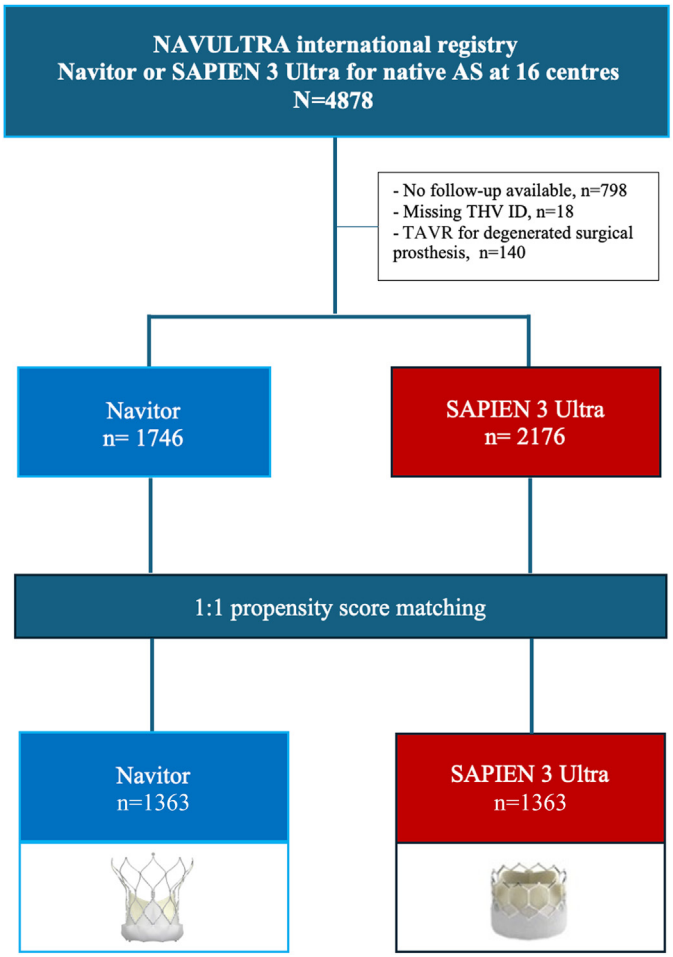
the ULTRA, which has an approximately 40% increased height designed to improve annular sealing and to reduce PVL. The ULTRA THV is available in 20-mm, 23-mm, and 26-mm sizes.

STUDY OUTCOMES AND DEFINITIONS. The primary outcomes of this analysis were death from any cause and the composite of death from any cause, disabling stroke and repeat hospitalization for heart failure (HF) at 1 year.

Secondary outcomes of interest were technical success, 30-day device success and 30-day early safety. The incidence of selected procedural complications and clinical outcomes at 30 days and 1 year were also considered. All clinical outcomes and procedural complications were assessed according to Valve Academic Research Consortium-3 (VARC-3) criteria.[6] Technical success was defined as: 1) freedom from mortality; 2) successful access, delivery of the device, and retrieval of the delivery system; 3) correct positioning of a single THV into the proper anatomical location; and 4) freedom from surgery or intervention related to the device or a major vascular, access-related, or cardiac structural complication at exit from the procedure room. Device success was defined as: 1) technical success; 2) 30-day freedom from mortality; 3) 30-day freedom from surgery or intervention related to the device or a major vascular, access-related, or cardiac structural complications; and 4) intended performance of the valve (mean gradient <20 mm Hg, peak velocity <3 m/s, and less than moderate aortic regurgitation). Early safety was defined as: 1) freedom from all-cause mortality; 2) freedom from all stroke; 3) freedom from VARC type 2 to 4 bleeding; 4) freedom from major vascular, access-related, or cardiac structural complications; 5) freedom from acute kidney injury stage 3 or 4; 6) freedom from moderate or severe aortic regurgitation; 7) freedom from permanent pacemaker implantation (PPI) caused by procedure-related conduction abnormalities; and 8) freedom from surgery or intervention related to the device at 30 days. Echocardiographic outcomes were evaluated before discharge, at 30 days, and at 1 year. PVL severity was assessed according to VARC-3 criteria and classified as follows: none, trace, mild, moderate, or severe.[6]

STATISTICAL ANALYSIS. All continuous variables are expressed as the mean ± SD and are compared using the unpaired Student's *t*-test. All categorical variables are compared using chi-square test or the Fisher exact test. Missing baselines covariates were estimated using multiple imputation chain method (n = 5).[7] The PS was used to adjust for differences in baseline characteristics and potential confounders that may lead to biased estimates of treatment outcomes. A 1-to-1 nearest-neighbor matching algorithm without replacement (caliper = 0.2) was performed to identify PS-matched pairs. This was done by means of a nonparsimonious multivariable logistic regression including the following 38 covariates: age, sex, body mass index, hypertension, Society of Thoracic Surgeons Predicted Risk of Mortality score, functional NYHA functional class III or IV, diabetes, chronic obstructive pulmonary disease, severe liver disease, atrial fibrillation, peripheral vascular disease, prior stroke, coronary artery disease, prior myocardial infarction, prior percutaneous coronary intervention, previous coronary artery bypass grafting, other previous cardiac surgery, estimated glomerular filtration

FIGURE 1 Study Flowchart



Study flow illustrating the derivation of the unmatched and propensity-matched patient cohorts from the NAVULTRA registry. AS = aortic stenosis; TAVR = transcatheter aortic valve replacement; THV = transcatheter heat valve.

rate, dialysis, porcelain aorta, prior PPI, baseline left bundle branch block, baseline right bundle branch block, baseline first degree atrioventricular block, left ventricular ejection function, transaortic max gradient, transaortic mean gradient, aortic valve area, moderate-to-severe mitral regurgitation, moderate-to-severe tricuspid regurgitation, moderate-to-severe aortic regurgitation, severe pulmonary hypertension, anesthesia type, aortic valve area, aortic valve perimeter, sinus of Valsalva mean diameter, eccentric annulus index, left ventricular outflow tract (LVOT), and aortic valve calcium distribution at the pre-TAVR computed tomography. Matching was performed within each imputed dataset using the observed and imputed covariate values. The balance on the matched datasets was assessed by computing the standardized mean difference for each covariate. Finally, the treatment effects estimated in each of the matched datasets were pooled together using Rubin's rules.[8]

Prespecified primary and secondary outcomes were compared between the NAV and ULTRA valve groups in both the overall and PS-matched cohorts. The risk of adverse events 1 year after TAVR was compared for both cohorts using Cox proportion hazards regression and Kaplan-Meier analysis. The impact of the competing risk of death on disabling stroke incidence and HF rehospitalization rates was assessed using cumulative incidence function analysis. Finally, sensitivity analyses were performed for the main clinical outcomes using propensity matching on the completed data without any missing values in covariates, the inverse probability weighting by PS, and the use of the PS as a covariate. Statistical analysis was performed using R version 4.2.0 (R Foundation for Statistical Computing) and SPSS Statistics version 25 for Macintosh (IBM). PS and matching procedures were conducted using the MatchThem package in R.[8]

RESULTS

BASELINE CHARACTERISTICS. A total of 4,878 patients who underwent transfemoral TAVR were included in the NAVULTRA registry from November 2018 to April 2024. Patients without follow-up after discharge, those with missing THV ID, and those with a prior aortic valve prosthesis were excluded, resulting in 1,746 patients who underwent TAVR with NAV and 2,176 with ULTRA (**Figure 1**).

Before PS matching, patients treated with NAV were older (81 ± 6.2 years of age vs 80.7 ± 7.3 years of age; $P < 0.01$) and more likely to be female (68.1% vs 46.0%; $P < 0.01$). They had a lower body mass index (26.7 ± 4.8 kg/m^2 vs 27.6 ± 5.6 kg/m^2; $P < 0.01$) and a higher Society of Thoracic Surgeons Predicted Risk of Mortality (4.3 ± 3.0 vs 3.9 ± 3.0; $P < 0.01$). Pre-TAVR computed tomography assessment revealed that ULTRA patients had a larger aortic annulus area (444 ± 71 mm^2 vs 430 ± 71 mm^2; $P < 0.01$) and perimeter (74.47 ± 6.10 mm vs 75.94 ± 6.17 mm; $P < 0.01$) and were more likely to have bicuspid valve anatomy (7.1% vs 2.0%; $P < 0.01$) compared with NAV patients. Heavily aortic leaflet calcification was more frequent in ULTRA-treated patients (36.8% vs 30.8%; $P < 0.01$), while severe LVOT calcification was significantly higher in NAV patients (3.6% vs 0.4%; $P < 0.01$). Baseline characteristics of the unmatched population are reported in **Table 1**.

From the entire cohort, a 1-to-1 PS matching analysis based on clinical and anatomical characteristics and anesthesia type resulted in 1,363 matched pairs. There were no significant differences in baseline characteristics between the propensity-matched NAV and ULTRA groups, including the degree of aortic valve and LVOT calcification (Supplemental Figure 1).

PROCEDURAL CHARACTERISTICS AND IN-HOSPITAL OUTCOMES. Procedural characteristics and in-hospital outcomes for the unadjusted and PS-matched populations are presented in **Table 2**. In the PS-matched population, predilatation and postdilatation were more frequently performed with NAV compared with ULTRA (for predilatation, OR: 13.9; 95% CI: 11.2-17.4; $P < 0.01$; for postdilatation, OR: 4.39; 95% CI: 3.06-6.31; $P < 0.01$). Overall, procedural complications were rare, with no significant differences between groups. In-hospital mortality during the index admission was similar between groups (OR: 1.09; 95% CI: 0.50-2.40; $P = 0.813$). There were also no differences in the rates of major vascular complications (OR: 0.77; 95% CI: 0.33-1.79; $P = 0.539$), life-threatening bleeding (OR: 1.91; 95% CI: 0.55-6.65; $P = 0.302$), cardiac tamponade (OR: 0.77; 95% CI: 0.21-3.25; $P = 0.776$), or conversion to open heart surgery (OR: 0.66; 95% CI: 0.08-5.15; $P = 0.696$) between the two groups. The rates of annulus rupture were very low across the entire cohort, with only 1 and 2 cases, respectively.

The rates of new left bundle branch block (OR: 1.78; 95% CI: 1.42-2.23; $P < 0.01$) and new PPI (OR: 2.44; 95% CI: 1.93-3.10; $P < 0.01$) were significantly higher in NAV recipients compared with those receiving ULTRA in both the unmatched and matched populations. Additionally, the NAV group had a significantly longer length of hospitalization (NAV: 4.0 ± 5.1 days vs ULTRA: 3.4 ± 5.0 days; $P < 0.01$).

TABLE 1 Baseline Characteristics of Registry Patients Before PS Matching

	Missing (%)	Overall (N = 4,878)	Navitor (n = 1,746)	SAPIEN 3 Ultra (n = 2,176)	*P* Value
Age, y	–	80.3 ± 6.9	81 ± 6.2	80 ± 7.3	<0.01
Female	–	2,007 (51.2)	1,006 (68.1)	1,001 (46.0)	<0.01
Body mass index, kg/m^2	1.8	27.19 ± 5.22	26.68 ± 4.77	27.59 ± 5.51	<0.01
Body surface area, m^2	1.7	1.82 ± 0.22	1.80 ± 0.21	1.83 ± 0.22	<0.01
STS PROM	23.2	4.01 ± 3.01	4.28 ± 3.08	3.89 ± 2.97	0.01
NYHA functional class III or IV	4.6	1,944 (49.6)	753 (44.1)	1,191 (58.6)	<0.01
Hypertension	0.2	3,096 (78.9)	1,369 (78.4)	1,727 (79.5)	0.438
Diabetes mellitus	0.2	1,312 (33.5)	539 (30.9)	773 (35.6)	<0.01
COPD	0.4	642 (16.4)	307 (17.6)	335 (15.5)	0.078
Severe liver disease	3.8	54 (1.4)	17 (1.0)	37 (1.8)	0.04
Porcelain aorta	8.0	79 (2.0)	33 (2.3)	46 (2.2)	0.704
Atrial fibrillation	–	892 (22.7)	380 (21.8)	512 (23.5)	0.190
Prior PCI	1.0	884 (22.5)	400 (22.9)	484 (22.6)	0.832
Peripheral vascular disease	0.7	496 (12.6)	213 (13.80)	283 (12.3)	0.504
Previous stroke	–	361 (9.2)	129 (7.4)	232 (10.6)	<0.01
CAD	0.2	1,595 (40.7)	580 (33.3)	1,015 (46.7)	<0.01
Prior MI	0.2	550 (14.0)	209 (11.9)	341 (15.7)	0.01
Prior CABG	0.1	238 (6.1)	88 (5.0)	150 (6.9)	0.015
Other prior cardiac surgery	9.9	130 (3.3)	58 (3.5)	72 (3.8)	0.579
Dialysis	–	79 (2.0)	27 (1.5)	52 (2.4)	0.061
eGFR <30 mL/min	2.1	308 (7.9)	124 (7.2)	184 (8.7)	0.07
eGFR, mL/min/1.73 m^2	2.1	60.34 ± 22.45	54.03 ± 23.68	53.07 ± 23.36	0.631
Hemoglobin, g/dL	6.0	12.07 ± 2.63	12.30 ± 1.87	11.89 ± 3.13	<0.01
Severe pulmonary hypertension	9.9	261 (6.7)	133 (9.7)	128 (10.0)	0.800
Previous pacemaker	–	360 (9.1)	218 (12.4)	142 (6.5)	<0.01
RBBB	13.5	328 (8.4)	114 (8.8)	214 (10.2)	0.161
First-degree AV block	13.7	367 (9.4)	130 (10.0)	237 (11.3)	0.237
Baseline LBBB	13.5	256 (6.5)	105 (8.0)	151 (7.2)	0.358
Peak gradient, mm Hg	24.0	74.42 ± 20.93	75.31 ± 19.59	73.85 ± 21.72	0.06
Mean gradient, mm Hg	2.8	46.39 ± 13.75	47.36 ± 13.34	45.61 ± 14.04	<0.01
AVA, cm^2	9.5	0.70 ± 0.19	0.69 ± 0.17	0.72 ± 0.20	<0.01
LVEF, %	3.3	55.74 ± 10.78	55.33 ± 10.05	56.09 ± 11.33	<0.05
Moderate or severe AR	5.6	485 (12.4)	236 (13.8)	249 (12.5)	0.206
Moderate or severe MR	4.9	591 (15.8)	194 (11.4)	397 (19.6)	<0.01
Moderate or severe TR	20	518 (13.2)	121 (9.9)	397 (20.7)	<0.01
Aortic annulus area, mm^2	13.8	438 ± 70	430 ± 71	444 ± 71	<0.01
Annulus perimeter, mm	14.7	75.24 ± 6.18	74.47 ± 6.10	75.94 ± 6.17	<0.01
Sinus of Valsalva, mm	31.9	31.18 ± 3.37	30.83 ± 3.16	31.51 ± 3.53	<0.01
Bicuspid aortic valve	4.3	181 (4.6)	35 (2.0)	146 (7.1)	<0.01
Eccentricity of annulus	23.1	0.81 ± 0.08	0.80 ± 0.07	0.81 ± 0.08	<0.01
Aortic valve calcification[a]					
Moderate	33.4	877 (22.4)	277 (27.6)	600 (37.3)	<0.01
Heavily	33.4	902 (23.0)	309 (30.8)	593 (36.8)	<0.01
LVOT calcification[b]					
Moderate	44	115 (2.9)	67 (8.3)	48 (3.4)	<0.01
Severe	44	34 (0.9)	29 (3.6)	5 (0.4)	<0.01

Values are n (%) or mean ± SD. [a]Aortic valve calcification was in a semiquantitative fashion: mild, small isolated spots; moderate, multiple larger spots; heavily, extensive calcifications of all cusps. [b]LVOT calcification was assessed in a semiquantitative fashion: mild, 1 nodule of calcium extending <5 mm in any dimension and covering <10% of the perimeter of the LVOT; moderate, 2 nodules of calcification or 1 extending >5 mm in any direction or covering >10% of the perimeter of the LVOT; severe, multiple nodules of calcification of single focus extending >1 cm in length or covering >20% of the perimeter of the LVOT.

AR = aortic regurgitation; AV = atrioventricular; AVA = aortic valve area; CABG = previous coronary artery bypass grafting; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; MI = myocardial infarction; MR = mitral regurgitation; PCI = percutaneous coronary intervention; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; RBBB = right bundle branch block; TR = tricuspid regurgitation.

TABLE 2 Procedural and In-Hospital Outcomes of Unadjusted and Propensity-Matched Cohorts

	Navitor (n = 1,746)	SAPIEN 3 Ultra (n = 2,176)	Unadjusted		Propensity Matched	
			OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
General anesthesia	79 (4.5)	285 (13.1)	0.31 (0.24-0.40)	<0.01	0.92 (0.67-1.27)	0.649
Predilatation	1,308 (79)	453 (25.4)	10.93 (9.34-12.84)	<0.01	13.97 (11.20-17.4)	<0.01
Postdilatation	511 (30.8)	160 (9.9)	4.50 (3.70-5.49)	<0.01	4.39 (3.06-6.31)	<0.01
Contrast dye, mL	123.9 ± 72.4	121.5 ± 79.5	1.56 (−5.52 to 8.65)	0.411	1.56 (−5.52 to 8.65)	0.660
In-hospital death	17 (1.0)	26 (1.2)	0.81 (0.43-1.49)	0.509	1.09 (0.50-2.40)	0.813
Cardiac tamponade	5 (0.4)	9 (0.6)	0.80 (0.24-2.34)	0.701	0.77 (0.21-3.25)	0.776
Conversion to open heart surgery	2 (0.1)	5 (0.2)	0.49 (0.07-2.31)	0.405	0.66 (0.08-5.15)	0.696
Annulus rupture	1 (0.05)	2 (0.09)	0.62 (0.03-6.50)	0.699	0.99 (0.33-2.93)	0.988
Second THV implanted	17 (0.7)	16 (0.9)	1.33 (0.66-2.66)	0.418	0.99 (0.43-2.31)	0.995
Vascular complications						
Major	13 (0.74)	28 (1.3)	0.57 (0.29-1.09)	0.101	0.77 (0.33-1.79)	0.539
Bleeding						
Life threatening (type 3)	12 (0.7)	10 (0.5)	01.49 (0.64-3.56)	0.346	1.91 (0.55-6.65)	0.302
Major (type 2)	10 (0.6)	37 (1.7)	0.33 (0.16-0.64)	<0.01	0.45 (0.19-1.05)	0.07
New pacemaker	311 (17.8)	181 (8.3)	2.38 (1.97-2.90)	<0.01	2.44 (1.93-3.10)	<0.01
New onset of AF	35 (2.0)	49 (2.2)	0.89 (0.57-1.37)	0.595	0.92 (0.54-1.55)	0.742
New LBBB	24.9 (321/1299)	14.9 (314/2096)	1.88 (1.58-2.24)	<0.01	1.78 (1.42-2.23)	<0.01
AKI 3	1.5 (20/1,315)	0.6 (14/2,156)	2.36 (1.19-4.79)	0.01	2.80 (0.93-8.40)	0.07
New dialysis	8 (0.45)	9 (0.4)	1.10 (0.41-2.90)	0.833	1.15 (0.27-4.94)	0.849
VARC-3 technical success	1,630 (93.3)	2,067 (95)	0.74 (0.56-0.97)	0.03	0.76 (0.53-1.10)	0.150
LOS, d	4.05 ± 5.1	3.43 ± 5.01	0.62 (0.29-0.94)[a]	<0.01	0.54 (0.11-0.96)[a]	0.01
Echocardiographic assessment (discharge)						
Peak gradient, mm Hg	14.19 ± 6.52	20.7 ± 9.7	−7.98 (−8.60 to −7.31)[a]	<0.01	−6.38 (−7.54 to −5.22)[a]	<0.01
Mean gradient, mm Hg	7.88 ± 3.54	11.78 ± 5.6	−4.40 (−4.70 to −4.09)[a]	<0.01	−3.78 (−4.10 to −3.42)[a]	<0.01
AVA, cm^2	2.14 ± 0.57	1.85 ± 0.60	0.29 (0.23-0.34)[a]	<0.01	0.26 (0.21-0.31)[a]	<0.01
None/trace PVL	986 (56.7)	1,596 (73.9)	0.46 (0.40-0.53)	<0.01	0.50 (0.42-0.59)	<0.01
Mild PVL	685 (39.5)	541 (25.1)	1.94 (1.70-2.23)	<0.01	1.78 (1.50-2.10)	<0.01
Moderate PVL or greater	67 (3.8)	21 (1.0)	4.08 (2.53-6.84)	<0.01	3.92 (1.98-7.77)	<0.01

Values are n (%), mean ± SD, or % (n/N). [a]Indicates mean change.

AKI = acute kidney injury; AF = atrial fibrillation; LOS = length of stay; PVL = paravalvular leak; THV = transcatheter heart valve; VARC-3 = Valve Academic Research Consortium-3; other abbreviations as in Table 1.

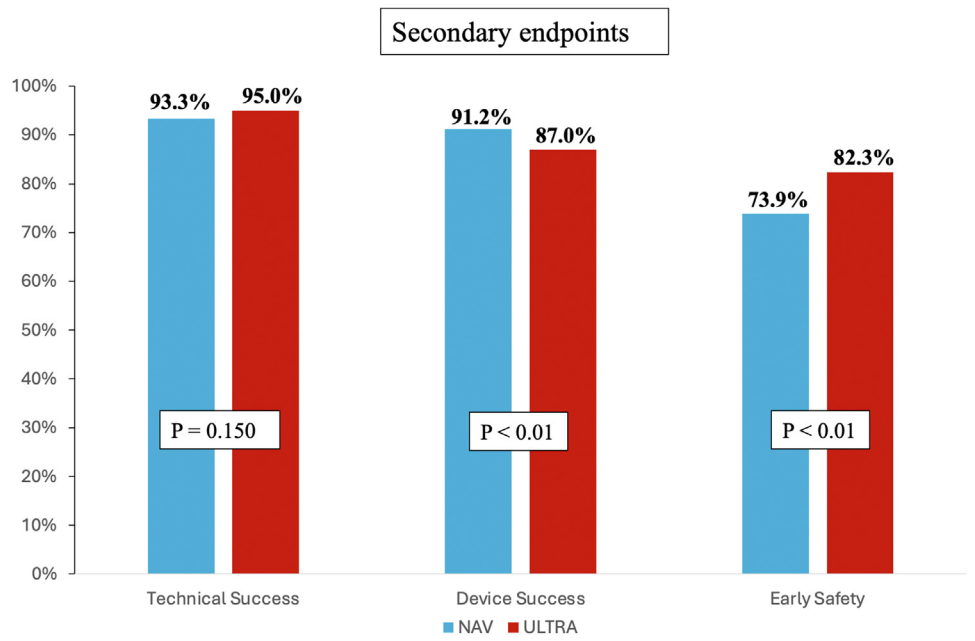
Among the secondary outcomes (Figure 2, Table 3), the rate of technical success was high and comparable between the two groups (93.3% for NAV vs 95.0% for ULTRA; $P = 0.150$). The device success rate was high in both groups, with a statistically significant difference favoring the NAV group (91.2% for NAV vs 87.0% for ULTRA; $P < 0.01$). However, the rate of the early safety endpoint was significantly higher with ULTRA (82.6%) compared with NAV (73.9%; OR: 0.55; 95% CI: 0.45-0.67; $P < 0.01$).

CLINICAL OUTCOMES AT 30 DAYS AND 1 YEAR. At 30 days, no significant differences were observed between patients treated with ULTRA and NAV regarding all-cause mortality, disabling and nondisabling stroke, or repeat hospitalization for HF. However, the NAV group had a higher incidence of new PPI (Table 4).

Clinical outcomes at 1 year are shown for the unadjusted and propensity-matched population in Table 4.

At 1 year, the rate of death from any cause occurred in 9.7% of patients receiving NAV and 9.9% in those with ULTRA (HR: 0.93; 95% CI: 0.84-1.28; $P = 0.757$) (Supplemental Figure 2). Similarly, there was no significant difference in the rate of the composite endpoint of death from any cause, stroke, or HF rehospitalization at 1 year after the procedure (Central Illustration). There was also no significant difference in the rate of repeat procedure between patients in the NAV and ULTRA groups (HR: 4.24; 95% CI: 0.47-37.60; $P = 0.360$). The rate of disabling stroke was low and comparable in both groups (1.8% ULTRA vs 1.5% NAV; $P = 0.911$), whereas the rate of HF hospitalization was significantly higher in the NAV group compared with the ULTRA group (4.6% vs 2.8%;

FIGURE 2 Secondary Endpoints Between Intra-Annular Self-Expanding vs Balloon-Expandable Transcatheter Heart Valves



Comparison of Valve Academic Research Consortium-3 early composite endpoints between intra-annular Navitor (NAV) and SAPIEN 3 Ultra (ULTRA) devices.

$P < 0.01$). These findings were consistent after accounting for the competing risks of all-cause death.

The propensity-matched analysis confirmed that there were no significant differences in the rates of any death (HR: 1.08; 95% CI: 0.80 to 1.47; $P = 0.585$), cardiac death (HR: 1.05; 95% CI: 0.74 to 1438; $P = 0.781$), disabling stroke (HR: 0.99; 95% CI: 0.49-2.00; $P = 0.997$), and nondisabling stroke (HR: 1.48; 95% CI: 0.76-2.87; $P = 0.248$). However, the rate of hospitalization for HF (HR: 1.6; CI: 1.06-2.72; $P < 0.01$) and new PPI (HR: 2.14; 95% CI: 1.69-2.72; $P < 0.01$) was significantly higher in NAV recipients compared with those receiving ULTRA in both the unmatched and matched populations (Table 4, Supplemental Figure 3).

Echocardiographic outcomes. Early echocardiographic data after TAVR of the unadjusted and propensity-matched cohorts are shown in Table 2. In the unadjusted population, ULTRA more frequently achieved none/trivial PVL compared with NAV (OR: 0.46; 95% CI: 0.40-0.53; $P < 0.01$), whereas the rate of mild PVL was higher in the NAV group (OR: 1.94; 95% CI: 1.70-2.23; $P < 0.01$). The ULTRA device was associated with a lower incidence of moderate or greater PVL compared with NAV (3.8% for NAV vs 1.0% for ULTRA; $P < 0.01$), but the ULTRA

TABLE 3 Secondary Outcomes

			Unadjusted		Propensity Matched	
	Navitor	SAPIEN 3 Ultra	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
VARC-3 technical success	1,630 (93.3)	2,067 (95.0)	0.74 (0.56-0.97)	0.03	0.76 (0.53-1.10)	0.150
VARC-3 device success	1,594 (91.2)	1,894 (87.0)	1.44 (1.27-1.93)	<0.01	1.49 (1.12-1.99)	<0.01
VARC-3 early safety	1,291 (73.9)	1,806 (82.3)	0.58 (0.50-0.68)	<0.01	0.55 (0.45-0.67)	<0.01

Values are n (%).
VARC-3 = Valve Academic Research Consortium-3.

TABLE 4 Clinical Outcomes of Unadjusted and Propensity-Matched Populations at 30 Days and 1 Year

			Unadjusted		Propensity Matched	
	Navitor	SAPIEN 3 Ultra	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
At 30 d						
All-cause death	28 (1.6)	45 (2.1)	0.89 (0.55-1.57)	0.597	1.11 (0.58-2.12)	0.755
CV death	23 (1.3)	33 (1.5)	0.89 (0.53-2.11)	0.680	1.07 (0.53-2.11)	0.854
Disabling stroke	14 (0.9)	18 (0.8)	1.10 (0.57-2.13)	0.758	1.37 (0.35-2.02)	0.714
Nondisabling stroke	19 (1.1)	17 (0.8)	1.47 (0.78-2.74)	0.238	1.37 (0.61-3.08)	0.438
Hospitalization for HF	27 (1.5)	19 (0.9)	1.71 (0.95-3.08)	0.07	1.86 (0.80-4.28)	0.143
New PPI	334 (19.1)	216 (9.9)	2.05 (1.72-2.42)	<0.01	2.11 (1.65-2.70)	<0.01
Repeat procedure	3 (0.2)	1 (0.05)	5.59 (0.65-47.89)	0.116	2.60 (0.27-24.56)	0.399
At 1 y						
All-cause death	124 (9.7)	145 (9.9)	0.93 (0.84-1.28)	0.757	1.08 (0.80-1.47)	0.585
Composite endpoint[a]	179 (13.6)	188 (12.6)	1.13 (0.94-1.36)	0.171	1.19 (0.89-1.58)	0.218
Cardiac death	75 (5.7)	86 (5.8)	0.99 (0.76-1.30)	0.977	1.05 (0.74-1.48)	0.781
Disabling stroke	20 (1.5)	30 (1.8)	0.45 (0.57-1.64)	0.911	0.99 (0.49-2.00)	0.997
Nondisabling stroke	29 (1.9)	22 (1.2)	1.68 (0.98-2.85)	0.06	1.48 (0.76-2.87)	0.248
Hospitalization for HF	60 (4.6)	39 (2.8)	1.66 (1.16-2.37)	<0.01	1.69 (1.06-2.72)	0.03
New PPI	346 (20.6)	221 (10.6)	0.70 (1.75-2.45)	<0.01	2.14 (1.69-2.72)	<0.01
Repeat procedure	5 (0.3)	1 (0.05)	7.19 (0.86-59.74)	0.07	4.24 (0.47-37.60)	0.194

Values are n (%). Data are reported as Kaplan-Meier estimates at the specific time point. [a]Any death, disabling stroke, or repeat hospitalization for HF.
CV = cardiovascular; HF = heart failure; PPI = permanent pacemaker implantation; VARC-3 = Valve Academic Research Consortium-3.

yielded higher mean postprocedural aortic valve gradients than the NAV (11.8 mm Hg vs 7.9 mm Hg; $P < 0.01$).

In the propensity-matched analysis, ULTRA confirmed a lower incidence of any PVL compared with NAV, including mild and moderate PVL (for mild PVL, OR: 1.78; 95% CI: 1.50-2.10; $P < 0.01$; for moderate PVL, OR: 3.92; 95% CI: 1.98-7.77; $P < 0.01$). The SE NAV was associated with lower residual transprosthetic gradients and a larger effective orifice area (mean difference: 0.26; 95% CI: 0.21-0.31; $P < 0.01$; mean difference: −3.78; 95% CI: −4.10 to −3.42; $P < 0.01$) (Supplemental Figures 4 and 5). These echocardiographic findings were consistent at 30 days (Supplemental Table 1).

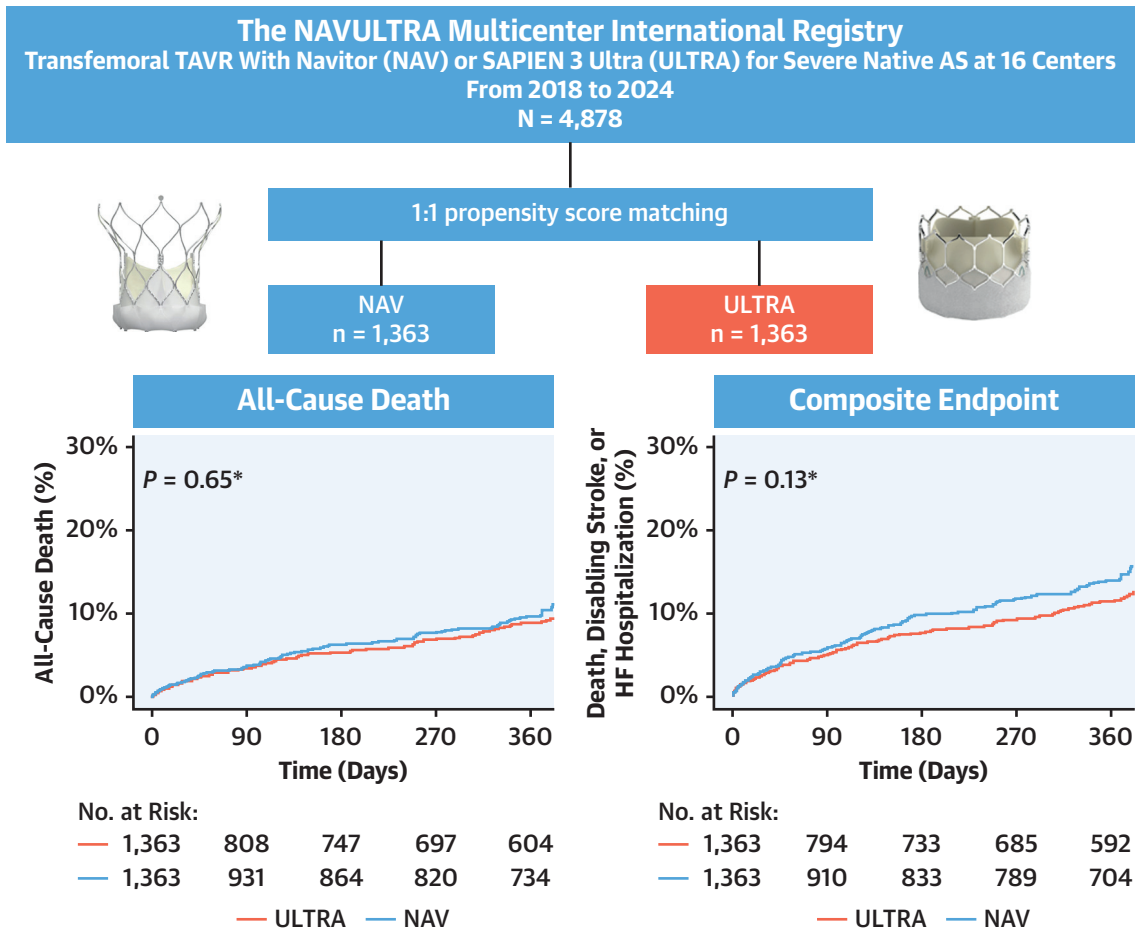
At 1 year, in both the unadjusted and the propensity matched populations (Supplemental Table 2), the absence of PVL was significantly more frequent with ULTRA devices compared with NAV devices (OR: 0.70; 95% CI: 0.54-0.91; $P < 0.01$), whereas there was no significant difference in the rate of moderate or greater PVL (OR: 0.89; 95% CI: 0.31-2.82; $P = 0.896$). Mild PVL was more frequent in the NAV group (OR: 1.53; 95% CI: 0.31-2.82; $P < 0.05$). In contrast, the ULTRA was associated with higher mean transprosthetic gradients compared with the NAV (12.09 mm Hg vs 7.87 mm Hg; $P < 0.01$) (Supplemental Figures 6 and 7).

Sensitivity analyses. The results of the sensitivity analyses are presented in the Supplemental Table 3. Using different PS methods, the results were largely consistent with the primary analysis.

DISCUSSION

The major findings of the present analysis comparing intra-annular SE NAV and BE ULTRA THVs in an unselected, real-world population from an international multicenter registry are as follows: 1) there were no significant differences between SE and BE with respect to 1-year rates of death from any cause and the composite endpoint of any death, disabling stroke, and repeat hospitalization due to HF, but new PPI and rehospitalization for HF were more frequently in patients with an SE THV at 1 year; 2) the VARC-3 technical success rate was >90% for both devices, with no significant difference between groups; 3) the VARC-3 device success was achieved in >85% for both devices, but the BE device had a lower rate of VARC-3 device success, mainly because of higher residual mean transprosthetic gradient; 4) the SE device had a lower rate of VARC-3 early safety, mainly because of higher rates of new PPI; 5) the SE device demonstrated better echocardiographic hemodynamic performance in terms of a lower mean transvalvular gradient and a larger effective orifice area than the BE device; and 6) the incidence of moderate or greater PVL was rare in both devices, but any paravalvular regurgitation, including mild and moderate, was more common in patients with an SE device than those with a BE device.

CENTRAL ILLUSTRATION **1-Year Clinical Primary Outcomes of TAVR With NAV or ULTRA**



Cannata S, et al. JACC Cardiovasc Interv. 2025;18(12):1557–1568.

Study design and Kaplan-Meier curves of all-cause death and primary composite endpoint and at 1 year. *The Kaplan-Meier curves in the figure are derived from a single imputed dataset and should be considered representative of the main results presented in the paper. AS = aortic stenosis; EOA = effective orifice area; HF = heart failure; NAV = Navitor; NAVULTRA = Navitor and SAPIEN 3 Ultra; PPI = permanent pacemaker implantation; PVL = paravalvular leak; TAVR = transcatheter aortic valve replacement; ULTRA = SAPIEN 3 Ultra.

Over recent years, various studies have compared different TAVR platforms to investigate the potential benefits of specific device types.[9-11] The NAVULTRA registry is the first study to report outcomes in patients undergoing TAVR who received intra-annular SE or BE devices. The principal aim of the NAVULTRA registry was to compare the effectiveness of the SE NAV and BE ULTRA devices in a real-world setting at 1 year, using the latest VARC-3 endpoint definitions. In our propensity-matched cohort, the rates of any death and the composite endpoint at 1 year were similar for TAVR with ULTRA and NAV THVs. Similarly, there were no differences in cardiac death, any stroke, disabling stroke, or repeat procedures

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JUNE 23, 2025:1557-1568

between the two groups at 1 year. However, NAV recipients had a higher rate of HF rehospitalization and new PPI implantation at 1 year (**Central Illustration**). The increased risk of rehospitalization for HF in the NAV group may be attributed to multiple factors, including the higher rates of any PVL, new PPI, and new onset left bundle branch block. It is recognized that moderate-to-severe PVL is associated with increased mortality and HF rehospitalization.[12-15] A recent meta-analysis showed that even mild PVL may impact mortality and rehospitalization regardless of the type of THV, though data remain controversial.[16,17] New-onset left bundle branch block and new PPI may also adversely affect long-term clinical outcomes, although the data remain conflicting.[18-21] Dyssynchronization induced by new onset left bundle branch block or pacing may negatively affect left ventricular reverse remodeling, potentially resulting in a higher risk of HF rehospitalizations.[21] However, at this stage, the possibility of chance or residual confounding cannot be excluded.

In the NAVULTRA registry, both intra-annular devices demonstrated high and comparable rates of technical success (87.4% vs 85.9%) in an unselected real-world population of TAVR candidates. Despite similar technical success rates, VARC-3 device success favored SE devices in our analysis, owing to the higher residual transvalvular gradient in the BE group. However, VARC-3 early safety significantly favored BE devices due to the higher rate of new PPI in the SE group. New PPI remains a concern following TAVR, as it has been associated with worse clinical outcomes, including mortality and hospitalization for HF. The rates of new PPI at 30 days and 1 year in the SE group are in line with those reported in previous studies.[5]

In terms of echocardiographic performance, the SE NAV, despite its intra-annular design—which is often considered hemodynamically disadvantageous—demonstrated a lower residual transprosthetic gradient and larger EOAs compared with the intra-annular BE ULTRA. These results are comparable to the performance of supra-annular self-expanding devices.[10,11] The clinical relevance of higher residual transvalvular gradients, with potentially less symptomatic benefit, faster THV deterioration, and a need for reintervention, is still a matter of debate.[22] Recent analysis from the FRANCE-2 (French Aortic National CoreValve and Edwards 2) registry showed increased mortality among patients with persistently elevated gradients at 1 year.[23] Nevertheless, in the present analysis there is no significant difference between the two groups in the occurrence of mortality at 1 year. Conversely, the BE ULTRA exhibited better performance in terms of PVL; the risk of any paravalvular regurgitation, including mild and moderate, was less common in patients with a BE device than in those with an SE device.

Notably, in terms of in-hospital outcomes, both predilation and postdilation were performed more frequently with the NAV compared with the ULTRA. However, this did not impact on complication rates, such as stroke or annulus rupture. The post-TAVR length of stay was significantly longer in the NAV group compared with the ULTRA group, which may be attributed to the higher incidence of conduction abnormalities and new PPI after TAVR.

Finally, the overall rates of all-cause mortality, cardiac death, and disabling stroke at 30 days were very low in our study (**Table 4**), consistent with previous studies evaluating NAV and ULTRA devices.[3-5]

It is important to note that the results of this study are exploratory and need to be corroborated in dedicated clinical trials. In this context, results from the ongoing ENVISION (Safety and Effectiveness of NAVITOR in Transcatheter Aortic Valve Implantation; NCT05932615) clinical trial will be of paramount importance. Although both platforms demonstrated equivalent outcomes at 1 year, the intra-annular SE valves exhibited superior hemodynamic performance with lower residual transprosthetic gradients, albeit at the cost of increased PVL, PPI, and rehospitalization for HF. As we await more conclusive data in the coming years, this analysis provides valuable insights into current best practices for device selection.

Superior hemodynamic valve performance appears to impact on device durability with significant differences emerging beyond 5 years post-TAVR. It may therefore play a particularly relevant role in younger, more active patients with longer life expectancy. In this context, the next generation of BE THVs, the SAPIEN 3 Ultra RESILIA, showed improved hemodynamics with lower gradients compared with the ULTRA.[24] In many regions, the current clinical choice is now between SAPIEN 3 Ultra RESILIA and NAV.

Conversely, PVL has historically been associated with increased mortality, highlighting the role of anatomical factors—such as calcium burden and distribution—which impact on PVL incidence and should be carefully considered in device selection. Additionally, the need for new PPI has been linked to worse clinical outcomes, including increased mortality and HF hospitalizations, reinforcing its importance in THV selection. As TAVR planning evolves, it is increasingly crucial to consider the advantages and potential drawbacks of each device in the context of individual patient characteristics to achieve optimal outcomes.

STUDY LIMITATIONS. This study has the inherent limitations of nonrandomized, observational, retrospective studies without an independent adjudication of clinical events and an independent core laboratory to assess PVL severity. Although we applied a propensity-matched approach based on 38 variables to overcome differences in baseline characteristics and potential confounders, residual confounding remains a source of bias that cannot be excluded. We did not collect the postimplantation height, which could have affected clinical outcomes. Last, selection bias in the THV choice should be acknowledged.

CONCLUSIONS

The NAVULTRA registry showed that in patients undergoing TAVR with NAV and ULTRA devices there were comparable rates of all-cause mortality and the composite endpoint of mortality, rehospitalization for HF, or disabling stroke at 1 year. However, differences were observed in secondary clinical endpoints and valve hemodynamic performance. These findings warrant further investigation in dedicated randomized clinical trials that directly compare the two intra-annular devices.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Van Mieghem has received research grants from Abbott Vascular, Boston Scientific, Edwards Lifesciences, Medtronic, Meril, Pie Medical, PulseCath BV, and Teleflex; and served as a consultant for Abbott, Abiomed, Alleviant Medical Inc., AncorValve, Anteris, Approxima Srl, Bolt Medical, Boston Scientific, Daiichi-Sankyo, LUMA Vision, Materialise, Medtronic, Pie Medical, Polares, PulseCath BV, and Siemens. Dr De Backer has received institutional research grants and consulting fees from Abbott, Boston Scientific, and Medtronic. Dr Byrne has served on the advisory board or as a physician proctor for Abbott and Edwards Lifesciences; and received educational grants from Edwards Lifesciences. Dr Barbanti has served as a consultant for Boston Scientific, Edwards Lifesciences, and Medtronic. Dr Nombela-Franco has served as a proctor for Abbott Vascular and Edwards Lifesciences. Dr Maisano has received grant and/or research institutional support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific, NVT, Terumo, and Venus; has received consulting fees and honoraria (personal and institutional) from Abbott, Boston Scientific, Medtronic, Edwards Lifesciences, Xeltis, CardioValve, Occlufit, Simulands, Mtex, Venus, Squadra, Valgen, and CroiValve; has also royalty income from and IP rights with Edwards Lifesciences; and is a shareholder (including share options) of Magenta, Transseptalsolutions, and 4Tech. Dr Lorusso has received research grant support from Medtronic and LivaNova; received speaker fees from Abiomed; served on the medical advisory board of Xenios and Eurosets; and served as a consultant for Medtronic and LivaNova. Dr Tamburino has served as a consultant for Medtronic. Dr Gandolfo has served as a proctor for Edwards Lifesciences. Dr Latib has served on the advisory board or as a consultant for Medtronic, Boston Scientific, Philips, Edwards Lifesciences, Abbott, Philips, Tresquare, and Anteris. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? Limited data exist on outcomes after TAVR with SE NAV compared with BE ULTRA.

WHAT IS NEW? In this real-world, multicenter study, we found that the two TAVR platforms, NAV and ULTRA, were associated with similar 1-year clinical outcomes, but the NAV devices yielded higher rates of PVL, rehospitalization for HF, and new PPI. Transprosthetic gradients were significantly lower in patients receiving the NAV THV.

WHAT IS NEXT? Randomized clinical trials with longer follow-up are needed to explore the differences between the two devices, aiming for a patient-specific approach to ensure optimized patient outcomes.

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KEY WORDS intra-annular, Navitor, SAPIEN 3 Ultra, TAVR

APPENDIX For a list of participating centers and supplemental tables and figures, please see the online version of this paper.