

Viešoji įstaiga Klaipėdos jūrininkų ligoninė  
(Adresatas (perkančioji organizacija))

**PASIŪLYMAS**  
**DĖL PERKATETERINIŲ BŪDU IMPLANTUOJAMŲ BIOLOGINIŲ AORTOS VOŽTUVŲ**  
**SU ĮVEDIMO SISTEMA PIRKIMO**

2020-04-03 Nr. \_\_\_\_\_

(Data)

Kaunas

(Sudarymo vieta)

Tiekėjo pavadinimas /Jeigu dalyvauja ūkio subjektų grupė, surašomi visi dalyvių pavadinimai/	UAB „Sorimpeksas“
Tiekėjo adresas /Jeigu dalyvauja ūkio subjektų grupė, surašomi visi dalyvių adresai/	Šiaulių g. 16 A, Kaunas
Už pasiūlymą atsakingo asmens vardas, pavardė	Daiva Macijauskienė
Telefono numeris	8 37 361766
Fakso numeris	8 37 324447
El. pašto adresas	<a href="mailto:daiva@sorimpeksas.com">daiva@sorimpeksas.com</a>
Tiekėjo (įmonės) kodas	135733248

Vykdant sutartį pasitelksiu šiuos subteikėjus (subteikėjus):

*Pastaba. Pildoma, jei tiekėjas ketina pasitelkti subrangovą (-us), subteikėją (-us), ar subteikėją (-us)/*

Subteikėjo (-ų) pavadinimas (-ai)	
Subteikėjo (-ų) adresas (-ai)	
Įsipareigojimų dalis (procentais), kuriai ketinama pasitelkti subteikėją (-us)	
Sutarties objekto dalis (-ys), kuriai(-oms) ketinama pasitelkti subteikėją (-us)	

1. Šiuo pasiūlymu pažymime, kad sutinkame su visomis pirkimo sąlygomis, nustatytomis pirkimo dokumentuose (jų paaiškinimuose, papildymuose).

2. Teikdami šį pasiūlymą patvirtiname, kad esame tinkamai įsisteigę ir teisėtai veikiame pagal Lietuvos Respublikos įstatymus, taip pat esame atlikę visus teisinius veiksmus, būtinus, kad pirkimo sutartis būtų tinkamai sudaryta ir galiotų, ir turime visus teisės aktais numatytus leidimus, licencijas, darbuotojus, reikalingus prekėms tiekti. Siūlome šias prekes, kurios visiškai atitinka pirkimo techninėje specifikacijoje nurodytus reikalavimus:

Dalies Nr.	PREKĖS PAVADINIMAS IR REIKALAUJAMOS SAVYBĖS (prekės aprašymas)	Perkamas preliminarius kiekis vienetais	Siūlomų prekių parametrai ir jų reikšmės pagal 2 stulpelio reikalavimus bei tai patvirtinančio dokumento pavadinimas, psl. Nr., kuriame aprašytas nurodytas parametras	Gamintojas, Prekės kodas kataloge	Vnt. kaina € be PVM	Bendra kaina € be PVM (3 * 6)	PVM procento dydis	Bendra kaina € su PVM (7+PVM)
1	2	3	4	5	6	7	8	9
1.	<p><b>Perkateteriniu būdu implantuojamas biologinis aortos vožtuvas su įvedimo sistema, leidžiančia repozicionuoti vožtuvą</b></p> <ul style="list-style-type: none"> <li>- Pilnai sukomplektuotas rinkinys – vožtuvas ir jo įvedimo sistema</li> <li>- Implantavimui aortos vožtuvo pozicijoje</li> <li>- Per a. femoralis, per a. subclavia arba per tiesioginę aortos punkciją</li> <li>- Savaime išsiplečiantis nitinolo rėmelis su įsiūtu vožtuvo protezu. Pastebėjus pozicionavimo klaidą, įvedimo sistema leidžia vožtuvą pakartotinai suspausti ir vėl išskleisti pakeitus poziciją (ne mažiau 3 kartų)</li> <li>- Vožtuvai turi dengti tokius anatominius parametrus: natyvinis vožtuvo perimetras nuo 55+- 2 mm iki 96 +- 2 mm, natyvinis vožtuvo diametras 18-30 mm</li> <li>- Vožtuvo diametras 23-34 mm</li> <li>- Vožtuvo burės yra biologiniai audiniai</li> <li>- Galimybė rinktis vožtuvą su išoriniu biologinio audinio sluoksniu, paravulvuliniais pratekėjimams mažinti.</li> <li>- Turi būti randomizuotų tyrimų publikacijos tarptautiniuose specializuotose leidiniuose (pateikti tai patvirtinančius dokumentus)</li> <li>- CE sertifikatai (pateikti tai patvirtinančius dokumentus)</li> </ul>	23	<p><b>Perkateteriniu būdu implantuojamas biologinis aortos vožtuvas su įvedimo sistema, leidžiančia repozicionuoti vožtuvą</b></p> <ul style="list-style-type: none"> <li>- Pilnai sukomplektuotas rinkinys – vožtuvas ir jo įvedimo sistema</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 1 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO- 1 psl.</li> <li>- Implantavimui aortos vožtuvo pozicijoje</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 1 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO- 1 psl.</li> <li>- Per a. femoralis, per a. subclavia arba per tiesioginę aortos punkciją</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 4 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO - 4 psl.</li> <li>1,2 p.d. Konfidencialu. Brošiura Evolut R Patient Ed Product Access Tear Sheet–1 psl.</li> <li>- Savaime išsiplečiantis nitinolo rėmelis su įsiūtu vožtuvo protezu. Pastebėjus pozicionavimo klaidą, įvedimo sistema leidžia vožtuvą pakartotinai suspausti ir vėl išskleisti pakeitus poziciją ( 3 kartus)</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 1,10 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO- 1,10 psl.</li> <li>- Vožtuvai dengia tokius anatominius parametrus: natyvinis vožtuvo perimetras nuo 56,5 mm iki 94,2 mm, natyvinis vožtuvo diametras 18-30 mm</li> <li>- Vožtuvo diametras 23-34 mm</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU – 1 psl,</li> <li>1, 2 p.d. Konfidencialu. Brošiura Evolut R. Evolut pro – 2 psl.</li> <li>- Vožtuvo burės yra biologiniai audiniai</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU - 1 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO - 1 psl.</li> <li>- Galimybė rinktis vožtuvą su išoriniu biologinio audinio sluoksniu, paravulvuliniais pratekėjimams mažinti.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO – 1 psl.</li> <li>1, 2 p.d. Konfidencialu. Brošiura Evolut PRO. Paravulvulinis pratekėjimu maz.. 3,4 psl. Konfidencialu. Klinik.studija dėl paravulvulinio pratekėjimo -1 psl.</li> <li>- Yra randomizuotų tyrimų publikacijos tarptautiniuose specializuotose leidiniuose Konfidencialu. Evolut Low Risk - article (1 Publikacija), Thiele_EurHeartJ_2020__SOLVE-TAVI publication (2 publikacija), Notion - SAVR vs TAVR publication (3 Publikacija)</li> <li>- CE sertifikatai: Konfidencialu. CE</li> </ul>	Medtronic, Evolut R, Evolut PRO	12970.00	298310.00	5	313225.50

<b>Bendra pirkimo dalies kaina žodžiais: Trys šimtai trylika tūkstančių du šimtai dvidešimt penki eurai 50 ct</b>								
2.	<p><b>Perkateteriniu būdu implantuojamas biologinis aortos vožtuvas su įvedimo sistema, leidžiančia repozicionuoti vožtuvą</b></p> <ul style="list-style-type: none"> <li>- Pilnai sukomplektuotas rinkinys – vožtuvas ir jo įvedimo sistema</li> <li>- Implantavimui aortos vožtuvo pozicijoje</li> <li>- Per a. femoralis, per a. subclavia arba per tiesioginę aortos punkciją</li> <li>- Savaimė išsiplečiantis nitalo rėmelis su įsiūtu vožtuvo protezu. Pastebėjus pozicionavimo klaidą, įvedimo sistema leidžia vožtuvą pakartotinai suspausti ir vėl išskleisti pakeitus poziciją (ne mažiau 3 kartų)</li> <li>- Vožtuvai turi dengti tokius anatominius parametrus: natyvinius vožtuvo perimetrus nuo 55+- 2 mm iki 96 +- 2 mm, natyvinius vožtuvo diametras 18-30 mm</li> <li>- Vožtuvo diametras 23-34 mm</li> <li>- Vožtuvo burės yra biologiniai audiniai</li> <li>- Galimybė rinktis vožtuvą su išoriniu biologinio audinio sluoksniu, paravulvuliniam pratekėjimams mažinti.</li> <li>- Turi būti randomizuotų tyrimų publikacijos tarptautiniuose specializuotose leidiniuose (pateikti tai patvirtinančius dokumentus)</li> <li>- CE sertifikatai (pateikti tai patvirtinančius dokumentus)</li> </ul>	20	<p><b>Perkateteriniu būdu implantuojamas biologinis aortos vožtuvas su įvedimo sistema, leidžiančia repozicionuoti vožtuvą</b></p> <ul style="list-style-type: none"> <li>- Pilnai sukomplektuotas rinkinys – vožtuvas ir jo įvedimo sistema</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 1 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO- 1 psl.</li> <li>- Implantavimui aortos vožtuvo pozicijoje</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 1 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO- 1 psl.</li> <li>- Per a. femoralis, per a. subclavia arba per tiesioginę aortos punkciją</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 4 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO - 4 psl.</li> <li>1,2 p.d. Konfidencialu. Brošiura Evolut R Patient Ed Product Access Tear Sheet–1 psl.</li> <li>- Savaimė išsiplečiantis nitalo rėmelis su įsiūtu vožtuvo protezu. Pastebėjus pozicionavimo klaidą, įvedimo sistema leidžia vožtuvą pakartotinai suspausti ir vėl išskleisti pakeitus poziciją ( 3 kartus)</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU- 1,10 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO- 1,10 psl.</li> <li>- Vožtuvai dengia tokius anatominius parametrus: natyvinius vožtuvo perimetrus nuo 56,5 mm iki 94,2 mm, natyvinius vožtuvo diametras 18-30 mm</li> <li>- Vožtuvo diametras 23-34 mm</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU – 1 psl.</li> <li>1, 2 p.d. Konfidencialu. Brošiura Evolut R. Evolut pro – 2 psl.</li> <li>- Vožtuvo burės yra biologiniai audiniai</li> <li>1,2 p.d. Konfidencialu. Evolut R IFU - 1 psl.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO - 1 psl.</li> <li>- Galimybė rinktis vožtuvą su išoriniu biologinio audinio sluoksniu, paravulvuliniam pratekėjimams mažinti.</li> <li>1,2 p.d. Konfidencialu. Evolut PRO – 1 psl.</li> <li>1, 2 p.d. Konfidencialu. Brošiura Evolut PRO. Paravulvulinio pratekėjimo maz.. 3,4 psl. Konfidencialu. Klinik.studija dėl paravulvulinio pratekėjimo -1 psl.</li> <li>- Yra randomizuotų tyrimų publikacijos tarptautiniuose specializuotose leidiniuose Konfidencialu. Evolut Low Risk - article (1 Publikacija), Thiele_EurHeartJ_2020__SOLVE-TAVI publication (2 publikacija), Notion - SAVR vs TAVR publication (3 Publikacija)</li> <li>- CE sertifikatai: Konfidencialu. CE</li> </ul>	Medtronic, Evolut R, Evolut PRO	12970.00	259400.00	5	272370.00
<b>Bendra pirkimo dalies kaina žodžiais: Du šimtai septyniasdešimt du tūkstančiai trys šimtai septyniasdešimt eurų 00 ct</b>								

**Pastaba: atskirų pozicijų kaina** gali būti išreikšta po kablelio nurodant ne daugiau kaip keturis (4) ženklus. Bendra suma be PVM ir su PVM turi būti išreikšta cento tikslumu, po kablelio nurodant ne daugiau kaip 2 ženklus. 7 stulpelio suma apskaičiuojama: preliminarų kiekį (3 stulpelis) dauginant iš mato vieneto kainos eurais, be PVM (6 stulpelis). 8 stulpelyje nurodomas taikomo PVM dydis procentais. 9 stulpelio bendra kaina skaičiuojama prie 7 stulpelio kainos pridėdant PVM.

Tais atvejais, kai pagal galiojančius teisės aktus tiekėjui nereikia mokėti PVM, jis lentelės atitinkamos skilties nepildo ir nurodo priežastis, dėl kurių PVM nemoka.

7. Tiekėjai pasiūlyme turi nurodyti, kokia pasiūlyme pateikta informacija yra konfidenciali.

Šiame pasiūlyme pateikta ir konfidenciali informacija\* (Pildyti tuomet, jei bus pateikiama konfidenciali informacija):

Eil. Nr.	Pateikto dokumento pavadinimas	Dokumentas yra įkeltas pasiūlymo lango eilutėje „Prisegti dokumentai“
1.	Konfidencialu. CE	Dokumentas yra įkeltas pasiūlymo lango eilutėje „Prisegti dokumentai“
2.	Konfidencialu. Gamintojo įgaliojimas	Dokumentas yra įkeltas pasiūlymo lango eilutėje „Prisegti dokumentai“
2.	Konfidencialu. Brošiūros	Dokumentas yra įkeltas pasiūlymo lango eilutėje „Prisegti dokumentai“
3.	Konfidencialu. RC pažyma	Dokumentas yra įkeltas pasiūlymo lango eilutėje „Prisegti dokumentai“

\*Konfidencialia informacija gali būti, įskaitant, bet ja neapsiribojant, komercinė (gamybinė) paslaptis ir konfidencialieji pasiūlymų aspektai. Konfidencialia negalima laikyti informacijos nurodytos VPI 20 str. 2 d. Tiekėjas neturi teisės nurodyti, kad visa pasiūlyme pateikta informacija yra konfidenciali. Tiekėjas turi aiškiai nurodyti, kokie su pasiūlymu pateikti dokumentai laikytini konfidencialiais. **Jei tiekėjas nenurodo konfidencialios informacijos, laikoma, kad tokios tiekėjo pasiūlyme nėra.**

8. Kartu su pasiūlymu pateikiami šie dokumentai (pasirašydamas pasiūlymą saugiu elektroniniu parašu patvirtinu, kad dokumentų skaitmeninės kopijos yra tikros):

Eil.Nr	Pateiktų dokumentų pavadinimas	Dokumento puslapių skaičius
1.	Direktorius įgaliojimas	1
2.	EBVPD pažyma	13
3.	Konfidencialu. Brošiūros	52
4.	Evolut Low Risk - article (1 Publikacija)	10
5.	Thiele_EurHeartJ_2020__SOLVE-TAVI publication (2 publikacija)	11
6.	Notion - SAVR vs TAVR publication (3 Publikacija)	8
7.	RANDOMIZUOTŲ TYRIMŲ PUBLIKACIJŲ TARPTAUTINIuose SPECIALIZUOTOSE LEIDINIuose VERTIMAI	3

8.	Konfidencialu. Gamintojo įgaliojimas	2
9.	Konfidencialu. CE	2
10.	Konfidencialu. RC pažyma	2

7. Pasiūlymas galioja iki termino, nustatyto pirkimo dokumentuose.

Viešųjų pirkimų vadybininkė  
(Tiekėjo arba jo įgalioto asmens pareigų pavadinimas)      ( Parašas)

Daiva Macijauskienė  
( Vardas ir pavardė)

## ORIGINAL ARTICLE

# Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators\*

## ABSTRACT

**BACKGROUND**

Transcatheter aortic-valve replacement (TAVR) is an alternative to surgery in patients with severe aortic stenosis who are at increased risk for death from surgery; less is known about TAVR in low-risk patients.

**METHODS**

We performed a randomized noninferiority trial in which TAVR with a self-expanding supraannular bioprosthesis was compared with surgical aortic-valve replacement in patients who had severe aortic stenosis and were at low surgical risk. When 850 patients had reached 12-month follow-up, we analyzed data regarding the primary end point, a composite of death or disabling stroke at 24 months, using Bayesian methods.

**RESULTS**

Of the 1468 patients who underwent randomization, an attempted TAVR or surgical procedure was performed in 1403. The patients' mean age was 74 years. The 24-month estimated incidence of the primary end point was 5.3% in the TAVR group and 6.7% in the surgery group (difference, -1.4 percentage points; 95% Bayesian credible interval for difference, -4.9 to 2.1; posterior probability of noninferiority >0.999). At 30 days, patients who had undergone TAVR, as compared with surgery, had a lower incidence of disabling stroke (0.5% vs. 1.7%), bleeding complications (2.4% vs. 7.5%), acute kidney injury (0.9% vs. 2.8%), and atrial fibrillation (7.7% vs. 35.4%) and a higher incidence of moderate or severe aortic regurgitation (3.5% vs. 0.5%) and pacemaker implantation (17.4% vs. 6.1%). At 12 months, patients in the TAVR group had lower aortic-valve gradients than those in the surgery group (8.6 mm Hg vs. 11.2 mm Hg) and larger effective orifice areas (2.3 cm<sup>2</sup> vs. 2.0 cm<sup>2</sup>).

**CONCLUSIONS**

In patients with severe aortic stenosis who were at low surgical risk, TAVR with a self-expanding supraannular bioprosthesis was noninferior to surgery with respect to the composite end point of death or disabling stroke at 24 months. (Funded by Medtronic; ClinicalTrials.gov number, NCT02701283.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Popma at Interventional Cardiology, Beth Israel Deaconess Medical Center, 185 Pilgrim Rd., Boston, MA 02215, or at [jpopma@bidmc.harvard.edu](mailto:jpopma@bidmc.harvard.edu).

\*A complete list of investigators, institutions, and research personnel participating in the Evolut Low Risk Trial is provided in the Supplementary Appendix, available at [NEJM.org](http://NEJM.org).

This article was published on March 17, 2019, at [NEJM.org](http://NEJM.org).

DOI: 10.1056/NEJMoa1816885

Copyright © 2019 Massachusetts Medical Society.

**I**N PREVIOUS STUDIES, WE HAVE SHOWN that transcatheter aortic-valve replacement (TAVR) with the use of a self-expanding supraannular bioprosthesis is superior to medical therapy or surgery in patients with severe, symptomatic aortic stenosis who are at prohibitive or high risk for complications or death from surgery<sup>1-3</sup> and is a noninferior approach in patients deemed to be at intermediate surgical risk.<sup>4,5</sup> Societal guidelines have endorsed the use of TAVR in patients who are at increased risk for complications or death from surgery,<sup>6,7</sup> and the expanded use of TAVR in the United States is closely monitored.<sup>8</sup> The number of TAVR procedures performed in the United States has now surpassed the number of isolated surgical aortic-valve replacements.<sup>9</sup>

Use of TAVR in patients at low surgical risk requires compelling evidence of safety and effectiveness, given the low mortality and stroke incidence with aortic-valve surgery in relatively young, healthy patients.<sup>9</sup> Other outcomes, such as aortic-valve reintervention, coronary-artery obstruction, permanent pacemaker use, and longer-term valve durability, are metrics that also require scrutiny in this population. One small randomized study of TAVR with a self-expanding bioprosthesis as compared with surgery provides support for the safety of TAVR with a self-expanding bioprosthesis in low-risk patients up to 5 years after the procedure.<sup>10,11</sup>

The purpose of the current trial (Evolut Surgical Replacement and Transcatheter Aortic Valve Implantation in Low Risk Patients) was to evaluate the safety and effectiveness of TAVR with a self-expanding bioprosthesis as compared with surgical aortic-valve replacement in patients deemed to have a low risk of death with surgery.

## METHODS

### TRIAL DESIGN

This study was a multinational, randomized, non-inferiority clinical trial comparing the safety and efficacy of TAVR with those of surgery in patients with severe aortic stenosis who were deemed to be at low risk for death at 30 days with surgery. The trial was conducted in compliance with the International Conference on Harmonisation and the Declaration of Helsinki. Patients were enrolled at 86 centers in Australia, Canada, France, Japan, the Netherlands, New Zealand, and the United

States (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Local institutional review boards or medical ethics committees approved the protocol, available at NEJM.org.

Medtronic funded the trial and developed the protocol in collaboration with the executive committee (see Table S2 in the Supplementary Appendix for members of committees). Medtronic was responsible for site selection, data monitoring, and trial management. Paradigm Biostatistics performed the Bayesian end-point comparisons; an independent statistical consultant validated all end-point analyses. An independent data and safety monitoring board provided study oversight.

The principal investigators (the first and last authors) wrote the first draft of the manuscript; all the authors critically reviewed it, made revisions, and supported the decision to submit the manuscript for publication. The authors attest that the trial was performed according to the protocol and vouch for the accuracy and completeness of the data.

### PATIENT SELECTION

Eligible patients had severe aortic-valve stenosis with suitable anatomy for TAVR or surgery and no more than a predicted 3% risk of death by 30 days with surgery, as assessed by members of the local heart team. Aortic stenosis was defined as an aortic-valve area of 1.0 cm<sup>2</sup> or less (or aortic-valve area index of  $\leq 0.6$  cm<sup>2</sup> per square meter) or a mean gradient of 40 mm Hg or more or maximal aortic-valve velocity of 4.0 m or more per second as assessed by transthoracic echocardiography performed with the patient at rest. A detailed list of inclusion and exclusion criteria, including criteria for inclusion of asymptomatic patients, is provided in Table S3 in the Supplementary Appendix. The screening committee confirmed all decisions regarding patient selection (see the Methods section in the Supplementary Appendix). All patients provided written informed consent.

### STUDY PROCEDURES

Randomization was performed in a 1:1 ratio, with variable block sizes, with an electronic randomization system. Randomization was stratified by site and the need for coronary-artery revascularization. Patients assigned to TAVR were treated with one of three self-expanding, supraannular bioprostheses (CoreValve, Evolut R, or Evolut PRO;

Medtronic) (Fig. S1 in the Supplementary Appendix). The size and type of surgical valve were at the discretion of the surgeon, although candidates for mechanical valves were excluded. Patients were evaluated at baseline, at discharge, and at 1, 6, 12, 18, and 24 months after the procedure. All echocardiographic studies were assessed at an independent core laboratory (Mayo Clinic). Health-related quality of life was assessed with the Kansas City Cardiomyopathy Questionnaire (KCCQ). KCCQ summary scores range from 0 to 100, with higher scores indicating better health status; scores higher than 60 correlate with New York Heart Association (NYHA) class I or II, and a 10-point increase corresponds to moderate clinical improvement.<sup>12,13</sup>

#### STUDY END POINTS

The primary safety and effectiveness end point was a composite of death from any cause or disabling stroke at 24 months. Disabling stroke was defined by a score on the modified Rankin scale of 2 or more (with scores ranging from 0 [no symptoms] to 6 [death]) at 90 days and an increase of at least 1 category from baseline (i.e., before the stroke). There were seven prespecified secondary end points that were tested hierarchically for either noninferiority or superiority (see the Hierarchical Testing section in the Supplementary Appendix). Additional secondary safety end points included a composite of death, disabling stroke, life-threatening bleeding, major vascular complication, or stage 2 or 3 acute kidney injury at 30 days; and prosthetic-valve endocarditis, prosthetic-valve thrombosis, prosthetic-valve dysfunction requiring a repeat procedure, stroke, and life-threatening bleeding at 12 months. The full list of secondary end points is provided in the Methods section in the Supplementary Appendix.

An independent academic clinical-events committee (Baim Institute for Clinical Research, Boston) adjudicated all end points, using standard definitions (Table S4 in the Supplementary Appendix). End-point adjudication was blinded when feasible (for some end points, knowledge of treatment assignment was inherent in the end-point assessment).

#### STATISTICAL ANALYSIS

This trial used Bayesian adaptive statistical methods with noninformative prior distributions to assess the primary end point. We hypothesized

that TAVR would be noninferior to surgery with respect to the primary end point with a noninferiority margin of 6%. The primary end point was to be tested for the superiority of TAVR to surgery if the primary objective (noninferiority with respect to the primary end point) and all seven prespecified hierarchical secondary objectives met their designated success criterion (in the hierarchical testing order). The prespecified success criteria were a posterior probability greater than 0.972 for noninferiority and greater than 0.984 for superiority, criteria that were selected empirically through extensive simulations to achieve a type I error rate of no more than 0.05 for noninferiority testing and no more than 0.025 for superiority testing.

The estimated sample size of 1200 patients was selected on the basis of an assumed 15% incidence of death or disabling stroke at 24 months; 1468 patients were ultimately enrolled to permit completion of a randomized substudy of valve leaflet immobility and thrombosis and to meet Japanese regulatory requirements. A prespecified Bayesian interim analysis was to be performed 12 months after the 850th patient underwent the study procedure (see the Methods section in the Supplementary Appendix). For patients who did not complete 24 months of follow-up, we imputed their outcome according to a prespecified statistical model, which was based on the patient's last known clinical status. A sensitivity analysis was performed to account for missing data, including data for the patients who were lost to follow-up or withdrew from the study.

The primary analysis cohort was the as-treated population, which comprised patients who were randomly assigned to a group and who underwent an attempted procedure. Secondary analyses of the primary end point were also performed in the intention-to-treat population, the "implanted" population (patients in whom an aortic valve was implanted), and the per-protocol population. Details regarding the primary objective, analysis populations, sensitivity analyses, and hierarchical testing methods among secondary end points are provided in the Methods section in the Supplementary Appendix. We used a Bayesian analogue of a two-sample t-test to compare continuous variables with a noninformative prior distribution. Event rates are summarized as Bayesian posterior medians with 95% credible intervals, which were calculated from the 2.5th and 97.5th percentiles

of the posterior distributions. The Bayesian credible intervals for secondary end points use marginal posterior distributions that are probably narrower than those that are based on a true multidimensional posterior for the collection of outcomes. Caution should therefore be exercised in drawing inferences about absolute treatment effects with the 95% Bayesian credible intervals, owing to the multiplicity of secondary end-point comparisons.

## RESULTS

### **BASILINE CHARACTERISTICS**

From March 28, 2016, to November 27, 2018, a total of 1468 patients underwent randomization; 734 were assigned to TAVR and 734 were assigned to surgery. After randomization, the assigned procedure was not attempted in 12 patients assigned to TAVR and 53 patients assigned to surgery; in 3 patients assigned to surgery, TAVR was attempted instead (Fig. S2 and Results section in the Supplementary Appendix). The as-treated cohort included 1403 patients: 725 in the TAVR group and 678 in the surgery group.

Demographic and baseline characteristics and cardiac risk factors are shown in Table 1. The mean age of the patients was 74 years, 34.9% were women, and all the patients were at low surgical risk. There were no significant differences between the two treatment groups. Among patients who were assigned to the surgery group, the baseline characteristics of those who actually underwent surgery were similar to the characteristics of those who did not undergo surgery (Table S5 in the Supplementary Appendix). A detailed description of procedural end points is provided in the Results section in the Supplementary Appendix.

At this prespecified interim analysis, 12-month follow-up was available for 432 patients in the TAVR group and 352 in the surgery group; 24-month follow-up was available for 72 patients in the TAVR group and 65 patients in the surgery group. The median follow-up time in each group was 12.2 months.

### **PRIMARY SAFETY AND EFFECTIVENESS END POINT**

The incidence of death or disabling stroke at 24 months (the primary end point) was 5.3% in the TAVR group (95% Bayesian credible interval, 3.3 to 8.0) and 6.7% in the surgery group (95% Bayesian credible interval, 4.4 to 9.6). The prespecified

criterion for noninferiority was met (difference,  $-1.4$  percentage points; 95% Bayesian credible interval for the difference,  $-4.9$  to  $2.1$ ; posterior probability of noninferiority,  $>0.999$ ) (Fig. 1); the prespecified criterion for superiority was not met (posterior probability of superiority,  $0.779$ ). A noninferiority analysis using the intention-to-treat cohort yielded similar results. A sensitivity analysis that was performed to account for patients who were lost to follow-up also had similar results (details on these analyses are provided in Tables S6 through S8 and the Methods section in the Supplementary Appendix).

The 24-month estimated incidence of death from any cause was 4.5% in the TAVR group and 4.5% in the surgery group (difference,  $0$  percentage points; 95% credible interval for the difference,  $-3.2$  to  $3.2$ ). The 24-month estimated incidence of disabling stroke was 1.1% in the TAVR group and 3.5% in the surgery group (difference,  $-2.3$  percentage points; 95% credible interval for the difference,  $-4.8$  to  $-0.4$ ). No significant treatment-by-subgroup interactions were noted for the primary end point (Fig. S3 in the Supplementary Appendix).

### **SECONDARY SAFETY MEASURES**

The incidence of the secondary composite safety end point at 30 days was 5.3% in the TAVR group and 10.7% in the surgery group (Table 2). The incidence of death from any cause at 30 days was 0.5% in the TAVR group and 1.3% in the surgery group; causes of death are shown in Table S9 in the Supplementary Appendix. The ratio of observed to expected incidence of death from any cause by 30 days (with expected risk calculated on the basis of the Society of Thoracic Surgeons Predicted Risk of Mortality [STS-PROM] model) was 0.26 in the TAVR group and 0.68 in the surgery group. New atrial fibrillation at 30 days occurred in 7.7% of the patients in the TAVR group and in 35.4% in the surgery group (difference,  $-27.7$  percentage points; credible interval for the difference,  $-31.8$  to  $-23.6$ ), whereas permanent pacemaker implantation occurred in 17.4% of the patients in the TAVR group and in 6.1% in the surgery group (difference,  $11.3$  percentage points; credible interval for the difference,  $8.0$  to  $14.7$ ) (Table 2). Incidences of stroke, prosthetic-valve thrombosis, endocarditis, and reintervention were similar in the two groups at 12 months.

**Table 1. Characteristics of the Patients at Baseline.\***

Characteristic	As-Treated Analysis		Intention-To-Treat Analysis	
	TAVR (N=725)	Surgery (N=678)	TAVR (N=734)	Surgery (N=734)
Age — yr	74.1±5.8	73.6±5.9	74.0±5.9	73.8±6.0
Female sex — no. (%)	261 (36.0)	229 (33.8)	266 (36.2)	246 (33.5)
NYHA class — no. (%)				
I	76 (10.5)	63 (9.3)	77 (10.5)	73 (9.9)
II	467 (64.4)	422 (62.2)	476 (64.9)	456 (62.1)
III	181 (25.0)	190 (28.0)	180 (24.5)	202 (27.5)
IV	1 (0.1)	3 (0.4)	1 (0.1)	3 (0.4)
STS-PROM — %†	1.9±0.7	1.9±0.7	1.9±0.7	1.9±0.7
Diabetes mellitus — no. (%)	228 (31.4)	207 (30.5)	228 (31.1)	224 (30.5)
Serum creatinine >2 mg/dl — no. (%)	3 (0.4)	1 (0.1)	3 (0.4)	1 (0.1)
Dialysis — no. (%)	0	1 (0.1)	0	1 (0.1)
Hypertension — no./total no. (%)	614/724 (84.8)	559/677 (82.6)	622/733 (84.9)	608/733 (82.9)
Peripheral arterial disease — no./total no. (%)	54/718 (7.5)	56/678 (8.3)	55/727 (7.6)	62/733 (8.5)
Cerebrovascular disease — no. (%)	74 (10.2)	80 (11.8)	74 (10.1)	84 (11.4)
Chronic obstructive pulmonary disease — no./total no. (%)	104/695 (15.0)	117/649 (18.0)	106/703 (15.1)	121/703 (17.2)
Cardiac risk factors				
SYNTAX score‡	1.9±3.7	2.1±3.9	1.9±3.7	2.1±3.8
Previous coronary-artery bypass surgery — no. (%)	18 (2.5)	14 (2.1)	18 (2.5)	17 (2.3)
Previous percutaneous coronary intervention — no. (%)	103 (14.2)	87 (12.8)	102 (13.9)	93 (12.7)
Preexisting pacemaker or defibrillator — no. (%)	23 (3.2)	26 (3.8)	25 (3.4)	28 (3.8)
Previous myocardial infarction — no. (%)	48 (6.6)	33 (4.9)	49 (6.7)	39 (5.3)
Previous atrial fibrillation or atrial flutter — no./total no. (%)	111/722 (15.4)	98/678 (14.5)	113/731 (15.5)	109/734 (14.9)
Aortic-valve gradient — mm Hg§	47.0±12.1	46.6±12.2	47.2±12.3	46.7±12.2
Aortic-valve area — cm <sup>2</sup> §	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.2
Left ventricular ejection fraction — %§	61.7±7.9	61.9±7.7	61.7±7.9	61.9±7.7

\* Plus–minus values are means ±SD. There were no significant differences between the treatment groups. Percentages may not total 100 because of rounding. To convert the values for serum creatinine to micromoles per liter, multiply by 88.4. NYHA denotes New York Heart Association, and TAVR transcatheter aortic-valve replacement.

† The Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) provides an estimate of the risk of death at 30 days among patients undergoing surgical aortic-valve replacement on the basis of several demographic and procedural variables.

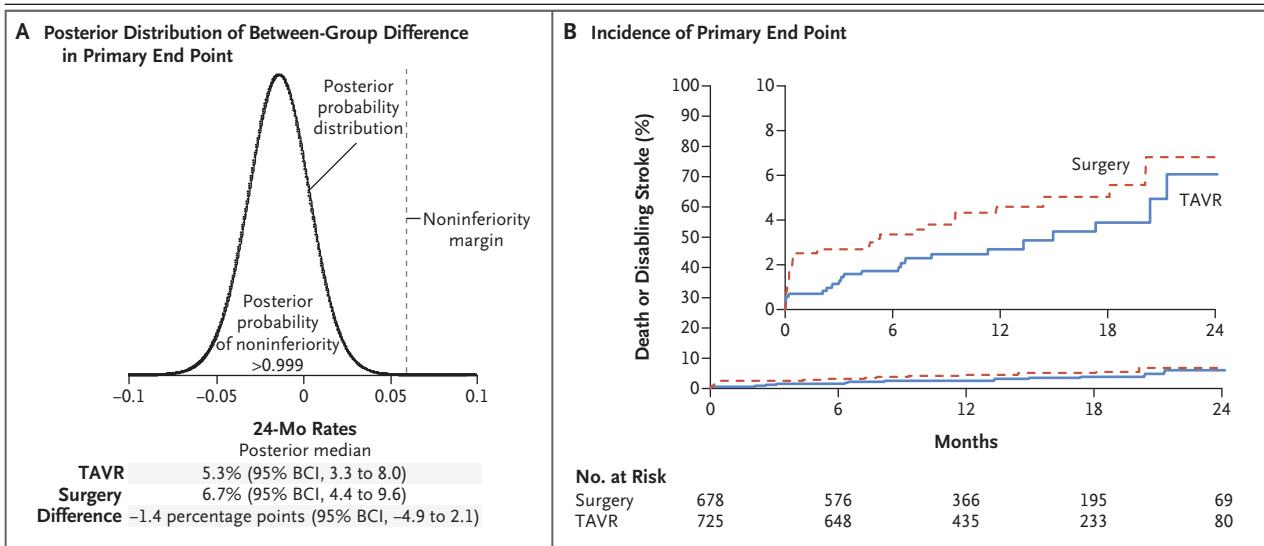
‡ The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score is a measure of the severity and extent of coronary artery disease. Low SYNTAX scores (<18) are associated with a higher success rate with PCI, scores between 18 and 27 with an intermediate success rate, and scores higher than 27 with a low success rate.

§ These data were reported by the individual trial site.

## SECONDARY EFFECTIVENESS MEASURES

Results of hierarchical analyses of the secondary effectiveness end points are provided in Table 3; all these end points met the prespecified test threshold. Symptoms graded by NYHA class decreased significantly from baseline in both groups, and this reduction in symptoms persisted throughout the 12-month follow-up period (Fig. S4 in

the Supplementary Appendix). Hospitalization for heart failure during the 12-month follow-up period occurred in 3.2% of the patients in the TAVR group and in 6.5% in the surgery group (difference, –3.4 percentage points; 95% credible interval for the difference, –5.9 to –1.0). The KCCQ overall summary score (±SD) measuring quality of life was 88.7±14.2 in the TAVR group



**Figure 1. Posterior Distribution and Time-to-Event Curves for the Primary End Point.**

The posterior distribution for the difference between the treatment groups in the incidence of death from any cause or disabling stroke at 24 months (the primary end point), shown in Panel A, confirmed that the noninferiority criterion for the primary end point was met. BCI denotes Bayesian credible interval, and TAVR transcatheter aortic-valve replacement. Panel B shows Kaplan–Meier time-to-event curves for the primary end point. The inset shows the same data on an enlarged y axis.

and  $78.6 \pm 18.9$  in the surgery group at 30 days, with no difference between groups observed at 12 months (Table S10 in the Supplementary Appendix). Among patients who were discharged from the hospital after undergoing TAVR, there was no significant difference in the incidence of death by 12 months between those who received a new permanent pacemaker and those who did not (3.4% and 1.2%, respectively).

#### ECHOCARDIOGRAPHIC FINDINGS

Aortic-valve hemodynamics improved from baseline in both groups (Fig. 2). Mean aortic-valve gradients were lower at 12 months in the TAVR group than in the surgery group; the mean effective orifice area was larger in the TAVR group than in the surgery group (Table 3). Moderate or severe total aortic regurgitation was present at 30 days in 3.5% of the patients in the TAVR group and in 0.5% in the surgery group. Severe patient–prosthesis mismatch occurred at 12 months in 1.8% of the patients in the TAVR group and in 8.2% in the surgery group (Table S11 in the Supplementary Appendix).

#### DISCUSSION

Our study, which used an adaptive Bayesian design, showed that among patients deemed to be

at a low risk for death from surgery, TAVR with a self-expanding supraannular bioprosthesis was noninferior to surgery with respect to the risk of death or disabling stroke at 24 months. TAVR with a self-expanding supraannular bioprosthesis was associated with a lower incidence of disabling stroke, acute kidney injury, bleeding events, and atrial fibrillation than surgery but with a higher incidence of aortic regurgitation and permanent pacemaker use. Both TAVR and surgery provided functional improvement at 12 months, but the TAVR group had better recovery at 30 days, as indicated by the KCCQ score.

Our study group has conducted a series of clinical studies that have compared TAVR with a self-expanding supraannular bioprosthesis with surgery in patients at various degrees of surgical risk.<sup>2,5,14</sup> The current interim analysis includes patients at the lowest reported risk from surgery among these trials (mean STS-PROM, 1.9%). The 30-day incidence of death in both groups was very low (0.5% in the TAVR group and 1.3% in the surgery group) with a low ratio of observed-to-expected incidence of death in both groups (0.26 in the TAVR group and 0.68 in the surgery group), a finding that is probably attributable to the use of best practices by our heart teams. We selected the primary end point of death from any cause or disabling stroke at 24 months owing to

**Table 2. Clinical End Points at 30 Days and at 12 Months.\***

End Point	30 Days			12 Months		
	TAVR	Surgery	Difference, TAVR–Surgery (95% BCI)	TAVR	Surgery	Difference, TAVR–Surgery (95% BCI)
	% of patients	% of patients	percentage points	% of patients	% of patients	percentage points
Death from any cause or disabling stroke	0.8	2.6	–1.8 (–3.2 to –0.5)	2.9	4.6	–1.8 (–4.0 to 0.4)
Death from any cause	0.5	1.3	–0.8 (–1.9 to 0.2)	2.4	3.0	–0.6 (–2.6 to 1.3)
Death from cardiovascular cause	0.5	1.3	–0.8 (–1.9 to 0.2)	1.7	2.6	–0.9 (–2.7 to 0.7)
All stroke	3.4	3.4	0.0 (–1.9 to 1.9)	4.1	4.3	–0.2 (–2.4 to 1.9)
Disabling	0.5	1.7	–1.2 (–2.4 to –0.2)	0.8	2.4	–1.6 (–3.1 to –0.3)
Nondisabling	3.0	1.7	1.2 (–0.3 to 2.9)	3.4	2.2	1.1 (–0.6 to 2.9)
Transient ischemic attack	0.6	0.8	–0.2 (–1.2 to 0.7)	1.7	1.8	–0.2 (–1.6 to 1.3)
30-Day composite safety end point†	5.3	10.7	–5.4 (–8.3 to –2.6)	NA	NA	NA
Life-threatening or disabling bleeding	2.4	7.5	–5.1 (–7.5 to –2.9)	3.2	8.9	–5.7 (–8.4 to –3.1)
Major vascular complication	3.8	3.2	0.6 (–1.4 to 2.5)	3.8	3.5	0.3 (–1.7 to 2.3)
Acute kidney injury stage 2 or 3	0.9	2.8	–1.8 (–3.4 to –0.5)	0.9	2.8	–1.8 (–3.4 to –0.5)
Atrial fibrillation	7.7	35.4	–27.7 (–31.8 to –23.6)	9.8	38.3	–28.5 (–32.8 to –24.1)
Permanent pacemaker implantation	17.4	6.1	11.3 (8.0 to 14.7)	19.4	6.7	12.6 (9.2 to 16.2)
Myocardial infarction	0.9	1.3	–0.4 (–1.5 to 0.7)	1.7	1.6	0.1 (–1.3 to 1.5)
Coronary-artery obstruction	0.9	0.4	0.5 (–0.3 to 1.4)	0.9	0.4	0.5 (–0.3 to 1.4)
Endocarditis	0.1	0.2	–0.1 (–0.7 to 0.3)	0.2	0.4	–0.2 (–0.9 to 0.5)
Valve thrombosis	0.1	0.1	0.0 (–0.4 to 0.4)	0.2	0.3	–0.1 (–0.9 to 0.5)
Aortic reintervention	0.4	0.4	0.0 (–0.8 to 0.7)	0.7	0.6	0.0 (–1.0 to 0.9)
Hospitalization for heart failure	1.2	2.5	–1.3 (–2.8 to 0.1)	3.2	6.5	–3.4 (–5.9 to –1.0)

\* Values represent the estimated incidence (median of the posterior probability distribution as calculated by Bayesian analysis). Caution should be exercised regarding drawing inferences about absolute treatment effects with the 95% Bayesian credible interval (BCI), owing to multiple secondary end-point comparisons.

† The 30-day composite safety end point was a composite of death, disabling stroke, life-threatening bleeding, major vascular complication, or stage 2 or 3 acute kidney injury.

the implications of these results for patients and providers considering options for aortic-valve replacement. The estimated 24-month incidence of death from any cause was low (4.5%) in both groups, a finding that reinforced the fact that our study included healthier patients with severe aortic-valve disease.

Neurologic complications associated with aortic-valve replacement are increasingly recognized as critical outcome measures in studies comparing transcatheter and surgical procedures.<sup>15,16</sup> We performed functional neurologic assessments before and after both procedures; a very small number of patients (<2%) in the TAVR group received an embolic protection device (see the Supplementary Appendix). Although the incidence of stroke was similar in the two groups, disabling stroke by 30 days occurred less often in the TAVR

group, and the incidence remained lower at 24 months; these findings are similar to those in previous randomized trials of TAVR involving patients at increased surgical risk.<sup>2,4</sup>

Although aortic-valve hemodynamics were substantially improved from baseline in both groups, we found lower aortic-valve gradients and larger aortic-valve areas in the TAVR group, findings that are probably related to the supraannular design of the self-expanding bioprostheses.<sup>2,4,14,17-19</sup> Although 22.1% of the patients in the surgery group received small (19-mm or 21-mm) prostheses, the mean aortic-valve areas were large (2.0 cm<sup>2</sup>), and the incidence of 12-month severe prosthesis–patient mismatch (8.2%) was less than in previous reports.<sup>20,21</sup> Nonetheless, valve areas were larger, and the frequency of prosthesis–patient mismatch was lower, with TAVR. In contrast, rates of aortic

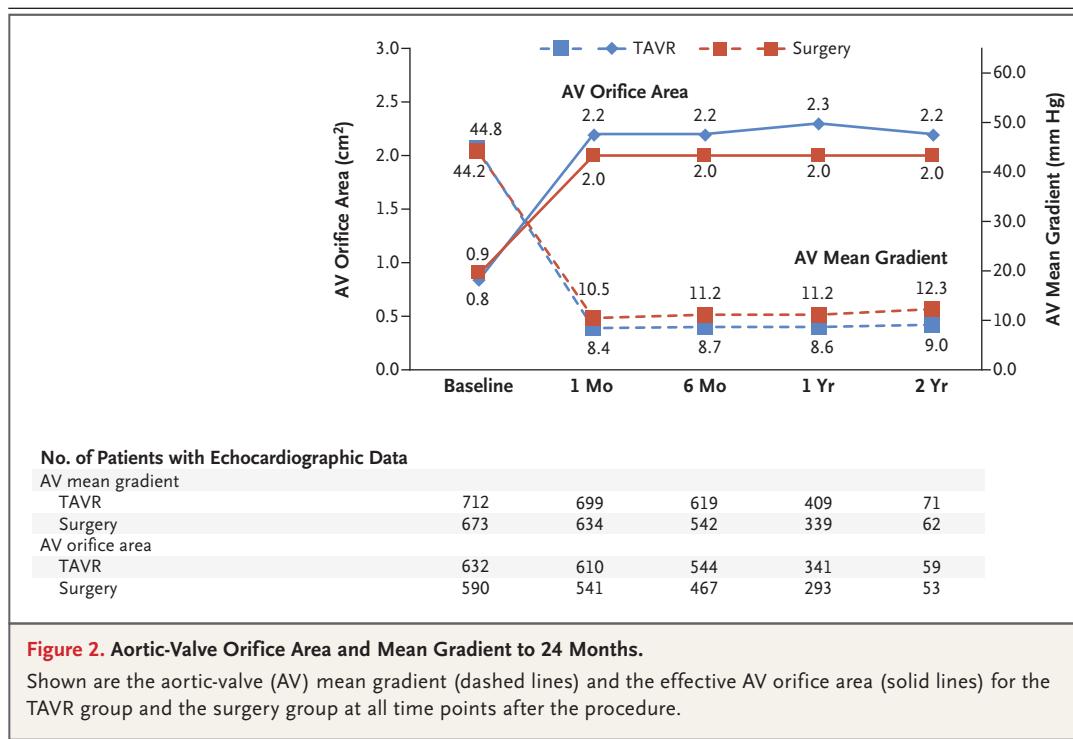
**Table 3. Hierarchical Secondary Noninferiority and Superiority Objectives.\***

Criterion	Hypothesis	Analysis Cohort	TAVR	Surgery	Difference, TAVR–Surgery (90% BCI)	Posterior Probability	Threshold	Test Result
<b>Noninferiority</b>								
Mean gradient at 12 mo (mm Hg)	TAVR < [surgery + 5 mm Hg]†	Implanted	8.6±3.7 (409)	11.2±4.9 (339)	-2.6 (-3.1 to -2.1)	>0.999	0.95	Passed
Mean effective orifice area at 12 mo (cm <sup>2</sup> )	TAVR > [surgery - 0.1 cm <sup>2</sup> ]†	Implanted	2.3±0.7 (341)	2.0±0.6 (293)	0.3 (0.2 to 0.4)	>0.999	0.95	Passed
Mean NYHA class change from baseline to 12 mo	TAVR > [surgery - 0.375]†	As-treated	0.9±0.7 (428)	1.0±0.7 (342)	-0.1 (-0.2 to 0.0)	>0.999	0.95	Passed
Mean KCCQ change from baseline to 12 mo	TAVR > [surgery - 5 points]‡	As-treated	22.2±20.3 (428)	20.9±21.0 (347)	1.3 (-1.2 to 3.8)	>0.999	0.95	Passed
<b>Superiority</b>								
Mean gradient at 12 mo (mm Hg)	TAVR < surgery	Implanted	8.6±3.7 (409)	11.2±4.9 (339)	-2.6 (-3.2 to -2.0)	>0.999	0.975	Passed
Mean effective orifice area at 12 mo (cm <sup>2</sup> )	TAVR > surgery	Implanted	2.3±0.7 (341)	2.0±0.6 (293)	0.3 (0.2 to 0.4)	>0.999	0.975	Passed
Mean KCCQ change from baseline to 30 days	TAVR > surgery	As-treated	20.0±21.1 (713)	9.1±22.3 (636)	10.9 (8.6 to 13.2)	>0.999	0.975	Passed

\* Plus-minus values are means ±SD. The numbers of patients with data are in parentheses. All noninferiority objectives were tested with a type I error standard of 0.05, and superiority tests were tested with a type I error of 0.025. If all the tests met their success criterion, the primary end point of death or disabling stroke at 24 months was tested for superiority with type I error rate of 0.025.

† Clinically meaningful differences of 5 mm Hg for mean gradient, 0.1 cm<sup>2</sup> for effective orifice area, and 0.375 for the NYHA class were determined by the Low Risk Trial Executive Committee.

‡ Kansas City Cardiomyopathy Questionnaire (KCCQ) summary scores range from 0 to 100, with higher scores indicating better health status; scores higher than 60 correlate with NYHA class I or II, and a 10-point increase corresponds to moderate clinical improvement. An increase of 5 points was deemed to be clinically meaningful.<sup>13</sup>



**Figure 2. Aortic-Valve Orifice Area and Mean Gradient to 24 Months.**

Shown are the aortic-valve (AV) mean gradient (dashed lines) and the effective AV orifice area (solid lines) for the TAVR group and the surgery group at all time points after the procedure.

regurgitation were higher in the TAVR group. Longer-term follow-up will be necessary to understand the implications of these various valve characteristics on structural valve deterioration and long-term outcomes. We found a low incidence (<1%) of bioprosthetic-valve thrombosis, endocarditis, or need for aortic-valve reintervention with both self-expanding and surgical bioprostheses.

Our study has several limitations. The most important limitation is that this prespecified interim analysis occurred when 850 patients had reached 12 months of follow-up, and complete 24-month follow-up of the entire cohort has not been reached. Definitive conclusions regarding the advantages and disadvantages of TAVR as compared with surgery await long-term clinical and echocardiographic follow-up, which is planned to continue through 10 years for all patients. Second, although the amount of missing data in the trial was small, some patients did not have complete follow-up data on NYHA functional class, KCCQ scores, and echocardiography. Third, end-point adjudication could not be performed

in a blinded manner for all end points, which may have resulted in bias in end-point assessment. Fourth, we excluded patients with bicuspid aortic valves and those who were candidates for mechanical valves. Finally, the latest-generation Evolut PRO bioprosthesis was used in only 22.3% of the patients who received TAVR.

In conclusion, in a randomized trial involving patients with severe aortic stenosis who were at low risk for death from surgery, TAVR with a self-expanding supraannular bioprosthesis was noninferior to surgical aortic-valve replacement with respect to death from any cause or disabling stroke at 24 months.

Supported by Medtronic.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

We thank Manuela Negoita, M.D., and Eric Vang, Ph.D., for providing scientific review, Jennifer Maloney, M.B.A., Joleen Perkins, B.S., Hang Nguyen, B.S., Sonia Diaz De Leon, M.S., and Charles Boldt, M.A., for study management, and Jane Moore, M.S., E.L.S., and Colleen Gilbert, Pharm.D., for providing editorial assistance with an earlier version of the manuscript.

## APPENDIX

The authors' affiliations are as follows: Beth Israel Deaconess Medical Center, Boston (J.J.P.); University of Michigan Hospitals, Ann Arbor (G.M.D., S.J.C.), and Spectrum Health Hospitals, Grand Rapids (J.C.H., W.M.) — both in Michigan; Riverside Methodist–Ohio Health, Columbus (S.J.Y.); University of Pittsburgh Medical Center Pinnacle Health, Harrisburg (M.M., H.G.), and the University of Pittsburgh, Pittsburgh (T.G.G.) — both in Pennsylvania; Aurora–Saint Luke's Medical Center, Milwaukee (D.O., T.B.); Houston Methodist DeBakey Heart and Vascular Center, Houston (N.S.K., M.J.R.); Abbott Northwestern Hospital (J.A., P.S.) and Medtronic (M.J.B., H.Q.), Minneapolis, Mayo Clinic, Rochester (J.K.O.), and Paradigm Biostatistics, Anoka (A.S.M.) — all in Minnesota; Morton Plant Hospital, Clearwater, FL (J. Rovin); Mount Sinai Health System, New York (D.H.A.), and Saint Francis Hospital, Roslyn (N.R., G.P.) — both in New York; Scripps Clinic and Research Foundation, La Jolla, CA (P.S.T.); University of Kansas Hospital, Kansas City (G.L.Z.); Yale New Haven Hospital, New Haven, CT (J.K.F.); Clinique Pasteur, Toulouse, France (D.T.); Johns Hopkins Hospital, Baltimore (J. Resar); Alfred Hospital, Melbourne, VIC, Australia (A.W.); McGill University Health Centre, Montreal (N.P.); and Winchester Medical Center, Winchester, VA (B.R.).

## REFERENCES

- Popma JJ, Adams DH, Reardon MJ, et al. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol* 2014;63:1972-81.
- Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790-8.
- Reardon MJ, Adams DH, Kleiman NS, et al. 2-Year outcomes in patients undergoing surgical or self-expanding transcatheter aortic valve replacement. *J Am Coll Cardiol* 2015;66:113-21.
- Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321-31.
- Reardon MJ, Kleiman NS, Adams DH, et al. Outcomes in the randomized CoreValve US Pivotal High Risk Trial in patients with a Society of Thoracic Surgeons risk score of 7% or less. *JAMA Cardiol* 2016;1:945-9.
- Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017;135(25):e1159-e1195.
- Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739-91.
- Grover FL, Vemulapalli S, Carroll JD, et al. 2016 Annual report of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *Ann Thorac Surg* 2017;103:1021-35.
- D'Agostino RS, Jacobs JP, Badhwar V, et al. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2019 update on outcomes and quality. *Ann Thorac Surg* 2019;107:24-32.
- Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the All-Comers NOTION randomized clinical trial. *J Am Coll Cardiol* 2015;65:2184-94.
- Thyregod HGH, Ihlemann N, Jørgensen TH, et al. Five-year clinical and echocardiographic outcomes from the Nordic Aortic Valve Intervention (NOTION) randomized clinical trial in lower surgical risk patients. *Circulation* 2019 February 1 (Epub ahead of print).
- Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol* 2000;35:1245-55.
- Spertus J, Peterson E, Conard MW, et al. Monitoring clinical changes in patients with heart failure: a comparison of methods. *Am Heart J* 2005;150:707-15.
- Gleason TG, Reardon MJ, Popma JJ, et al. 5-Year outcomes of self-expanding transcatheter versus surgical aortic valve replacement in high-risk patients. *J Am Coll Cardiol* 2018;72:2687-96.
- Gleason TG, Schindler JT, Adams DH, et al. The risk and extent of neurologic events are equivalent for high-risk patients treated with transcatheter or surgical aortic valve replacement. *J Thorac Cardiovasc Surg* 2016;152:85-96.
- Kleiman NS, Maini BJ, Reardon MJ, et al. Neurological events following transcatheter aortic valve replacement and their predictors: a report from the CoreValve Trials. *Circ Cardiovasc Interv* 2016;9(9):e003551.
- Little SH, Oh JK, Gillam L, et al. Self-expanding transcatheter aortic valve replacement versus surgical valve replacement in patients at high risk for surgery: a study of echocardiographic change and risk prediction. *Circ Cardiovasc Interv* 2016;9(6):e003426.
- Søndergaard L, Steinbrüchel DA, Ihlemann N, et al. Two-year outcomes in patients with severe aortic valve stenosis randomized to transcatheter versus surgical aortic valve replacement: the All-Comers Nordic Aortic Valve Intervention Randomized Clinical Trial. *Circ Cardiovasc Interv* 2016;9(6):e003665.
- Hahn RT, Leipsic J, Douglas PS, et al. Comprehensive echocardiographic assessment of normal transcatheter valve function. *JACC Cardiovasc Imaging* 2019;12:25-34.
- Head SJ, Mokhles MM, Osnabrugge RL, et al. The impact of prosthesis-patient mismatch on long-term survival after aortic valve replacement: a systematic review and meta-analysis of 34 observational studies comprising 27 186 patients with 133 141 patient-years. *Eur Heart J* 2012;33:1518-29.
- Herrmann HC, Daneshvar SA, Fonarow GC, et al. Prosthesis-patient mismatch in patients undergoing transcatheter aortic valve replacement: from the STS/ACC TVT Registry. *J Am Coll Cardiol* 2018;72:2701-11.

Copyright © 2019 Massachusetts Medical Society.

# Durability of Transcatheter and Surgical Bioprosthetic Aortic Valves in Patients at Lower Surgical Risk



Lars Søndergaard, MD, DMSc,<sup>a</sup> Nikolaj Ihlemann, MD, PhD,<sup>a</sup> Davide Capodanno, MD, PhD,<sup>b</sup> Troels H. Jørgensen, MD,<sup>a</sup> Henrik Nissen, MD, PhD,<sup>c</sup> Bo Juel Kjeldsen, MD, PhD,<sup>d</sup> Yanping Chang, MS,<sup>e</sup> Daniel Andreas Steinbrüchel, MD, DMSc,<sup>f</sup> Peter Skov Olsen, MD, DMSc,<sup>f</sup> Anna Sonia Petronio, MD,<sup>g</sup> Hans Gustav Hørsted Thyregod, MD, PhD<sup>f</sup>

## ABSTRACT

**BACKGROUND** Transcatheter aortic valve replacement (TAVR) is an alternative to surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis and intermediate or high surgical risk.

**OBJECTIVES** The aim of this study was to compare the durability of transcatheter and surgical bioprosthetic aortic valves using standardized criteria.

**METHODS** In the NOTION (Nordic Aortic Valve Intervention) trial, all-comer patients with severe aortic stenosis and lower surgical risk for mortality were randomized 1:1 to TAVR (n = 139) or SAVR (n = 135). Moderate/severe structural valve deterioration (SVD) was defined as a mean gradient  $\geq 20$  mm Hg, an increase in mean gradient  $\geq 10$  mm Hg from 3 months post-procedure, or more than mild intraprosthetic aortic regurgitation (AR) either new or worsening from 3 months post-procedure. Nonstructural valve deterioration (NSVD) was defined as moderate/severe patient-prosthesis mismatch at 3 months or moderate/severe paravalvular leakage. Bioprosthetic valve failure (BVF) was defined as: valve-related death, aortic valve reintervention, or severe hemodynamic SVD.

**RESULTS** At 6 years, the rates of all-cause mortality were similar for TAVR (42.5%) and SAVR (37.7%) patients (p = 0.58). The rate of SVD was higher for SAVR than TAVR (24.0% vs. 4.8%; p < 0.001), whereas there were no differences in NSVD (57.8% vs. 54.0%; p = 0.52) or endocarditis (5.9% vs. 5.8%; p = 0.95). BVF rates were similar after SAVR and TAVR through 6 years (6.7% vs. 7.5%; p = 0.89).

**CONCLUSIONS** In the NOTION trial through 6 years, SVD was significantly greater for SAVR than TAVR, whereas BVF was low and similar for both groups. Longer-term follow-up of randomized clinical trials will be necessary to confirm these findings. (Nordic Aortic Valve Intervention Trial; [NCT01057173](https://doi.org/10.1016/j.jacc.2018.10.083)) (J Am Coll Cardiol 2019;73:546-53)  
© 2019 by the American College of Cardiology Foundation.

Treatment for severe degenerative aortic stenosis prior to 2007 required surgical aortic valve replacement (SAVR), precluding patients who are at high or prohibitive surgical risk from receiving treatment. The introduction of transcatheter aortic valve replacement (TAVR) has provided a safe treatment option for many of these high- and extreme-risk surgical patients (1-4). Recent



Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on [JACC.org](https://www.jacc.org).

From the <sup>a</sup>Department of Cardiology, The Heart Centre, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; <sup>b</sup>Cardiothoracic and Vascular Department, Azienda Ospedaliero Universitaria "Policlinico-Vittorio Emanuele," University of Catania, Catania, Italy; <sup>c</sup>Department of Cardiology, Odense University Hospital, Odense, Denmark; <sup>d</sup>Department of Cardiothoracic and Vascular Surgery, Odense University Hospital, Odense, Denmark; <sup>e</sup>Coronary and Structural Heart Disease Management, Medtronic, Mounds View, Minnesota; <sup>f</sup>Department of Cardiothoracic Surgery, The Heart Centre, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; and the <sup>g</sup>Cardiothoracic and Vascular Department, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy. This work was supported by the Danish Heart Foundation (grant numbers: 09-10-AR76-A2733-25400, 12-04-R90-A3879-22733, and 13-04-R94-A4473-22762) and Medtronic. Dr. Søndergaard has received consultant fees and institutional research grants from Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, and Symetis. Dr. Ihlemann has received educational compensation from Medtronic. Dr. Jørgensen has received a research grant from Edwards Lifesciences. Dr. Kjeldsen has served as a proctor for Edwards Lifesciences. Ms. Chang is an employee and shareholder of Medtronic. Dr. Steinbrüchel has received research contracts from Medtronic and St. Jude Medical. Dr. Petronio is a consultant for Medtronic, Abbott, and Boston Scientific. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received August 20, 2018; revised manuscript received October 26, 2018, accepted October 30, 2018.

prospective, randomized clinical studies have further established the noninferiority of TAVR compared with SAVR in intermediate-risk patients (5-7). These data have led to the rapidly growing adoption of TAVR for treatment of severe, symptomatic aortic stenosis. However, the long-term durability of transcatheter prosthetic valves has become increasingly important as TAVR treatment moves to younger, lower-risk patients with longer life expectancies.

In both SAVR and TAVR studies assessing long-term outcomes, the durability of the implanted bioprosthesis has been defined in many dissimilar ways, spanning from the need for reoperation to integration of clinical and echocardiographic outcomes. Indeed, standardized definitions are needed to compare longevity of transcatheter and surgical bioprosthetic aortic valves. A recent consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI), the European Society of Cardiology (ESC), and the European Association for Cardiothoracic Surgery (EACTS) was developed in response to this need for classifying bioprosthetic valve durability that accounts for bioprosthetic valve dysfunction (BVD) and bioprosthetic valve failure (BVF). Furthermore, BVD is divided into structural valve deterioration (SVD) and nonstructural valve deterioration (NSVD) as well as valve thrombosis and endocarditis (8).

SEE PAGE 554

To evaluate the long-term durability of bioprosthetic valves, it is required that the treated patients have survival rates that are ideally longer than what is expected for the valve prostheses. The competing risk of a nonvalve-related death will otherwise create challenges in outcome interpretation, particularly when using actuarial analyses (9). The NOTION (Nordic Aortic Valve Intervention) trial was the first, and so far, the only trial to randomize all-comer patients with severe aortic valve stenosis who were mostly at lower surgical risk for mortality (mean Society of Thoracic Surgeons score of  $3.0 \pm 1.7\%$ ) and therefore also expected to live longer than patients in other trials (7). Patients were randomized to TAVR using the self-expanding CoreValve bioprosthesis (Medtronic, Minneapolis, Minnesota) or SAVR using any commercially available surgical bioprosthetic aortic valve. Follow-up through 6 years is now available. A post hoc analysis of prosthetic valve dysfunction (SVD and NSVD) and BVF based on the new standardized EAPCI/ESC/EACTS definitions was completed for surgical and transcatheter valves implanted in the NOTION trial and is presented herein.

## METHODS

NOTION is a physician-initiated, prospective, randomized, unblinded clinical trial conducted at 3 centers in Denmark and Sweden (10). The trial was conducted per the principles of the Declaration of Helsinki and was approved by each site's ethical review board.

All patients provided written informed consent. All data was 100% monitored by an independent monitoring unit. An independent clinical events committee adjudicated all clinical events at 1 year.

**PATIENTS.** Patients at least 70 years of age with severe aortic stenosis were assessed by the local heart team for inclusion in the study. Detailed inclusion and exclusion criteria have been previously described (7). Enrolled patients were randomized to SAVR (27% Mosaic, 29% Epic, 24% Trifecta, 10% Perimount, and 10% Sorin Mitroflow) or TAVR (100% first-generation CoreValve) and followed annually. All patients with an implanted prosthesis were included in this analysis. Annual echocardiographic assessments measured aortic valve mean gradient, effective orifice area (EOA), total aortic regurgitation (AR) and paravalvular leakage (PVL). There was no echocardiography core laboratory used in the NOTION trial; thus, all echocardiographic data were analyzed and reported by the individual study sites.

**VALVE DURABILITY DEFINITIONS.** BVD was defined as 1 or more of the following: SVD, NSVD, bioprosthetic valve thrombosis, or endocarditis. SVD was defined as moderate/severe hemodynamic SVD (mean gradient  $\geq 20$  mm Hg, increase in mean gradient  $\geq 10$  mm Hg from 3 months post-procedure, or  $>$  mild intraprosthetic AR either new or worsening from 3 months post-procedure). NSVD was defined as moderate/severe patient-prosthesis mismatch (PPM) at 3 months or moderate/severe PVL. Moderate/severe PPM was defined as an indexed EOA  $\leq 0.85$  cm<sup>2</sup>/m<sup>2</sup>. Endocarditis was diagnosed according to the modified Duke Criteria (11). BVF was defined as at least 1 of the following: valve-related death (death caused by BVD or sudden unexplained death following diagnosis of BVD), aortic valve reintervention (TAVR or SAVR following diagnosis of BVD), or severe hemodynamic SVD (mean gradient  $\geq 40$  mm Hg, increase in mean gradient  $\geq 20$  mm Hg from 3 months post-procedure, or severe intraprosthetic AR either new or worsening from 3 months post-procedure).

**STATISTICAL ANALYSIS.** Categorical variables were compared with the use of the chi-square or Fisher exact test, as appropriate. Continuous variables were

## ABBREVIATIONS AND ACRONYMS

**SAVR** = surgical aortic valve replacement

**SVD** = structural valve deterioration

**TAVR** = transcatheter aortic valve replacement

**TABLE 1 Baseline Characteristics of the Implanted Cohort of the NOTION Trial**

	TAVR (n = 139)	SAVR (n = 135)	p Value
Age, yrs	79.4 ± 4.9	78.8 ± 4.6	0.326
BMI, kg/m <sup>2</sup>	26.6 ± 4.3	26.6 ± 4.1	0.983
Male	52.5	53.3	0.893
NYHA functional class III/IV	46.4	46.3	0.986
STS score	3.0 ± 1.7	3.0 ± 1.6	0.882
STS score			0.832
<4%	82.7	81.5	
4%-10%	15.8	18.5	
>10%	1.4	0.0	
Logistics EuroSCORE II	2.0 ± 1.3	2.0 ± 1.2	0.906
Diabetes mellitus	17.3	20.7	0.463
Creatinine >2 mg/dl	1.4	0.7	>0.999
Peripheral vascular disease	4.3	6.7	0.393
Prior stroke	5.8	9.6	0.228
Chronic lung disease	12.2	11.9	0.923
Permanent pacemaker	3.6	4.4	0.721
Atrial fibrillation/flutter	29.0	24.8	0.439

Values are mean ± SD or %

BMI = body mass index; NOTION = Nordic Aortic Valve Intervention; NYHA = New York Heart Association; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

presented as mean ± SD and compared using Student's *t*-test. Ordinal variables were compared using the Mantel-Haenszel test. BVF and SVD rates were estimated using the cumulative incidence function with death as the competing risk for SVD and nonvalve-related deaths as the competing risk for BVF. The cumulative incidence functions were compared between treatment groups using Gray's test. All testing used a 2-sided alpha level of 0.05. All statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

## RESULTS

Patients were enrolled in the NOTION trial from December 2009 to April 2013. For the implanted

cohort, there were 139 patients in the TAVR group and 135 in the SAVR group (3 patients randomized to TAVR were converted to SAVR because of complications during the procedure and are included in the SAVR group for this analysis). Follow-up is complete through 5 years with 100% compliance in both groups (98 TAVR and 97 SAVR patients); of these, 50 TAVR and 50 SAVR patients had 6 years of data available. Baseline characteristics are shown in **Table 1**. Most patients were at low risk for complications as evidenced by a Society of Thoracic Surgeons score <4% in 82.1% of patients. There were no significant differences in demographics or medical history between implanted TAVR and SAVR patients. The distribution of bioprosthetic valve types and sizes is shown in **Table 2**.

At 6 years, the Kaplan-Meier rates of all-cause mortality were similar for TAVR (42.5%) and SAVR (37.7%) patients (log-rank *p* = 0.58). Forward flow hemodynamics remained at consistent levels through 6 years (**Figure 1**). The EOA was significantly greater for TAVR than SAVR at all time points post-procedure with an EOA of 1.53 cm<sup>2</sup> vs 1.16 cm<sup>2</sup> for surgical valves at 6 years (*p* = 0.002). Aortic mean gradient was 9.9 mm Hg for TAVR and 14.7 mm Hg for SAVR at 6 years (*p* = 0.001).

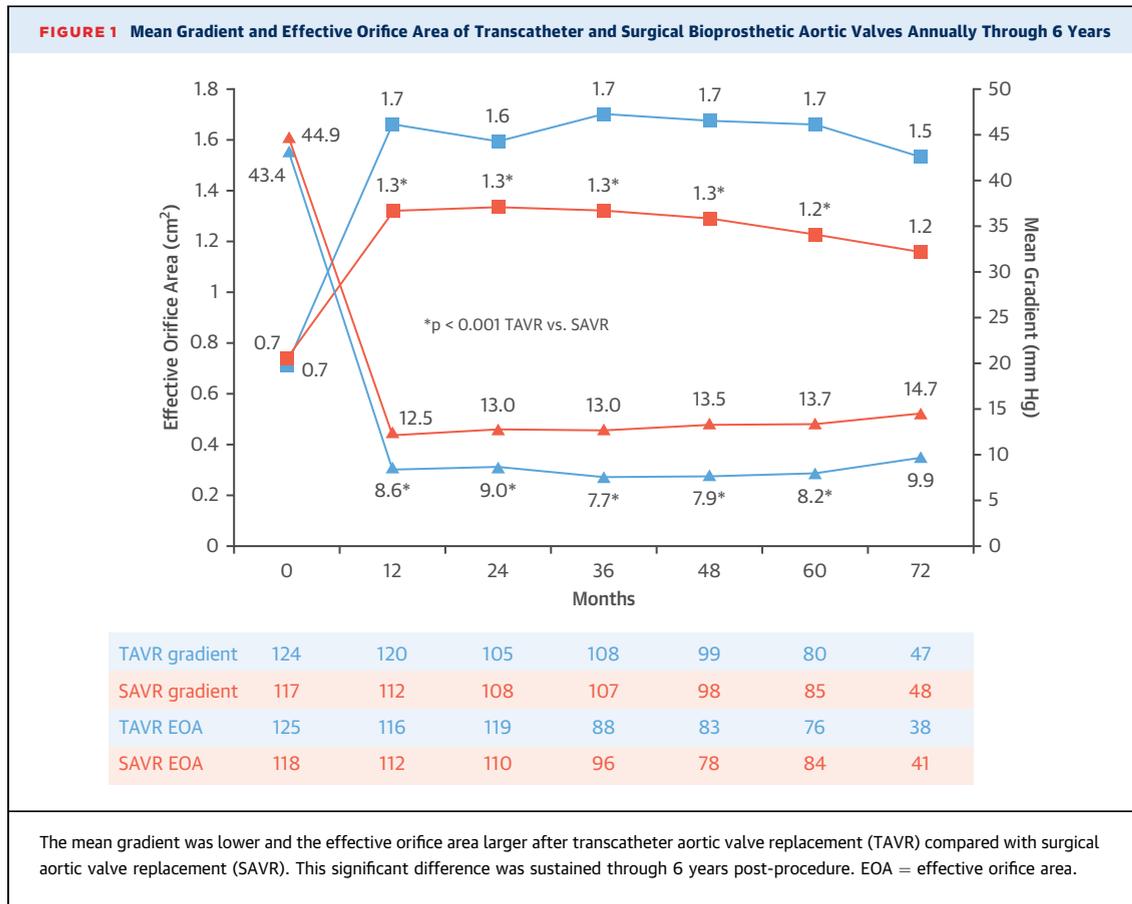
**BIOPROSTHETIC VALVE DYSFUNCTION.** The rate of BVD and its components through 6 years for the TAVR and SAVR patients is shown in **Table 3**. There were no significant differences between TAVR and SAVR patients for BVD (56.1% vs. 66.7%; *p* = 0.07), NSVD (54.0% vs. 57.8%; *p* = 0.52), or definite endocarditis (5.8% vs. 5.9%; *p* = 0.95). There was no evidence of thrombosis reported in either group.

**STRUCTURAL VALVE DETERIORATION.** There was significantly more moderate/severe SVD according to the EAPCI/ESC/EACTS definition through 6 years for the SAVR group than the TAVR group (24.0% vs. 4.8%; *p* < 0.001) (**Central Illustration**), which was primarily related to differences in measures of moderate hemodynamic SVD (**Table 4**). A mean gradient of ≥20 mm Hg through 6 months post-procedure was

**TABLE 2 Transcatheter and Surgical Valve Sizes**

Surgical Valve Types	19 mm	21 mm	23 mm	25 mm	27 mm	All
Mosaic	18.2 (2/11)	28.6 (12/42)	17.4 (8/46)	42.4 (14/33)	33.3 (1/3)	27.4 (37/135)
Epic	27.3 (3/11)	26.2 (11/42)	37.0 (17/46)	21.2 (7/33)	33.3 (1/3)	28.9 (39/135)
Trifecta	54.5 (6/11)	26.2 (11/42)	23.9 (11/46)	9.1 (3/33)	33.3 (1/3)	23.7 (32/135)
Perimount	0.0 (0/11)	14.3 (6/42)	13.0 (6/46)	6.1 (2/33)	0.0 (0/3)	10.4 (14/135)
Sorin Mitroflow	0.0 (0/11)	4.8 (2/42)	8.7 (4/46)	21.2 (7/33)	0.0 (0/3)	9.6 (13/135)
All	11	42	46	33	3	135
CoreValve Sizes	23 mm	26 mm	29 mm	31 mm		
	1.4 (2/139)	38.1 (53/139)	42.4 (59/139)	7.9 (11/139)		

Values are % (n/N) or n.



observed in 2.9% versus 22.2% of patients receiving TAVR and SAVR, respectively ( $p < 0.0001$ ). However, 1 TAVR and 9 SAVR patients had a mean gradient of  $\geq 20$  mm Hg at the time of the 3-month echocardiography. To account for this observation, a modified SVD definition was applied and showed a cumulative incidence for a mean gradient of  $\geq 20$  mm Hg AND an increase in mean gradient  $\geq 10$  mm Hg after 3 months post-procedure of 1.4% for TAVR and 12.4% for SAVR ( $p < 0.001$ ) (Figure 2).

**NONSTRUCTURAL VALVE DETERIORATION.** There was no significant difference in NSVD between the TAVR and SAVR patients through 6 years (Table 5). TAVR patients had more moderate PVL (20.9% vs. 1.5%;  $p < 0.0001$ ) post-procedure, but less severe PPM at 3 months post-procedure (12.2% vs. 28.1%;  $p = 0.001$ ) than SAVR patients at 3 months. Change over time was minimal for both PVL and PPM.

**BIOPROSTHETIC VALVE FAILURE.** TAVR and SAVR patients experienced a similar degree of BVF through 6 years (7.5% vs. 6.7%;  $p = 0.89$ ), as shown in Figure 3. There were no statistically significant differences in the frequency of the components of BVF between TAVR and SAVR groups: valve-related deaths (5.0% vs. 3.7%;  $p = 0.59$ ), reintervention (2.2% vs. 0.7%;  $p = 0.62$ ), and severe hemodynamic SVD (0.7% vs. 3.0%;  $p = 0.21$ ).

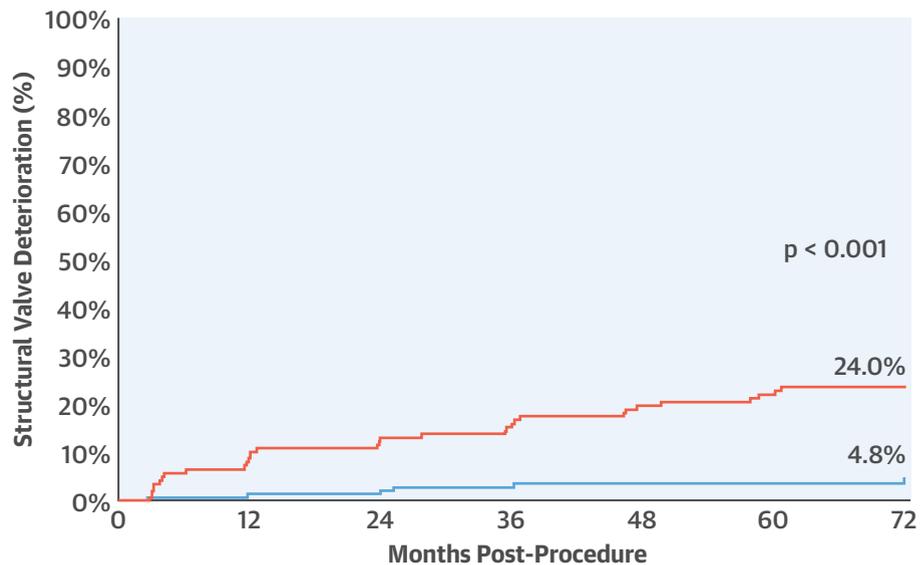
## DISCUSSION

Long-term assessment of BVD and BVF after TAVR has only been possible in recent years, and there are few reports of transcatheter bioprostheses durability directly compared with surgical bioprostheses

**TABLE 3 Bioprosthetic Valve Dysfunction and Its Components Through 5 Years**

	TAVR (n = 139)	SAVR (n = 135)	p Value
Bioprosthetic valve dysfunction	56.1	66.7	0.073
Components			
Structural valve deterioration	4.8	24.0	<0.0001
Nonstructural valve deterioration	54.0	57.8	0.52
Thrombosis	0.0	0.0	NA
Endocarditis	5.8	5.9	0.95

Values are %.  
 Abbreviations as in Table 1.

**CENTRAL ILLUSTRATION** Cumulative Incidence of Structural Valve Deterioration Through 6 Years

Number at risk:

139	134	130	125	114	106	84	44
135	119	113	104	95	81	70	32

— Transcatheter Aortic Valve Replacement    — Surgical Aortic Valve Replacement

Søndergaard, L. et al. *J Am Coll Cardiol.* 2019;73(5):546-53.

The cumulative incidence of structural valve deterioration was significantly lower after transcatheter aortic valve replacement compared with surgical aortic valve replacement through 6 years follow-up.

**TABLE 4** Structural Valve Deterioration and Its Components Through 6 Years

	TAVR (n = 139)*	SAVR (n = 135)*	p Value
Baseline hemodynamic parameters*			
3-month mean gradient	8.33 ± 3.93	12.15 ± 4.45	<0.0001
3-month central AR			
None/trace	99.2	98.2	
Mild	0.8	1.8	
Moderate	0.0	0.0	
Severe	0.0	0.0	
SVD	4.8	24.0	<0.001
Moderate hemodynamic SVD			
Mean gradient ≥20 mm Hg	2.9	22.2	
Mean gradient ≥10 and <20 mm Hg change from 3 months	1.4	11.1	
Moderate central AR	0.0	0.0	
Severe hemodynamic SVD			
Mean gradient ≥40 mm Hg	0.0	1.5	
Mean gradient ≥20 mm Hg change from 3 months	0.7	3.0	
Severe central AR	0.0	0.0	

Values are mean ± SD or %. \*The 3-month echocardiography measurements are the first post-procedure measures in NOTION.

AR = aortic regurgitation; SVD = structural valve deterioration; other abbreviations as in Table 1.

durability. The NOTION trial is among the first to provide comparative data regarding bioprosthetic valve durability for TAVR and SAVR from a randomized clinical trial in patients with low surgical risk for mortality. Consistent clinical and hemodynamic outcomes through 6 years were observed.

Overall, there were no differences in NSVD between groups, although more PVL was seen after TAVR and more PPM after SAVR. SVD and NSVD rates remained relatively unchanged over time and are more likely the result of suboptimal valve sizing for both groups than actual deterioration of the prostheses. The PVL rate in the NOTION trial is higher than contemporary reports of PVL after TAVR, probably due to the introduction of computed tomography (CT) scanning for sizing of the aortic annulus after NOTION was initiated and the use of the original CoreValve prosthesis without outer sealing skirt and possibility for resheathing. Rates of endocarditis were low and similar between groups, and no thromboembolic event or clinically detectable valve leaflet thrombosis was reported in either group.

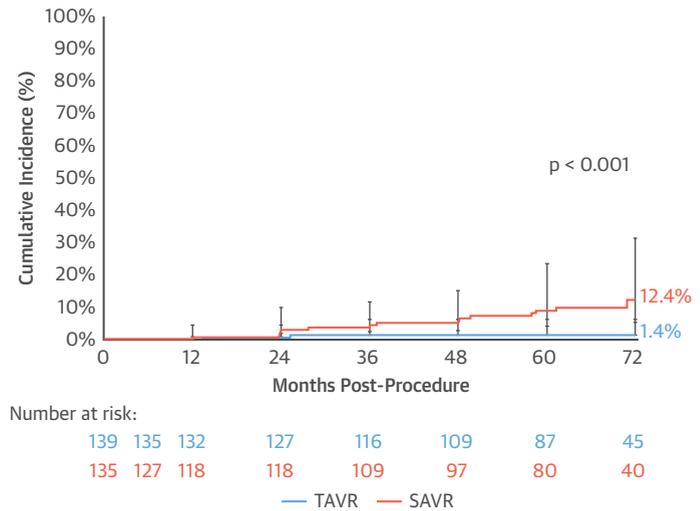
Four-dimensional volume-rendered CT was not used for detection of subclinical leaflet thrombosis (12). Importantly, there was also no difference in the patient-oriented components of BVF, including valve-related death, reintervention, and severe hemodynamic deterioration.

Causes of BVD include leaflet tear, calcification, pannus deposition, flail or fibrotic leaflet, endocarditis, and thrombosis. In surgical stented bioprostheses, SVD has been most commonly caused by calcification of the valve, which leads to stiffening and aortic valve restenosis or, more common in nonstented bioprostheses, leaflet tears and aortic valve insufficiency. Because SVD develops slowly over time, rates remain low for 5 to 10 years after SAVR (13). However, most long-term studies enroll elderly patients, and results are confounded by high noncardiac mortality rates. Furthermore, many of these studies report explantation rates due to SVD, but they do not employ a clear definition of hemodynamic parameters of SVD (13,14). A recent article from Bourguignon et al. (15), provides clearer criteria for the assessment of severe SVD (mean gradient > 40 mm Hg or severe AR) and reports severe SVD in 153 of 2,559 patients (5.9%) at a mean follow-up of 6.7 ± 4.8 years after Carpentier-Edwards Perimount bioprosthetic valve (Edwards Lifesciences, Irvine, California) implantation (15). The late linearized mortality rate was 6.0%/valve-year. Calcification and leaflet tears were the predominant causes of SVD.

Detailed analysis of transcatheter and surgical bioprosthetic aortic valve durability found significantly more moderate/severe SVD in the SAVR group, primarily related to higher aortic valve mean gradients, compared with the TAVR group. To account for the number of patients with a mean gradient ≥20 mm Hg already at the time of the 3-month post-procedure echocardiography, we looked at the proportion of patients with both a mean gradient ≥20 mm Hg AND an increase in mean gradient ≥10 mm Hg from the 3-month measurement. Future modifications of the EAPCI/ESC/EACTS consensus statement may account for observations that small surgical bioprostheses may have a mean gradient ≥20 mm Hg early after valve implantation.

SVD is typically detected by echocardiography and reflects irreversible valve dysfunction (15-17). A recent study of 152 patients implanted with a CoreValve bioprosthesis using the same standardized definitions proposed by Capodanno et al. (8) reported no severe SVD with follow-up to 8.9 years (18). There were 5 reinterventions related to PVL resulting in an estimated actuarial rate of BVF of 7.9% at 8 years.

**FIGURE 2** Cumulative Incidence of SVD Defined as a Mean Gradient of ≥20 mm Hg and an Increase in Mean Gradient ≥10 mm Hg After 3 Months Post-Procedure



This modified definition of structural valve deterioration (SVD) takes into account the proportion of patients who had a mean gradient ≥20 mm Hg at the 3-month post-procedure echocardiogram. The rate of SVD by this definition is lower for surgical aortic valve replacement (SAVR) but remains significantly greater than the SVD rate for transcatheter aortic valve replacement (TAVR) through 6 years.

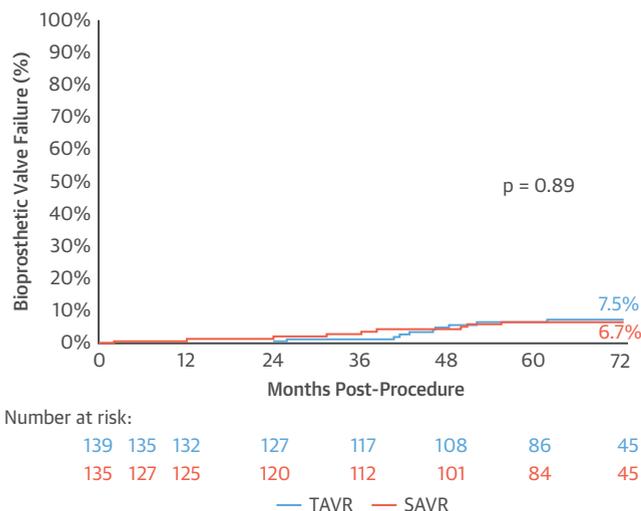
Stable hemodynamics and 5-year rates of SVD have also been reported by the Italian (4.2%) and Canadian (3.4%) registries, although again, definitions vary (19,20). However, these studies included patients with limited life-expectancy who were therefore likely to die before the occurrence of SVD or BVF. Furthermore, all studies were without an SAVR control group.

In surgery, bioprosthetic aortic valves are more commonly used over mechanical valves, partly due to patient preferences to avoid lifelong anticoagulation therapy. However, particularly younger patients face

**TABLE 5** Nonstructural Valve Deterioration and Its Components Through 6 Years

	TAVR (n = 139)	SAVR (n = 135)	p Value
Nonstructural valve deterioration	54.0	57.8	0.52
Components			
Moderate/severe PPM at 3 months	43.2	57.8	
Moderate PPM at 3 months	30.9	29.6	
Severe PPM at 3 months	12.2	28.1	
Moderate/severe PVL	21.6	1.5	
Moderate PVL	20.9	1.5	
Severe PVL	0.7	0.0	

Values are %.  
 PPM = patient-prosthesis mismatch; PVL = paravalvular leak; other abbreviations as in Table 1.

**FIGURE 3** Cumulative Incidence of Bioprosthetic Valve Failure Through 6 Years

There was no significant difference in bioprosthetic valve failure (BVF) between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR) through 6 years.

the risk of bioprosthetic valve deterioration and need for reintervention. Although this can be performed as a less-invasive transcatheter valve-in-valve procedure, the risk-benefit ratio needs to be acceptable. Similar, durability is an important factor for TAVR, particularly when expanding the therapy to younger, lower-risk patients with longer life-expectancy. Ideally, the durability for transcatheter bioprosthetic valves should be at least as good as for surgical bioprostheses. To compare different bioprostheses used for SAVR and TAVR, standardized definitions of prosthetic valve dysfunction and failure need to be applied. Furthermore, prospective and preferably randomized patient cohorts with a life-expectancy allowing long-term follow-up are needed.

**STUDY LIMITATIONS.** NOTION enrolled patients from 2009 to 2013 when echo-based sizing of the aortic annulus was standard of care instead of CT sizing, which could have affected patient outcomes. Surgeons in the trial did not use annular enlargement techniques or an algorithm to avoid patient-prosthesis mismatch. In addition, echocardiographic measurements were not adjudicated by an echocardiography core laboratory. Valve durability was assessed through 6 years of follow-up, but not all patients were eligible for 6-year follow-up at the time of this analysis. TAVR was performed with the self-expanding CoreValve bioprosthesis; thus, results may not be generalizable to balloon-expandable

transcatheter bioprostheses. CoreValve may have a favorable design with regard to the supra-annular leaflet position, which provides a larger effective opening area than transcatheter heart valves with an intra-annular leaflet position.

## CONCLUSIONS

Through 6-year follow-up of the NOTION trial, adequate hemodynamic valve performance was maintained for both groups. SVD was significantly greater for SAVR compared with TAVR mainly due to higher mean valve gradients present shortly after the procedure. Overall, NSVD was similar for both groups, although rates of PVL and PPM differed between TAVR and SAVR. Bioprosthetic valve failure rates were low and similar for the self-expanding transcatheter and surgical valves implanted, with no valve thrombosis and similar rates of endocarditis for both groups. Although follow-up is medium-term, the low rates of SVD and BVF after implantation of the self-expanding CoreValve bioprosthesis are encouraging. Longer-term follow-up of randomized clinical trials will be necessary to confirm these early results.

**ACKNOWLEDGMENTS** The authors thank study nurses Line M. Kristensen, Lisette L. Larsen, Ane L. Johansen, Ida Rosenlund and Eva-Lena Pommer and Colleen Gilbert, PharmD, of Medtronic Inc. for copy-editing and formatting of the manuscript; and all patients participating in the trial.

**ADDRESS FOR CORRESPONDENCE:** Dr. Lars Søndergaard, Department of Cardiology, Section 2011, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark. E-mail: [Lars.Soendergaard.01@regionh.dk](mailto:Lars.Soendergaard.01@regionh.dk). Twitter: [@Rigshospitalet](https://twitter.com/Rigshospitalet).

## PERSPECTIVES

### COMPETENCY IN PATIENT CARE AND

**PROCEDURAL SKILLS:** In patients with severe aortic stenosis at low surgical risk, the rate of structural deterioration of bioprosthetic valves is greater within the first 6 years after SAVR than TAVR, while the rates of bioprosthetic valve failure, endocarditis, and all-cause mortality were low and similar with both methods.

**TRANSLATIONAL OUTLOOK:** Further studies are needed to clarify the pathophysiological mechanisms responsible for the different rates of structural valve deterioration after SAVR compared with TAVR.

## REFERENCES

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597-607.
2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187-98.
3. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790-8.
4. Popma JJ, Adams DH, Reardon MJ, et al. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. *J Am Coll Cardiol* 2014;63:1972-81.
5. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609-20.
6. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321-31.
7. Thyregod HG, Steinbruchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: one-year results from the all-comers Nordic Aortic Valve Intervention (NOTION) Randomized Clinical Trial. *J Am Coll Cardiol* 2015;65:2184-94.
8. Capodanno DM, Petronio AS, Prendergast B, et al. Standardised definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical bioprosthetic valves. A consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) in collaboration with the European Society of Cardiology (ESC). *Eur Heart J* 2017;38:3382-90.
9. Capodanno D. Transcatheter aortic valve durability and the dark side of Kaplan-Meier analysis. *EuroIntervention* 2016;12:821-2.
10. Thyregod HG, Søndergaard L, Ihlemann N, et al. The Nordic Aortic Valve Intervention (NOTION) trial comparing transcatheter versus surgical valve implantation: study protocol for a randomised controlled trial. *Trials* 2013;14:11.
11. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. *Am J Med* 1994;96:200-9.
12. Søndergaard L, De Backer O, Kofoed KF, et al. Natural history of subclinical leaflet thrombosis affecting motion in bioprosthetic aortic valves. *Eur Heart J* 2017;38:2201-7.
13. Johnston DR, Soltesz EG, Vakil N, et al. Long-term durability of bioprosthetic aortic valves: implications from 12,569 implants. *Ann Thorac Surg* 2015;99:1239-47.
14. Forcillo J, El Hamamsy I, Stevens LM, et al. The perimount valve in the aortic position: twenty-year experience with patients under 60 years old. *Ann Thorac Surg* 2014;97:1526-32.
15. Bourguignon T, Bouquiaux-Stablo AL, Candolfi P, et al. Very long-term outcomes of the Carpentier-Edwards Perimount valve in aortic position. *Ann Thorac Surg* 2015;99:831-7.
16. Lang RM, Badano LP, Tsang W, et al., for the American Society of Echocardiography, European Association of Echocardiography. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. *J Am Soc Echocardiogr* 2012;25:3-46.
17. Lancellotti P, Pibarot P, Chambers J, et al. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016;17:589-90.
18. Holy EW, Kebernik J, Abdelghani M, et al. Long-term durability and hemodynamic performance of a self-expanding transcatheter heart valve beyond 5 years after implantation: a prospective observational study applying the standardized definitions of structural deterioration and valve failure. *EuroIntervention* 2018;14:e390-6.
19. Barbanti M, Petronio AS, Etori F, et al. 5-year outcomes after transcatheter aortic valve implantation with corevalve prosthesis. *J Am Coll Cardiol Intv* 2015;8:1084-91.
20. Toggweiler S, Humphries KH, Lee M, et al. 5-year outcome after transcatheter aortic valve implantation. *J Am Coll Cardiol* 2013;61:413-9.

---

**KEY WORDS** aortic bioprosthesis, aortic stenosis, aortic valve durability, transcatheter aortic valve replacement

**RANDOMIZUOTŲ TYRIMŲ PUBLIKACIJŲ TARPTAUTINIUIOSE SPECIALIZUOTOSE LEIDINIUIOSE VERTIMAI**

Eil. Nr.	Leidinio pavadinimas	Straipsnio pavadinimas	Svarbių pastraipų ir/ar išvadų ir/ar santraukų vertimas. Kiti paaiškinimai
1	The new england journal of medicine. „ClinicalTrials.gov“ numeris, NCT02701283 Publikuotas 2019 m. kovo 17d. NEJM.org.	Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients  <b>LOW RISK TRAIL</b>	<p>Savaime išsiplečiantis TAVI vožtuvas mažos rizikos pacientams. <b>PAGRINDIMAS: Transkaterinio aortos vožtuvo pakeitimas (TAVI)</b> yra alternatyva kardiologinei operacijai, pacientams su sunkia aortos stenozė, kuriems dėl kardiologinės operacijos padidėja mirties rizika; mažiau žinoma apie TAVI, mažos rizikos pacientams šia tema.</p> <p><b>METODAI.</b> Atlikta atsitiktinių imčių tyrimas, kuriame TAVR, savaime išsiplečiančio vožtuvo supraanulinius bioprotezas buvo lyginamas su chirurginiu aortos vožtuvo pakeitimu pacientams, su sunkia aortos stenozė esant mažai chirurginei rizikai. 850 pacientų buvo stebimi 12 mėnesių. Išanalizuoti <u>pirminiai išėičių rezultatai</u>, mirtis ar <u>neįgalumą sąlygojantis insultas</u> po 24 mėnesių, naudojant "Bayesian" metodus.</p> <p><b>REZULTATAI.</b> Iš 1468 atsitiktinių imčių pacientų, 1403 buvo atlikta TAVI ar chirurginė operacija. Vidutinis pacientų amžius buvo 74 metai. Apskaičiuotas 24 mėnesių pradinių rezultatų dažnis TAVI grupėje buvo 5,3% vs. 6,7% - chirurgijos grupėje (skirtumas, -1,4 procentiniai punktai; 95% patikimas "Bayesian" intervalas dėl skirtumo, nuo -4,9 iki 2,1; tikimybė &gt; 0,999). Po 30 dienų pacientams, kuriems buvo atlikta TAVR, palyginti su chirurgija, rečiau pasireiškė neįgalumą sąlygojantis insultas (0,5% v.s 1,7%), kraujavimo komplikacijos (2,4% v.s 7,5%), ūmus inkstų pažeidimas (0,9% vs. 2,8 proc.); prieširdžių virpėjimas (7,7 proc., vs. 35,4 proc.); didesnis vidutinio ar sunkaus aortos regurgitacijos dažnis (3,5 proc., vs. 0,5 proc.); širdies stimulatoriaus implantacija (17,4 proc., vs. 6,1 proc.). Po 12 mėnesių TAVR grupės pacientams buvo mažesni aortos vožtuvų gradientas, nei chirurginės grupės pacientams (8,6 mm Hg vs 11,2 mm Hg) ir didesnė efektyvi regurgitacinė anga (2,3 cm<sup>2</sup> vs. 2,0 cm<sup>2</sup>).</p> <p><b>IŠVADOS.</b> Pacientai su sunkia aortos stenozė ir nedidele chirurgine rizika, TAVR su savaime išsiplečiančiu viršžiediniu bioprotezu buvo netinkami kardiologijai atsižvelgiant į <u>galutinį vertinimą</u> - mirtį ar neįgalumą</p>

			sąlygojantį insultą po 24 mėnesių.
2	European Society of Cardiology, European Heart Journal (2020) 0, 1–11 CLINICAL RESEARCH doi:10.1093/eurheartj/ehaa036	Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial  <b>SOLVE-TAVI</b> trial	<p><b>Tikslas.</b>TAVI tapo žinoma gydymo galimybe pacientams su simptomatine aortos stenozė. Techniniai vožtuvų konstrukcijos pokyčiai atitiko ankstesnius apribojimus, tokius kaip: suboptimalus dislokavimas, laidumo sutrikimai ir paravalvulinis nuotėkiai. Tačiau duomenų yra nedaug, kurie lygintų naujos kartos savaime išsiplečiantį (SIV) ir balionu plečiamą vožtuvus (BIV).</p> <p><b>Metodai ir rezultatai</b> SOLVE-TAVI daugiacentris, atviras, atsitiktinių imčių tyrimas, kuriame dalyvavo 447 pacientai su aortos stenozė, atliekant transfemoralinį TAVI, lyginant SIV („Evolut R“, „Medtronic Inc.“, Mineapolis, MN, JAV) su BIV („Sapien“ 3, Edwards Lifesciences, Irvine, CA, JAV). Pirminiai išėičių rezultatai, mirtingumas dėl visų priežasčių ir insultas, vidutinė/sunki protezo vožtuvo regurgitacija ir nuolatinė širdies stimulatoriaus implantacija po 30 dienų (ekvivalentiškumo riba 10% su 0,05). Pirminiai galutiniai išėičių rezultatai - 2006 m 28,4% SIV vs. 26,1% BIV pacientams atitiko nustatytus lygiavertiškumo kriterijus [normos skirtumas - 2,39 (90 pasikliautinis intervalas, CI nuo -9,45 iki 4,66); P = 0,04]. Atskirų komponentų įvykiai buvo šie: <u>mirtingumas dėl visų priežasčių</u> 3,2% vs. 2,3% [normos skirtumas -0,93 (90% CI -4,78 iki 2,92); P &lt;0,001], insultas 0,5% vs. 4,7% [skirtumas 4,20 (90% CI 0,12 iki 8,27); P = 0,003], vidutinio/sunkaus paravalvulinių nuotėkių 3,4% vs. 1,5% [skirtumas -1,89 (90% CI nuo -5,86 iki 2,08); P = 0,0001] ir nuolatinio širdies stimulatoriaus implantacija 23,0% vs. 19,2% [skirtumas -3,85 (90% CI nuo -10,41 iki 2,72) SIV vs BIV pacientams; p= 0,06].</p> <p><b>Išvada</b> Pacientams su aortos stenozė ir kuriems atliekama transfemoralinė TAVI, naujosios kartos SIV ir BIV pirminiai išėičių rezultatai susiję su vožtuvu yra lygiaverčiai. Šios išvados patvirtina saugų šios naujosios kartos TAVI prietaisų pritaikymą daugumai pacientų, turintys tam tikras specifines savybes, atsižvelgiant į individualią vožtuvo anatomiją.</p>

3	<p>JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL .73, NO.5,2019</p>	<p>Durability of Transcatheter and Surgical Bioprosthetic Aortic Valves in Patients at Lower Surgical Risk</p> <p><b>NOTION</b></p>	<p><b>PAGRINDINĖ INFORMACIJA</b> Transkatterinio aortos vožtuvo keitimas (TAVR) yra alternatyva chirurginiam aortos vožtuvo pakeitimui (SAVR) pacientams, kuriems yra sunki aortos stenozė ir vidutinė ar didelė chirurginė rizika.</p> <p><b>TIKSLAS.</b> Palyginti transkateterio ir chirurginio bioprotezinio aortos vožtuvo patvarumą naudojant standartizuotus kriterijus.</p> <p><b>METODAI.</b> NOTION tyrime visiems pacientams, kuriems yra sunki aortos stenozė ir mažesnė chirurginė mirštamumo rizika buvo atsitiktine tvarka paskirstyti 1: 1 į TAVR (n=139) arba SAVR (n= 135). Vidutinis/sunkus <u>struktūrinis vožtuvo pablogėjimas (SVD)</u> buvo apibrėžtas kaip vidutinis gradientas <math>\geq 20</math> mm Hg, padidėjęs vidutinis gradientas <math>\geq 10</math> mm, 3 mėnesiai po procedūros, arba daugiau nei lengva intraprotezinė aortos regurgitacija (AR), naujas arba pasunkėjusi, 3 mėnesiai po procedūros. Nestruktūrinis vožtuvo pablogėjimas (NVP) buvo apibūdinamas kaip vidutinio sunkumo/sunkus paciento protezo neatitikimas po 3 mėnesių arba vidutinio sunkumo/sunkus su paravalvuliniais pratekėjimais. <u>Bioprotezinis vožtuvo prastas funkcionavimas (BVF)</u> buvo apibūdinamas kaip: mirtis, aortos vožtuvo pakartotinė intervencija ar sunkus hemodinamikos pažeidimas. <b>REZULTATAI</b> Po 6 metų, visų priešasčių mirštamumas TAVI (42,5%) ir SAVR (37,7%) buvo panašus (p=0,58). SVD dažnis buvo didesnis SAVR nei TAVRI(24,0% vs. 4,8%; p &lt;0,001), tuo tarpu nebuvo skirtumo NSVD (57,8% vs. 54,0%; p=0,52) ar endokardito (5,9% vs. 5,8%; p= 0,95). BVF rodikliai buvo panašūs po SAVR ir TAVI po 6 m. (6,7% vs. 7,5%; p=0,89).</p> <p><b>IŠVADOS.</b> NOTION tyrimo, po 6 m SVD buvo reikšmingai didesnis SAVR grupėje nei TAVI, tuo tarpu BVF buvo mažas ir panašus abiejose grupėse. Reikalingos ilgesnio laikotarpio atsitiktinių imčių klinikinių tyrimų stebėjimo, patvirtinti šias išvadas.</p>
---	---	---	--

# Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial

Holger Thiele <sup>1,2,\*†</sup>, Thomas Kurz <sup>3,4†</sup>, Hans-Josef Feistritzer<sup>1,2</sup>, Georg Stachel <sup>1,2</sup>, Philipp Hartung<sup>1,2</sup>, Ingo Eitel <sup>3,4</sup>, Christoph Marquetand <sup>3,4</sup>, Holger Nef<sup>5</sup>, Oliver Doerr <sup>5</sup>, Alexander Lauten<sup>4,6</sup>, Ulf Landmesser<sup>4,6</sup>, Mohamed Abdel-Wahab<sup>1,2</sup>, Marcus Sandri<sup>1,2</sup>, David Holzhey<sup>1,2</sup>, Michael Borger<sup>1,2</sup>, Hüseyin Ince<sup>7</sup>, Alper Öner<sup>7</sup>, Roza Meyer-Saraei<sup>3,4</sup>, Harm Wienbergen <sup>8</sup>, Andreas Fach<sup>8</sup>, Norbert Frey<sup>4,9</sup>, Inke R. König<sup>4,10</sup>, Reinhard Vonthein <sup>10</sup>, Yvonne Rückert<sup>2</sup>, Anne-Kathrin Funkat<sup>2</sup>, Suzanne de Waha-Thiele<sup>3,4,‡</sup>, and Steffen Desch<sup>1,2,4,‡</sup>; on behalf of the SOLVE-TAVI Investigators

<sup>1</sup>Heart Center Leipzig at University of Leipzig, Strümpellstr. 39, 04289 Leipzig, Germany; <sup>2</sup>Leipzig Heart Institute, Russenstraße 69a, D-04289 Leipzig, Germany; <sup>3</sup>University Clinic Schleswig-Holstein and University Heart Center Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany; <sup>4</sup>German Center for Cardiovascular Research (DZHK), Ratzeburger Allee 160, D-23538 Lübeck, Germany; <sup>5</sup>Medizinische Klinik I, Abteilung für Kardiologie, Universitätsklinikum Marburg/Gießen, Klinikstr. 33, D-35392 Gießen, Germany; <sup>6</sup>Universitätsklinikum Charité, Campus Benjamin Franklin, Hindenburgdamm 30, D-12200 Berlin, Germany; <sup>7</sup>Medizinische Klinik I im Zentrum für Innere Medizin (ZIM), Universitätsklinikum Rostock, Ernst-Heydemann-Str. 6, D-18057 Rostock, Germany; <sup>8</sup>Klinikum Links der Weser, Herzzentrum Bremen, Senator-Wessling-Str. 1, D-28277 Bremen, Germany; <sup>9</sup>Department of Cardiology, University Clinic Schleswig-Holstein, Campus Kiel, Schittenhelmstr. 12, D-24105 Kiel, Germany; and <sup>10</sup>Institut für Medizinische Biometrie und Statistik, Universität zu Lübeck, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, D-23562 Lübeck, Germany

Received 5 July 2019; revised 9 October 2019; editorial decision 10 January 2020; accepted 23 January 2020

## Aims

Transcatheter aortic valve implantation (TAVI) has emerged as established treatment option in patients with symptomatic aortic stenosis. Technical developments in valve design have addressed previous limitations such as suboptimal deployment, conduction disturbances, and paravalvular leakage. However, there are only limited data available for the comparison of newer generation self-expandable valve (SEV) and balloon-expandable valve (BEV).

## Methods and results

SOLVE-TAVI is a multicentre, open-label, 2 × 2 factorial, randomized trial of 447 patients with aortic stenosis undergoing transfemoral TAVI comparing SEV (Evolut R, Medtronic Inc., Minneapolis, MN, USA) with BEV (Sapien 3, Edwards Lifesciences, Irvine, CA, USA). The primary efficacy composite endpoint of all-cause mortality, stroke, moderate/severe prosthetic valve regurgitation, and permanent pacemaker implantation at 30 days was powered for equivalence (equivalence margin 10% with significance level 0.05). The primary composite endpoint occurred in 28.4% of SEV patients and 26.1% of BEV patients meeting the prespecified criteria of equivalence [rate difference -2.39 (90% confidence interval, CI -9.45 to 4.66);  $P_{\text{equivalence}} = 0.04$ ]. Event rates for the individual components were as follows: all-cause mortality 3.2% vs. 2.3% [rate difference -0.93 (90% CI -4.78 to 2.92);  $P_{\text{equivalence}} < 0.001$ ], stroke 0.5% vs. 4.7% [rate difference 4.20 (90% CI 0.12 to 8.27);  $P_{\text{equivalence}} = 0.003$ ], moderate/severe paravalvular leak 3.4% vs. 1.5% [rate difference -1.89 (90% CI -5.86 to 2.08);  $P_{\text{equivalence}} = 0.0001$ ], and permanent pacemaker implantation 23.0% vs. 19.2% [rate difference -3.85 (90% CI -10.41 to 2.72) in SEV vs. BEV patients;  $P_{\text{equivalence}} = 0.06$ ].

\* Corresponding author. Tel: +49 341 865 1428, Fax: +49 341 865 1461, Email: holger.thiele@medizin.uni-leipzig.de

† The first two authors should be considered as shared first authors.

‡ The last two authors should be considered as shared senior authors.

## Conclusion

In patients with aortic stenosis undergoing transfemoral TAVI, newer generation SEV and BEV are equivalent for the primary valve-related efficacy endpoint. These findings support the safe application of these newer generation percutaneous valves in the majority of patients with some specific preferences based on individual valve anatomy.

## Keywords

Transcatheter aortic valve implantation • Transcatheter aortic valve replacement • Aortic stenosis • Pacemaker implantation • Stroke • Prognosis

## Introduction

Transcatheter aortic valve implantation (TAVI) has emerged as a valuable and effective alternative to surgical aortic valve replacement (SAVR) in symptomatic aortic stenosis in the spectrum from high to intermediate and most recently also low surgical risk.<sup>1–3</sup> Based on several randomized trials in inoperable, high- and intermediate surgical risk patients several TAVI devices have gained European and US approval. In particular, two valve types have been widely used: self-expandable valve (SEV) and balloon-expandable valve (BEV).

Despite advances, initial TAVI devices had limitations, including the inability of retrieval or repositioning after full expansion, haemodynamic compromise during implantation or large access sheath size. The need for permanent pacemaker implantation is another important limitation in particular for SEV although the impact on outcome is undetermined.<sup>4</sup> Furthermore, paravalvular leakage (PVL) can occur and there is a higher mortality associated with moderate or severe PVL.<sup>5</sup> Accordingly, the current challenge is to further decrease rates in mortality, stroke, bleeding, need for permanent pacemaker implantation, and also PVL among other complications. Even though newer generation SEV<sup>6</sup> and BEV<sup>7</sup> devices have been developed to address possible drawbacks of first-generation devices which led to a frequent adoption of these devices in clinical practice,<sup>8</sup> randomized trials evaluating outcomes in patients treated with newer generation SEV and BEV are very limited. The current available evidence comparing different valve types includes only two small to modestly sized randomized controlled trials ( $n = 240$  comparing first-generation SEV and BEV<sup>9</sup>; and  $n = 912$  comparing a mechanically expanded valve with first- and second-generation SEV).<sup>10</sup>

Accordingly, aim of this randomized trial was to compare the newer generation SEV (Evolut R, Medtronic Inc., Minneapolis, MN, USA) and BEV (Sapien 3, Edwards Lifesciences, Irvine, CA, USA) in a multicentre trial with respect to equivalence in safety and efficacy in high-risk patients with symptomatic aortic stenosis undergoing transfemoral TAVI.

## Methods

### Study design and oversight

The comparison of second-generation self-expandable vs. balloon-expandable valves and general vs. local anaesthesia in Transcatheter Aortic Valve Implantation (SOLVE-TAVI) trial is an investigator-initiated  $2 \times 2$  factorial, open-label, randomized, multicentre study conducted at seven German sites to compare newer generation SEV (Evolut R, Medtronic Inc., Minneapolis, MN, USA) vs. BEV (Sapien 3, Edwards Lifesciences, Irvine, CA, USA). Results of the concurrent, interlaced trials of the valve and anaesthesia strategy are reported separately based on

different primary endpoints in both trials. SOLVE-TAVI is co-ordinated by the Heart Center Leipzig at University of Leipzig in co-operation with the Leipzig Heart Institute, Germany and the Center for Clinical Trials at University of Lübeck, Germany. The trial was designed by the first and senior authors and modified by the steering committee. Funding was partially provided by the German Heart Research Foundation and the Leipzig Heart Institute, Germany and by all participating sites.

The study was approved by ethics committees of all participating centres and national regulatory authorities. The trial organization included a steering committee, an independent data safety monitoring board, and a clinical event committee adjudicating all major clinical events. Echocardiographic data were analysed by the individual centres. In addition, PVL was also analysed by an independent core laboratory (blinded to treatment allocation). The first author had full access to all data and takes responsibility for integrity and data analysis. Data were maintained at the Center for Clinical Trials and the Institute for Medical Biometry and Statistics (IMBS), University of Lübeck, Lübeck, Germany, which performed all statistical analyses independently. All sites were monitored on site before and during the trial using the risk-based approach, and central data management queried frequently about implausible or missing values. The trial is registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT02737150).

### Patient selection

Patients with symptomatic aortic stenosis, age  $\geq 75$  years and high risk for conventional SAVR were eligible for enrolment. High risk was defined by logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE)  $\geq 20\%$  and/or Society of Thoracic Surgeons (STS) risk score  $\geq 10\%$  or other high-risk criteria by heart team consensus. A native aortic valve annulus size (18–29 mm) appropriate for the available valve sizes and suitability for transfemoral vascular access were also required.

Exclusion criteria were contraindication for a specific valve type; cardiogenic shock or haemodynamic instability; history of or active endocarditis; active infection requiring antibiotic treatment; life expectancy  $< 12$  months; active peptic ulcer or upper gastrointestinal bleeding  $< 3$  months; hypersensitivity or contraindication to aspirin, heparin, or clopidogrel; and participation in another trial. Written informed consent was provided by all patients.

By means of opaque sealed envelopes randomization was performed using permuted blocks of variable size and stratification for centre. The valves differ by design and instructions for use; therefore, the investigators performing the procedure were unblinded to the assigned treatment. However, clinical endpoint assessment was performed in a blinded manner.

### Treatment and follow-up

Apart from the valve type, all other interventions did not differ between groups. The technical aspects of the TAVI procedures followed the accepted standards and the implantation techniques of the specific valves. A pre-procedure computed tomography scan was standard in all institutions for native annulus measurement and also assessment of vascular access. All procedures have been performed by highly experienced

operators with a minimum overall experience of 50 TAVI procedures. The study was also performed in accordance with current national German recommendations on quality criteria for implementation of TAVI.<sup>11</sup>

Clinical follow-up was performed at discharge and 30 days and by protocol will also be continued at 6, 12, 24, and 60 months. Neurological assessments were performed after TAVI by neurologists and/or certified physicians to administer the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale.

## Study endpoints

The primary endpoint for the valve comparison was a composite of all-cause mortality, stroke, moderate or severe PVL, and permanent pacemaker implantation at 30-day follow-up.

Secondary endpoints of the current valve analysis included device success, early safety, clinical efficacy, time-related safety, and cardiovascular mortality according to the Valve Academic Research Consortium (VARC)-2 criteria.<sup>12</sup> In addition, the cardiovascular mortality at 30 days, individual components of the primary endpoint, mean length of primary hospital stay, quality of life according to the EuroQuol-5 questionnaire (EQ-5D), device time, and total procedural time were assessed.

## Statistical analysis

The study was powered for equivalence of the composite primary endpoint.<sup>13</sup> Based on clinical experience, an interaction between the valve and anaesthesia strategy was not expected. Thus, independent sample size calculations were performed with no adjustment for essentially conducting two studies. The final sample size was defined by the larger of these, i.e. the valve strategy, to be powered to detect the main effect of each intervention. Sample size calculations were performed using established sample size calculation software (nQuery 6.01) and were based on the available results of the CoreValve Evolut R CE study<sup>14</sup> and the Safety and Performance Study of the Edwards Sapien 3 Transcatheter Heart Valve trial.<sup>15</sup> Based on these data, an overall incidence of the combined endpoint of 15.0% had been anticipated in both groups. Equivalence of SEV and BEV was assumed within an equivalence margin of 10%. A difference >10% was judged to be clinically relevant for the primary endpoint. To reject the equivalence null hypothesis (two-sided  $\chi^2$  test; power 90%, significance level 0.05)  $2 \times 219 = 438$  evaluable patients were needed. The drop-out rate for the primary study endpoint assessment was assumed to be 1.0% resulting in a final study cohort consisting of 444 patients.

All analyses were performed according to the intention-to-treat principle. A per-protocol analysis was performed in case of cross-over. The full analysis set is the operationalization of the intention-to-treat principle which was defined as all randomized and treated patients regardless of protocol deviations. Randomized patients were not included in case of withdrawal of informed consent prior to treatment or if there was no treatment attempt (e.g. because of prior death) to avoid bias and to sharpen generalization. The denominator of proportions may differ because of missing values which were not imputed. The per-protocol set was defined as all randomized patients fulfilling all in- and no exclusion criteria receiving the allocated intervention.

Pre-specified subgroup analyses for the valve strategy were performed for sex, age (<80 vs.  $\geq 80$  years), presence or absence of coronary artery disease, left ventricular ejection fraction ( $\leq 35$  vs.  $> 35\%$ ), frailty (non/mild vs. moderate/severe), presence or absence of chronic renal insufficiency, body mass index ( $< 25$  kg/m<sup>2</sup> vs.  $\geq 25$  to  $30$  kg/m<sup>2</sup> vs.  $\geq 30$  kg/m<sup>2</sup>); STS score (<10% vs.  $\geq 10\%$ ); logistic EuroSCORE I (<20% vs.  $\geq 20\%$ ); aortic valve stenosis haemodynamic type (normal flow, high gradient vs. low flow, low gradient with reduced ejection fraction vs. paradoxical low

flow, low gradient, with normal ejection fraction); saturation of cerebral oxygen at start of TAVI procedure <50% vs.  $\geq 50\%$ , and general vs. local anaesthesia.

## Results

### Patients

From April 2016 to April 2018, 447 patients were randomized (Figure 1). A total of 225 patients were randomly assigned to SEV and 222 to BEV implantation. Of these, 438 patients underwent the TAVI procedure and were thus eligible for further analysis (Figure 1).

Patients were at high to intermediate risk with a mean age of over 80 years and a median logistic EuroSCORE I of 14.8% [interquartile range (IQR) 8.7–23.8%] and STS score of 4.7% (IQR 3.0–9.8%). Baseline characteristics are displayed in Table 1 and were well balanced between the two valve treatment groups (Table 1).

### Treatment

Procedural characteristics are shown in Table 2. Cross-over from SEV to BEV occurred in two patients (0.9%); to other valves in two patients and in the opposite direction in one patient (Figure 1). The use of transoesophageal echocardiography was infrequent and similar between both treatment groups (Table 2).

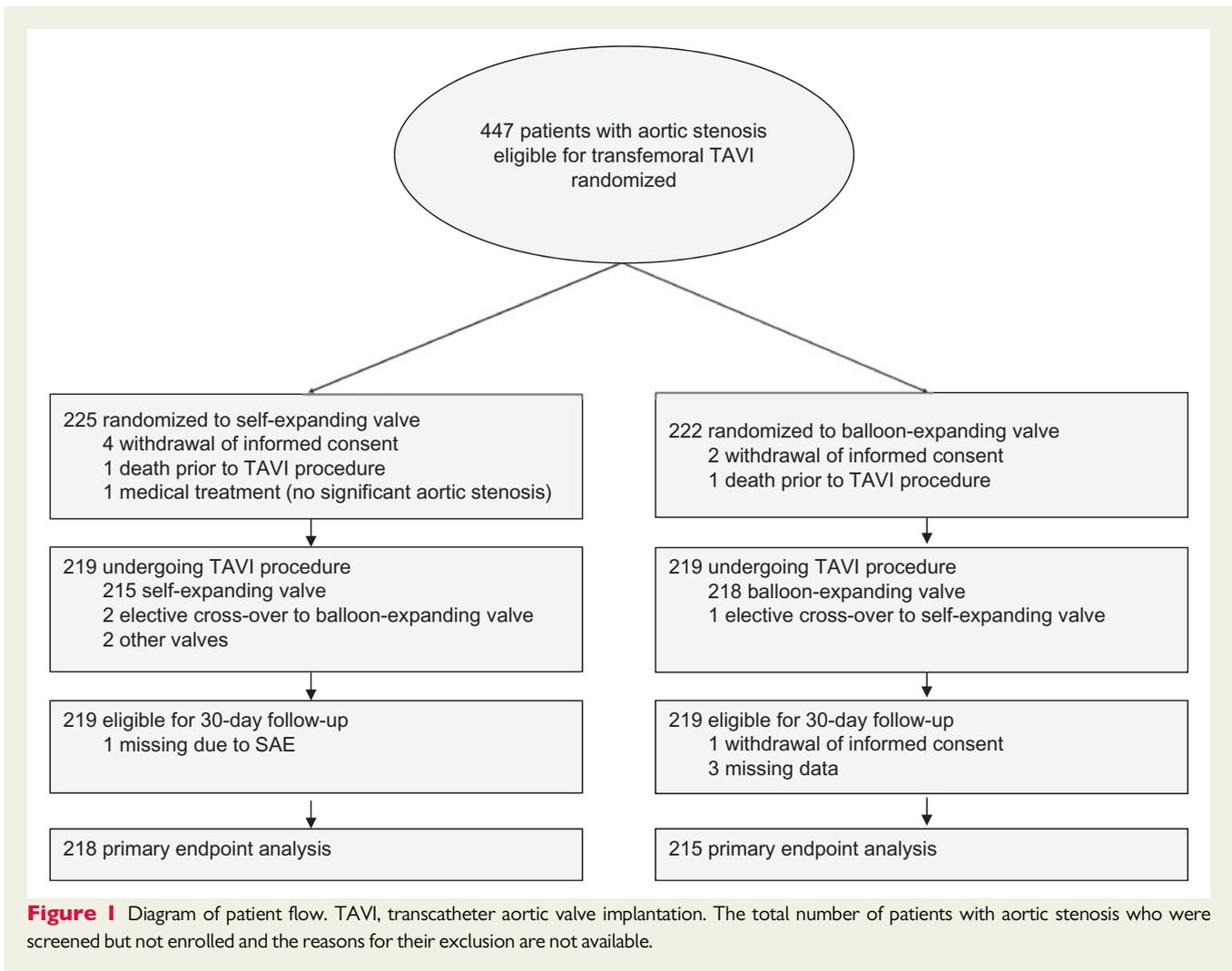
### Primary and secondary endpoints

Three patients in the BEV group were lost to follow-up with respect to the primary endpoint and one patient per group withdrew informed consent after TAVI (Figure 1). Consequently, 218 patients in the SEV and 215 patients in the BEV group were included in the primary endpoint analysis.

At 30 days, the rate of the composite primary endpoint of all-cause mortality, stroke, moderate or severe PVL, and permanent pacemaker implantation was equivalent between SEV and BEV [28.4% vs. 25.9%; rate difference -2.51 (90% confidence interval, CI -9.65 to 4.53);  $P_{\text{equivalence}} = 0.04$ ]. Only minor variation in the rate difference was observed when the analysis was performed in the per-protocol population [27.0% for SEV vs. 25.5% for BEV; rate difference: 1.48; 90% CI -8.61 to 5.65;  $P_{\text{equivalence}} = 0.03$ ]. Prespecified subgroup analyses revealed consistent results across all subgroups (Figure 2).

Analysis of the individual components of the primary endpoint were as follows (Take home figure): all-cause mortality 3.2% for SEV vs. 2.3% for BEV [rate difference -0.94 (90% CI -4.79 to 2.91);  $P_{\text{equivalence}} < 0.001$ ], stroke 0.5% for SEV vs. 4.7% for BEV [rate difference 4.20 (90% CI 0.11 to 8.28);  $P_{\text{equivalence}} = 0.003$ ], moderate/severe paravalvular leak 3.4% for SEV vs. 1.5% for BEV [rate difference -1.92 (90% CI -5.88 to 2.05);  $P_{\text{equivalence}} = 0.0001$ ], permanent pacemaker implantation 23.0% for SEV vs. 19.2% for BEV [rate difference -3.85 (90% CI -10.41 to 2.72);  $P_{\text{equivalence}} = 0.06$ ] (Table 3). Altogether, permanent pacemaker implantation rates were relatively high with similar indications between groups (Table 3).

Device time and total procedural time were similar between both treatment groups. However, fluoroscopy time and overall doses of contrast agent were higher in the SEV group in comparison to the BEV group (Table 2). There were no differences in major bleeding complications, acute kidney injury or the need and doses of vasopressors and inotropes between groups (Table 4).



Valve-related outcomes according to VARC-2 criteria with respect to device success and early safety fulfilled the criteria of equivalence (Table 4). However, clinical efficacy and time-related safety did not show equivalence (Table 4). Time-related safety was significantly better for the SEV (Table 4) which was mainly driven by a higher rate of patients with a gradient  $\geq 20$  mmHg in the BEV group at 30-day follow-up.

Overall quality of life according to the EQ-5D questionnaire was not statistically different between the two treatment groups. Pain was relieved by a median of one point compared with baseline in both groups in parallel (95% CI -1 to -0.5), while median self-care worsened by one point (95% CI 0.5–1) at 30 days in both groups. Little change was observed in mobility, anxiety, and usual activities (Figure 3).

## Discussion

In this randomized multicentre trial among high- to intermediate-risk aortic stenosis patients undergoing transfemoral TAVI, newer generation SEV in comparison to BEV met criteria for equivalence for the

composite primary efficacy endpoint at 30 days. All-cause mortality, stroke rates, and PVL were low. However, permanent pacemaker implantation in this specific high-risk population is still high with both valve types.

The number of TAVI procedures performed is steadily growing.<sup>17,18</sup> With the latest trials in low-risk patients showing superiority and non-inferiority of TAVI in comparison to SAVR,<sup>2,3</sup> valve design, device-related complications, and valve durability become even more important. Multiple companies continue to develop new valves in order to further reduce clinical complications. However, evidence on valve comparisons is limited. Currently, there are only two randomized trials comparing different valve types.<sup>9,10</sup> One trial was conducted in the early years of TAVI comparing first-generation SEV (CoreValve, Medtronic) and BEV (Sapien XT, Edwards)<sup>9,19</sup>; the second trial compared a mechanical expanding valve (Lotus, Boston Scientific Corp.) to mixed first- and second-generation SEV (CoreValve and Evolut R, Medtronic).<sup>10</sup> Similar to the SOLVE-TAVI trial, both trials also used a composite clinical endpoint. In the CHOICE trial ( $n = 241$ ) device success—according to the previous VARC criteria<sup>20</sup>—was superior with BEV vs. SEV mainly driven by less PVL.<sup>9</sup> In the REPRISSE III (Repositionable Percutaneous

**Table 1** Baseline characteristics

	Self-expanding valve (Evolut R) (n = 219)	Balloon-expandable valve (Sapien 3) (n = 219)
Age (years), mean ± SD	81.7 ± 5.3	81.5 ± 5.7
Male sex, n/total (%)	105/219 (47.9)	109/219 (49.8)
Risk scores		
STS score (%), median (IQR)	4.9 (2.9–9.9)	4.7 (3.1–9.4)
Log. EuroSCORE I (%), median (IQR)	14.9 (8.9–23.8)	14.8 (8.6–24.4)
EuroSCORE II (%), median (IQR)	4.1 (2.5–7.5)	3.8 (2.4–6.1)
Frailty, n/total (%)	93/216 (43.1)	80/217 (36.9)
Peripheral arterial disease, n/total (%)	29/218 (13.3)	26/220 (11.8)
Coronary artery disease, n/total (%)	127/219 (58.0)	116/219 (52.7)
Prior myocardial infarction, n/total (%)	19/219 (8.7)	22/219 (10.0)
Prior PCI, n/total (%)	84/219 (38.4)	79/219 (36.1)
Prior CABG, n/total (%)	26/219 (11.9)	18/219 (8.2)
Atrial fibrillation, n/total (%)	103/219 (47.0)	93/219 (42.5)
Prior pacemaker/implantable cardioverter defibrillator, n/total (%)	24/218 (11.0)	23/219 (10.5)
Prior stroke, n/total (%)	25/219 (11.4)	26/219 (11.9)
Renal insufficiency, n/total (%)	177/216 (81.9)	184/214 (86.0)
Pulmonary hypertension, n/total (%)	106/216 (49.1)	105/218 (48.2)
Chronic obstructive pulmonary disease, n/total (%)	30/219 (13.7)	29/217 (13.4)
Cardiovascular risk factors		
Diabetes, n/total (%)	79/218 (36.2)	68/219 (31.1)
Arterial hypertension, n/total (%)	193/219 (88.1)	204/219 (93.2)
Hyperlipoproteinemia, n/total (%)	100/218 (45.9)	80/217 (36.9)
Current smoking, n/total (%)	8/218 (3.7)	10/219 (4.6)
New York Heart Association class, n/total (%)		
I	25/216 (11.6)	17/218 (7.8)
II	50/216 (23.2)	56/218 (25.7)
III	122/216 (56.5)	130/218 (59.6)
IV	19/216 (8.8)	15/218 (6.9)
Baseline echocardiographic findings		
Aortic valve area (cm <sup>2</sup> ), median (IQR)	0.7 (0.6–0.9)	0.8 (0.6–0.9)
Mean aortic valve gradient (mmHg), median (IQR)	38.5 (30.0–50.5)	37.0 (26.5–47.5)
≥40 mmHg, n/total (%)	91/192 (52.6)	86/196 (43.9)
Left ventricular ejection fraction, n/total (%)		
>55%	120/211 (56.9)	119/208 (57.2)
45–55%	58/211 (27.5)	52/208 (25.0)
35–44%	21/211 (10.0)	18/208 (8.7)
<35%	12/211 (5.7)	19/208 (9.1)
Quality of life EuroQoL 5D 5L, median (IQR)		
Mobility	2 (1–3)	2 (1–4)
Self-care	1 (1–2)	1 (1–2)
Usual activities	2 (1–3)	2 (1–3)
Pain	2 (1–3)	3 (1–3)
Anxiety	1 (1–2)	1 (1–2)
VAS	60 (50–75)	60 (50–75)
Index	0.81 (0.68–0.91)	0.81 (0.60–0.91)

CABG, coronary artery bypass grafting; IQR, interquartile range; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; VAS, visual analogue scale.

Replacement of Stenotic Aortic Valve Through Implantation of Lotus Valve System—Randomized Clinical Evaluation) trial ( $n = 912$ ), all-cause mortality, disabling stroke, and moderate to severe PVL showed non-inferiority between both valve types.<sup>9,10</sup> However,

significantly more permanent pacemaker implantations were required with the mechanical expanding valve. In the current trial, permanent pacemaker implantation was added to the composite endpoint because of its clinical relevance. An equivalence design was

**Table 2** Procedural characteristics

	Self-expanding valve (Evolut R) (n = 219)	Balloon-expandable valve (Sapien 3) (n = 219)	P-value
Transoesophageal echocardiography, n/total (%)	41/214 (19.2)	38/213 (17.8)	0.73
Catecholamines, n/total (%)			
Norepinephrine	114/219 (52.1)	115/219 (52.5)	0.93
Epinephrine	19/219 (8.7)	18/219 (8.2)	0.86
Dobutamine	1/219 (0.5)	2/219 (0.9)	0.56
Duration of anaesthesia (min), median (IQR)	134 (110–155)	125 (102–154)	0.57
Anaesthesia type, n/total (%)			
Local anaesthesia	107/219 (48.9)	111/219 (50.7)	0.70
General anaesthesia	112/219 (51.1)	108/219 (49.3)	0.70
Final gradient after TAVI			
Invasive peak-to-peak (mmHg), median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.52
Invasive mean (mmHg), median (IQR)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.31
≥20 mmHg after one day at TOE, n/total (%)	2/185 (1.1%)	7/189 (3.7%)	0.17
≥20 mmHg after one month at TOE, n/total (%)	3/154 (2.0%)	10/159 (3.3%)	0.09
Device time (min), median (IQR)	57 (44–69)	57 (43–73)	0.80
Total procedural time (min), median (IQR)	110 (86–142)	107 (85–135)	0.40
Fluoroscopy time (min), median (IQR)	12 (9–16)	11 (8–15)	0.02
Contrast agent (ml), median (IQR)	110 (90–130)	90 (80–105)	<0.001
Major vascular complication, n/total (%)	11/218 (5.1)	14/219 (6.4)	0.54
Access site percutaneous closure device failure, n/total (%)	15/217 (6.9)	12/217 (5.5)	0.55
Life-threatening or disabling bleeding, n/total (%)	3/218 (1.4)	9/219 (4.1)	0.08
Major bleeding, n/total (%)	5/218 (2.3)	7/218 (3.2)	0.56
Time to echocardiography (days), median (IQR)	34.5 (27–55)	34 (28–50)	0.95

IQR, interquartile range; TAVI, transcatheter aortic valve implantation.

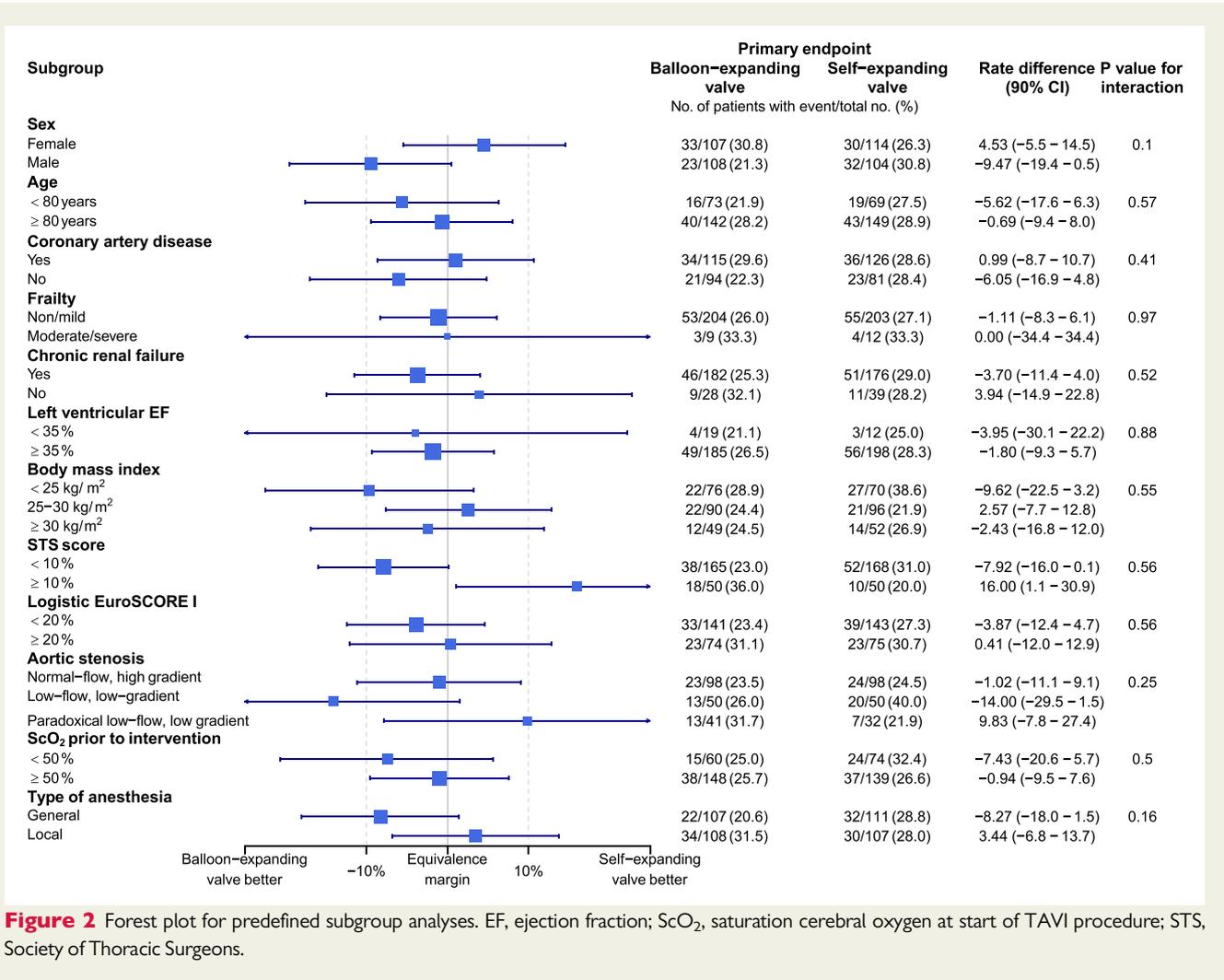
chosen because both newer generation valves were considered to have similar performance for the combined clinical endpoint.<sup>13</sup>

In addition to the above-mentioned two randomized trials, there are two registry-based trials with propensity matching to assess possible differences with SEV vs. BEV in 408 and 12 381 patients.<sup>8,21</sup> Therefore, the present randomized study significantly adds to the body of evidence of newer generation SEV vs. BEV by showing equivalence for a combined clinical endpoint consisting of four clinically relevant components. Currently, one other randomized trial has recently been published. In the SCOPE I trial, the SEV ACURATE neo did not show non-inferiority in comparison to the BAV Sapien 3 valve using a modified combined 30-day early safety and clinical efficacy endpoint. Results were mainly driven by higher rates of acute kidney injury and more PVL in the ACURATE neo SEV arm.<sup>22</sup> Furthermore, the SCOPE II trial (NCT03192813) compares the SEV ACURATE neo with the CoreValve Evolut R with respect to the primary composite endpoint of all-cause mortality or stroke at 1-year follow-up. This trial also has a non-inferiority design.

The lack of any difference in 30-day mortality rates between both valve types comes to no surprise based on the two previous randomized trials.<sup>9,10</sup> Interestingly, the 30-day all-cause mortality was low despite inclusion of a high-risk population and lower than in the CENTER matched comparison which also showed no difference in 30-day mortality between SEV and BEV.<sup>8</sup>

The low rate of moderate or severe PVL is in line with the expected rates based on registry studies of these new generation devices.<sup>14,15,23</sup> Moderate or severe PVL has been associated with an increased risk of mortality.<sup>24</sup> Therefore, PVL was included in the primary endpoint and was carefully assessed by a core lab. PVL can be a result of (i) under-sizing, (ii) malpositioning, or (iii) lack of a sealing zone due to calcification or irregularities from compression of the native valve. The advent of new sealing mechanisms in these new generation devices addresses the latter mechanism which led to a significant improvement in comparison to the first-generation comparison in the CHOICE trial.<sup>9</sup> The latest development in the CoreValve family (Evolut R Pro) has an additional external pericardial wrap to enhance annular sealing. However, no direct valve comparisons are available for this new device and PVL rates were similar to other devices and historical comparisons.<sup>25</sup>

Aortic valve area was increased and transvalvular pressure gradients were decreased with both valve types. However, gradients were smaller with the SEV because the leaflets reside in a less constrained supra-annular location. This is the reason why the secondary endpoint time-related safety according to VARC-2 criteria did not meet equivalence. The same finding has recently been observed in the low-risk trials comparing TAVI vs. conventional SAVR where the SEV Evolut R had larger valve area in comparison to surgical valves, whereas the BEV Sapien 3 valve had smaller valve areas in



**Figure 2** Forest plot for predefined subgroup analyses. EF, ejection fraction; ScO<sub>2</sub>, saturation cerebral oxygen at start of TAVI procedure; STS, Society of Thoracic Surgeons.

**Table 3** Primary endpoint and its components

	Self-expanding valve (Evolut R)	Balloon-expandable valve (Sapien 3)	Rate difference (90% CI)	P-value equivalence
Composite primary endpoint, <sup>a</sup> % (n/total)	28.4 (62/218)	25.9 (56/216)	-2.51 (-9.56 to 4.53)	0.04
All-cause mortality, % (n/total)	3.2 (7/217)	2.3 (5/219)	-0.94 (-4.79 to 2.91)	<0.0001
Stroke, % (n/total)	0.5 (1/210)	4.7 (10/214)	4.2 (0.11 to 8.28)	0.003
Moderate or severe prosthetic valve regurgitation, <sup>b</sup> % (n/total)	3.4 (7/208)	1.5 (3/207)	-1.92 (-5.88 to 2.05)	0.0002
Permanent pacemaker, % (n/total)	23.0 (49/213)	19.2 (41/214)	-3.85 (-10.4 to 2.72)	0.06

Results are displayed for the prespecified hierarchical testing against the equivalence margin 10% for the primary endpoint and its components.

<sup>a</sup>Composite of all-cause mortality, stroke, moderate or severe prosthetic valve regurgitation; permanent pacemaker implantation at 30-day follow-up.

<sup>b</sup>Moderate or severe paravalvular leak (PVL) based on core laboratory assessment.

comparison to surgical valves.<sup>2,3</sup> The long-term effect of haemodynamic differences between the SEV and BEV is unknown and the planned long-term follow-up will help elucidate this.

Stroke rates differ in TAVI trials mainly based on different patient cohorts and also intensity of follow-up and also if assessment by neurologists is performed. In the current trial, stroke rates

were numerically higher with BEV compared with SEV without reaching statistical significance in superiority testing. However, overall stroke rates in the SEV group were extremely low and much lower than reported in some high-risk studies, whereas the stroke rates in the BEV group were also in the lower range of these trials (range 6–10%).<sup>26–28</sup> Previous randomized trials did not

**Table 4** Clinical outcome at 30 days for other clinical endpoints

	Self-expanding valve (Evolut R)	Balloon-expandable valve (Sapien 3)	Rate difference (90% CI)
Indication for permanent pacemaker			
AV block III.° , % (n/total)	14.7 (32/218)	11.4 (25/219)	-3.26 (-8.81 to 2.28)
AV block II.° type Mobitz, % (n/total)	0.46 (1/ 218)	1.83 (4/219)	1.37 (-2.26 to 4.99)
AV block II.° type Wenckebach, % (n/total)	0.46 (1/218)	0.46 (1/219)	0 (-3.42 to 3.41)
AV block I.° , % (n/total)	2.75 (6/218)	4.11 (9/219)	1.36 (-2.64 to 5.35)
Left bundle branch block, % (n/total)	6.88 (15/218)	6.39 (14/219)	-0.49 (-4.98 to 4.00)
Sinus node arrest/higher degree SA-block, % (n/total)	0.92 (2/218)	0.91 (2/219)	0 (-3.49 to 3.49)
Bradyarrhythmias, % (n/total)	3.67 (8/218)	3.2 (7/219)	-0.47 (-4.41 to 3.46)
Valve-related outcome according to VARC-2 criteria <sup>a,12</sup>			
Device success, % (n/total)	93.6 (189/202)	91.0 (183/201)	2.52 (-2.42 to 7.45)
Early safety, % (n/total)	11.9 (26/219)	16.0 (35/219)	4.11 (-1.57 to 9.79)
Clinical efficacy, % (n/total)	33.8 (74/219)	37.0 (81/219)	-3.20 (-10.7 to 4.30)
Time-related safety, % (n/total)	17.8 (39/219)	26.0 (57/219)	8.22 (1.62 to 14.8)
Acute kidney injury <sup>b</sup> , % (n/total)	9.39 (20/213)	8.84 (19/215)	-0.55 (-5.50 to 4.39)
Delirium at 24 h or 48 h <sup>c</sup> , % (n/total)	10.4 (22/212)	13.6 (29/214)	3.22 (-2.24 to 8.69)
Need for inotropes, % (n/total)	78.5 (172/219)	80.4 (176/219)	-1.83 (-8.24 to 4.59)
Need for vasopressors, % (n/total)	79 (173/219)	80.8 (177/219)	-1.83 (-8.20 to 4.54)
Need for inotropes or vasopressors, % (n/total)	79 (173/219)	81.3 (178/219)	-2.28 (-8.63 to 4.07)

<sup>a</sup>Device success according to VARC-2 criteria<sup>12</sup>; absence of procedural mortality AND correct positioning of a single prosthetic heart valve into the proper anatomical location AND intended performance of the prosthetic heart valve (no prosthesis-patient mismatch) and mean aortic valve gradient <20 mmHg or peak velocity <3 m/s, AND no moderate or severe prosthetic valve regurgitation. Early safety according to VARC-2 criteria<sup>12</sup>; composite of all-cause mortality, all stroke (disabling and non-disabling), life-threatening bleeding, acute kidney injury (Stage 2 or 3, including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeat procedure. Clinical efficacy according to VARC-2 criteria<sup>12</sup>; composite of all-cause mortality, all stroke (disabling and non-disabling), requiring hospitalizations for valve-related symptoms or worsening congestive heart failure, New York Heart Association (NYHA) Class III or IV, valve-related dysfunction (mean aortic valve gradient  $\geq$ 20 mmHg, effective orifice area (EOA)  $\leq$ 0.9–1.1 cm<sup>2</sup> and/or Doppler velocity index (DVI) <0.35 m/s, and/or moderate or severe prosthetic valve regurgitation). Time-related safety according to VARC-2 criteria<sup>12</sup>; structural valve deterioration such as valve-related dysfunction (mean aortic valve gradient  $\geq$ 20 mmHg, EOA  $\leq$ 0.9–1.1 cm<sup>2</sup> and/or DVI <0.35 m/s), and/or moderate or severe prosthetic valve regurgitation requiring repeat procedure, prosthetic valve endocarditis, prosthetic valve thrombosis, thromboembolic events (e.g. stroke), bleeding, unless clearly unrelated to valve therapy (e.g. trauma).

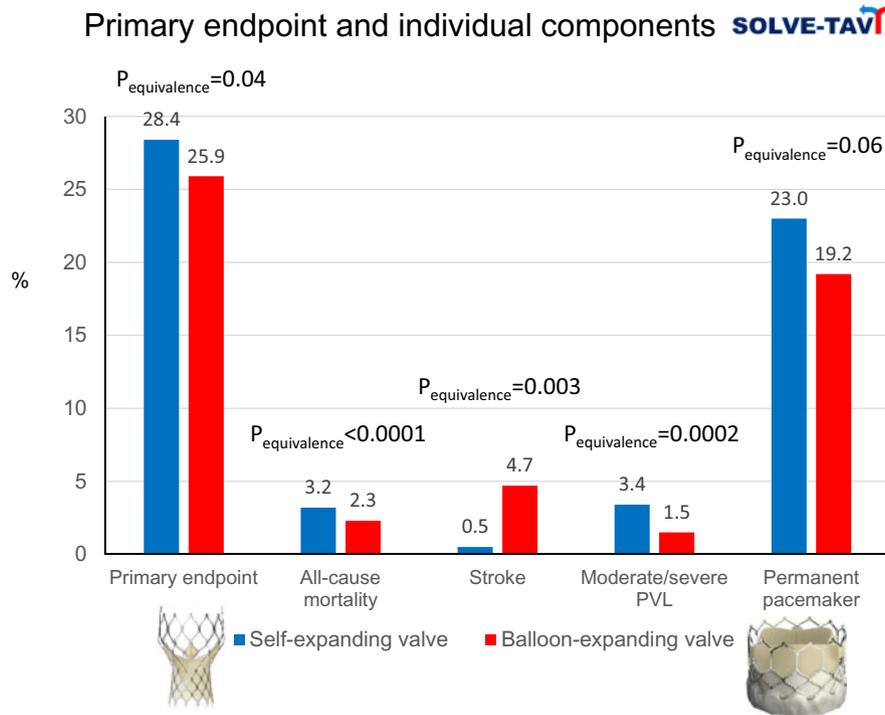
<sup>b</sup>Acute kidney injury according to VARC-2 criteria Stage 2 or 3.<sup>12</sup>

<sup>c</sup>Delirium assessed by Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) criteria.<sup>16</sup>

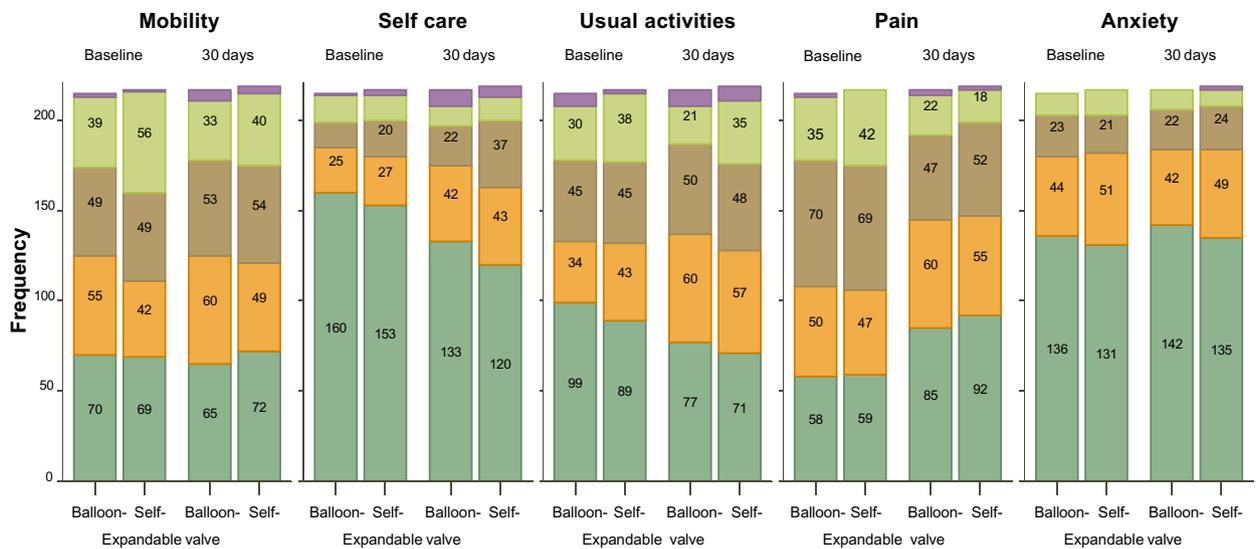
find differences in stroke rates between different valve types.<sup>9,10</sup> In contrast, the CENTER large-scale, propensity-matched study observed lower stroke rates with BEV compared with SEV and hypothesized that the implantation mechanism of SEV may generate more periprocedural strokes.<sup>8</sup> Therefore, the current finding may also be a chance finding. Intraprocedural strokes are potentially modifiable by the use of cerebral embolic protection devices. In a recent individual-patient-based meta-analysis using propensity matching cerebral embolic protection reduced stroke rates (1.9% vs. 5.4%,  $P=0.0028$ ).<sup>29</sup> Future studies are needed to characterize the adoption of cerebral embolic protection during TAVI in clinical practice and its effect on clinical outcome. Cerebral embolic protection was not used on a routine basis in the current trial and use of these devices was not systematically assessed in case report forms.

Initial results of these new valve designs suggested that implantation of these new devices is associated with a much lower need for permanent pacemaker implantation. Pacemaker implantation in patients treated with Evolut R was at 16.4% in an early registry and 18.1% in the recent CENTER registry, whereas in the same registry

Sapien 3 had a pacemaker rate of only 8.9%. Similar results have been observed in the recent intermediate and low-risk trials comparing TAVI vs. SAVR (Evolut R 17.4% and Sapien 3 8.5% and 6.6%, respectively).<sup>2,3,30</sup> In a recent systematic review, the SEV Evolut R and the BEV Sapien 3 required pacemaker implantation in a range of 14.7–26.7% and 4.0–24.0%, respectively.<sup>4</sup> Thus, the pacemaker implantation rate in SOLVE-TAVI is in the upper range of previously reported trials and registries. There were no differences in the indication for pacemaker implantation in both groups and it may be speculated that in some centres a more liberal indication has been applied for patients with long AV-block I.° and new left bundle branch block. Implantation depth and anatomical factors with more severe calcification may also have contributed to the relatively high pacemaker rate. Furthermore, implantation depth, need for additional balloon valvuloplasty, balloon and prosthesis size are well-known factors for pacemaker implantation which may be reduced with a further learning curve. In general, pacemaker implantation is associated with increased costs, longer hospital stay, and possibly patient morbidity. However, to date, it has not been associated with increased mortality.<sup>4</sup>



**Take home figure** Primary endpoint and components of the primary endpoint of the SOLVE-TAVI valve strategy comparison. PVL, paravalvular leakage.



**Figure 3** Quality of life for the five dimensions of the EuroQol 5D questionnaire at baseline and 30-day follow-up on 5-point Likert scales starting from no constraints (bottom bar) for self-expanding and balloon-expandable valve groups. Dark green, no constraints; Brown, slight constraints; Orange, moderate constraints; Light green, severe constraints; Purple, extreme constraints or unable to do.

Bleeding rates and access site complications were low and similar between both valve types. This is in contrast to the CENTER evaluation where patients treated with new generation BEV more often suffered from major or life-threatening bleedings than patients with

new generation SEV.<sup>8</sup> The early generation Edwards SAPIEN valve and also the first-generation CoreValve required large sheath sizes (22 Fr/24 Fr) which has been reduced to 14 Fr/16 Fr with the newest generation as used in the current trial.

This trial like all trials has some limitations. First, blinding was not possible due to the different valves chosen. Second, the present study included mainly high-risk patients undergoing TAVI. Therefore, the impact of the two different valve types on outcome in lower-risk cohorts cannot be extrapolated. Third, cerebral protection devices have not been used on a routine basis and no additional information on cerebral protection has been collected in the case report forms. Fourth, this trial was powered to show equivalence between both treatment groups for the composite clinical endpoint only.<sup>13</sup> Thus, the individual endpoints are not powered to show equivalence. The chosen equivalence margin of 10% was considered clinically meaningful but is surely considered by others too large for claiming equivalence in particular for the individual components of the primary endpoint and all other secondary endpoints. Finally, although the vast majority of patients can be successfully treated by either valve type from the present study, valve choice should take into account individual factors in which a specific valve type might be favoured (e.g. severe calcification, bicuspid anatomy, horizontal aorta, or the requirement of uncomplicated coronary access).

## Conclusions

Among high-risk patients with aortic stenosis, new generation SEV in comparison to BEV are equivalent with respect to the composite of all-cause mortality, stroke, permanent pacemaker implantation, and PVL. These findings support the safe application of these newer generation percutaneous valves which may be chosen on a general basis in the majority of patients with some specific preferences based on individual valve anatomy.

## Acknowledgements

We thank all patients for participation and all study nurses for the help in data acquisition and follow-up.

## Funding

This study was supported by the German Heart Research Foundation (grant number F/38/15) and the Leipzig Heart Institute, Leipzig, Germany.

**Conflict of interest:** none declared.

## References

- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Lung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2017;**38**:2739–2791.
- Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Généreux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR; PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;**380**:1695–1705.
- Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, Askew J, Sorajja P, Rovin J, Chetcuti SJ, Adams DH, Teirstein PS, Zorn GL, Forrest JK, Tchétché D, Resar J, Walton A, Piazza N, Ramlawi B, Robinson N, Petrossian G, Gleason TG, Oh JK, Boulware MJ, Qiao H, Mugglin AS, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019;**380**:1706–1715.
- van Rosendaal PJ, Delgado V, Bax JJ. Pacemaker implantation rate after transcatheter aortic valve implantation with early and new-generation devices: a systematic review. *Eur Heart J* 2018;**39**:2003–2013.
- Abdelghani M, Soliman Oll, Schultz C, Vahanian A, Serruys PW. Adjudicating paravalvular leaks of transcatheter aortic valves: a critical appraisal. *Eur Heart J* 2016;**37**:2627–2644.
- Manoharan G, Van Mieghem NM, Windecker S, Bosmans J, Bleiziffer S, Modine T, Linke A, Scholtz W, Chevalier B, Gooley R, Zeng C, Oh JK, Grube E. 1-year outcomes with the Evolut R self-expanding transcatheter aortic valve. From the international FORWARD Study. *JACC Cardiovasc Interv* 2018;**11**:2326–2334.
- Webb J, Gerosa G, Lefevre T, Leipsic J, Spence M, Thomas M, Thielmann M, Treede H, Wendler O, Walther T. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. *J Am Coll Cardiol* 2014;**64**:2253–2254.
- Vlastra W, Chandrasekhar J, Muñoz-García AJ, Tchétché D, de Brito FS Jr, Barbanti M, Kornowski R, Latib A, D'Onofrio A, Ribichini F, Baan J, Tijssen JGP, Trillo-Nouche R, Dumonteil N, Abizaid A, Sartori S, D'Errigo P, Tarantini G, Lunardi M, Orvin K, Pagnesi M, del Valle R, Modine T, Dangas G, Mehran R, Piek JJ, Delewi R. Comparison of balloon-expandable vs. self-expandable valves in patients undergoing transfemoral transcatheter aortic valve implantation: from the CENTER-collaboration. *Eur Heart J* 2019;**40**:456–465.
- Abdel-Wahab M, Mehili J, Frerker C, Neumann FJ, Kurz T, Tolg R, Zachow D, Guerra E, Massberg S, Schafer U, El-Mawardi M, Richardt G; CHOICE investigators. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. *JAMA* 2014;**311**:1503–1514.
- Feldman TE, Reardon MJ, Rajagopal V, Makkar RR, Bajwa TK, Kleiman NS, Linke A, Kereiakes DJ, Waksman R, Thourani VH, Stoler RC, Mishkel GJ, Rizik DG, Iyer VS, Gleason TG, Tchétché D, Rovin JD, Buchbinder M, Meredith IT, Götzberg M, Bjursten H, Meduri C, Salinger MH, Allocco DJ, Dawkins KD. Effect of mechanically expanded vs self-expanding transcatheter aortic valve replacement on mortality and major adverse clinical events in high-risk patients with aortic stenosis: the reprise III randomized clinical trial. *JAMA* 2018;**319**:27–37.
- Kuck KH, Eggebrecht H, Figulla HR, Haude M, Katus H, Möllmann H, Naber CK, Schunkert H, Thiele H, Hamm C. Qualitätskriterien zur Durchführung der transkathetären Aortenklappenimplantation (TAVI)—Positionspapier der Deutschen Gesellschaft für Kardiologie. *Kardiologie* 2015;**9**:11–26.
- Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es G-A, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J* 2012;**33**:2403–2418.
- Mascha E. Equivalence and noninferiority testing in anesthesiology research. *Anesthesiol* 2010;**113**:779–781.
- Popma JJ, Reardon MJ, Khabbaz K, Harrison JK, Hughes GC, Kodali S, George I, Deeb GM, Chetcuti S, Kipperman R, Brown J, Qiao H, Slater J, Williams MR. Early clinical outcomes after transcatheter aortic valve replacement using a novel self-expanding bioprosthesis in patients with severe aortic stenosis who are sub-optimal for surgery. Results of the Evolut R U.S. Study. *JACC Cardiovasc Interv* 2017;**10**:268–275.
- Webb J, Gerosa G, Lefevre T, Leipsic J, Spence M, Thomas M, Thielmann M, Treede H, Wendler O, Walther T. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. *J Am Coll Cardiol* 2014;**64**:2235–2243.
- Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard GR, Inouye SK. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 2001;**29**:1370–1379.
- Gaede L, Blumenstein J, Liebetrau C, Dörr O, Kim W-K, Nef H, Husser O, Elsässer A, Hamm CW, Möllmann H. Outcome after transvascular transcatheter aortic valve implantation in 2016. *Eur Heart J* 2018;**39**:667–675.
- Eggebrecht H, Mehta RH. Transcatheter aortic valve implantation (TAVI) in Germany: more than 100,000 procedures and now the standard of care for the elderly. *EuroIntervention* 2019;**14**:e1549–e1552.
- Abdel-Wahab M, Neumann FJ, Mehili J, Frerker C, Richardt D, Landt M, Jose J, Toelg R, Kuck KH, Massberg S, Robinson DR, El-Mawardi M, Richardt G, Investigators C. 1-year outcomes after transcatheter aortic valve replacement with balloon-expandable versus self-expandable valves: results from the CHOICE Randomized Clinical Trial. *J Am Coll Cardiol* 2015;**66**:791–800.
- Leon MB, Piazza N, Nikolsky E, Blackstone EH, Cutlip DE, Kappetein AP, Krucoff MW, Mack M, Mehran R, Miller C, Morel MA, Petersen J, Popma JJ, Takkenberg JJ, Vahanian A, van Es GA, Vranckx P, Webb JG, Windecker S, Serruys PW. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. *Eur Heart J* 2011;**32**:205–217.
- Chieffo A, Buchanan GL, Van Mieghem NM, Tchétché D, Dumonteil N, Latib A, van der Boon RMA, Vahdat O, Marcheix B, Farah B, Serruys PW, Fajadet J, Carrié D, de Jaegere PPT, Colombo A. Transcatheter aortic valve implantation

- with the Edwards SAPIEN versus the Medtronic CoreValve Revalving system devices: a multicenter collaborative study: the PRAGMATIC Plus Initiative (Pooled-Rotterdam-Milano-Toulouse In Collaboration). *J Am Coll Card* 2013;**61**: 830–836.
22. Lanz J, Kim WK, Walther T, Burgdorf C, Möllmann H, Linke A, Redwood S, Thilo C, Hilker M, Joner M, Thiele H, Conzelmann L, Conradi L, Kerber S, Schymik G, Prendergast B, Husser O, Stortecky S, Heg D, Juni P, Windecker S, Pilgrim T. Safety and efficacy of a self-expanding versus a balloon-expandable bioprosthesis for transcatheter aortic valve replacement in patients with symptomatic severe aortic stenosis: a randomised non-inferiority trial. *Lancet* 2019;**394**: 1619–1628.
  23. Grube E, Van Mieghem NM, Bleiziffer S, Modine T, Bosmans J, Manoharan G, Linke A, Scholtz W, Tchétché D, Finkelstein A, Trillo R, Fiorina C, Walton A, Malkin CJ, Oh JK, Qiao H, Windecker S; FORWARD Study Investigators. Clinical outcomes with a repositionable self-expanding transcatheter aortic valve prosthesis: the International FORWARD study. *J Am Coll Card* 2017;**70**:845–853.
  24. Kodali S, Pibarot P, Douglas PS, Williams M, Xu K, Thourani V, Rihal CS, Zajarias A, Doshi D, Davidson M, Tuzcu EM, Stewart W, Weissman NJ, Svensson L, Greason K, Maniar H, Mack M, Anwaruddin S, Leon MB, Hahn RT. Paravalvular regurgitation after transcatheter aortic valve replacement with the Edwards sapien valve in the PARTNER trial: characterizing patients and impact on outcomes. *Eur Heart J* 2015;**36**:449–456.
  25. Pagnesi M, Kim W-K, Conradi L, Barbanti M, Stefanini GG, Zeus T, Pilgrim T, Schofer J, Zweiker D, Testa L, Taramasso M, Hildick-Smith D, Abizaid A, Wolf A, Van Mieghem NM, Sedaghat A, Wöhrle J, Khogali S, Van der Heyden JAS, Webb JG, Estévez-Loureiro R, Mylotte D, MacCarthy P, Brugaletta S, Hamm CW, Bhadra OD, Schäfer U, Costa G, Tamburino C, Cannata F, Reimers B, Veulemans V, Asami M, Windecker S, Eitan A, Schmidt A, Bianchi G, Bedogni F, Saccocci M, Maisano F, Alsanjari O, Siqueira D, Jensen CJ, Naber CK, Ziviello F, Sinning J-M, Seeger J, Rottbauer W, Brouwer J, Alenezi A, Wood DA, Tzalamouras V, Regueiro A, Colombo A, Latib A. Transcatheter aortic valve replacement with next-generation self-expanding devices: a multicenter, retrospective, propensity-matched comparison of Evolut PRO Versus Acurate Neo transcatheter heart valves. *JACC Cardiovasc Interv* 2019;**12**:433–443.
  26. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermlinger J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;**370**:1790–1798.
  27. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;**363**:1597–1607.
  28. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;**364**:2187–2198.
  29. Seeger J, Kapadia SR, Kodali S, Linke A, Wöhrle J, Haussig S, Makkar R, Mehran R, Rottbauer W, Leon M. Rate of peri-procedural stroke observed with cerebral embolic protection during transcatheter aortic valve replacement: a patient-level propensity-matched analysis. *Eur Heart J* 2019;**40**:1334–1340.
  30. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;**374**:1609–1620.

# Europos bendrasis viešųjų pirkimų dokumentas (EBVPD)

## I dalis. Informacija apie pirkimo procedūrą ir perkančiąją organizaciją ar perkantįjį subjektą

### Informacija apie paskelbimą

**Skelbimo numeris OL S (tik tarptautiniams pirkimams):**

-

**Skelbimo numeris CVP IS (kur rasti?)**

479164

### Perkančiosios organizacijos / Perkančiojo subjekto tapatybė

**Oficialus pavadinimas:**

Viešoji įstaiga Klaipėdos jūrininkų ligoninė

**Šalis:**

Lietuva

### Informacija apie pirkimo procedūrą

**Procedūros tipas**

Atvira

**Pavadinimas:**

Perkateteriniu būdu implantuojamas biologinis aortos vožtuvas su įvedimo sistema

**Trumpas aprašymas:**

Perkateteriniu būdu implantuojamas biologinis aortos vožtuvas su įvedimo sistema

**Perkančiosios organizacijos ar perkančiojo subjekto (jei taikoma)**

**priskirtas dokumento numeris:**

479164

## II dalis. Informacija apie ekonominės veiklos vykdytoją

### A. Informacija apie ekonominės veiklos vykdytoją

**Tiekėjo pavadinimas arba vardas ir pavardė (jei fizinis asmuo):**

UAB "Sorimpeksas"

**Gatvė ir namo numeris:**

Šiaulių 16a.

**Pašto kodas:**

LT44353

**Miestas:**

Kaunas

**Šalis:**

Lietuva

**Interneto adresas (jei yra):**

-

**E. paštas:**

daiva@sorimpeksas.com

**Telefonas:**

+370 37 361766

**Asmuo ar asmenys ryšiams:**

Daiva Macijauskienė

**PVM mokėtojo kodas, jei yra:**

LT357332412

**Jei PVM mokėtojo kodo nėra, nurodykite kitą nacionalinį identifikacinį numerį (Lietuvoje - įmonės kodą)**

-

**Ar ekonominės veiklos vykdytojas yra labai maža, mažoji ar vidutinė įmonė?**

Taip

Ne

**Tik tuo atveju, kai pirkimas rezervuotas: ar ekonominės veiklos vykdytojas yra globojama darbo grupė (neįgaliųjų socialinė įmonė), socialinė įmonė? Ar jis vykdys sutartį pagal globojamų darbo grupių (neįgaliųjų socialinių įmonių) užimtumo programas?**

Taip

Ne

---

**Jei taikoma, ar ekonominės veiklos vykdytojas įtrauktas į oficialų patvirtintų ekonominės veiklos vykdytojų sąrašą arba ar jis turi lygiavertį sertifikatą (pvz., pagal nacionalinę (išankstinę) kvalifikacijos vertinimo sistemą)? Lietuvos tiekėjai renkasi „ne“**

Taip

Ne

- Be to, užpildykite trūkstamą informaciją IV dalies A, B, C arba D skirsniuose, atsižvelgdami į konkretų atvejį TIK jei to reikalaujama atitinkamame skelbime arba pirkimo dokumentuose:

**e) Ar ekonominės veiklos vykdytojas galės pateikti sertifikatą dėl socialinio draudimo įmokų ir mokesčių mokėjimo arba pateikti informaciją, kuri leistų perkančiajai organizacijai ar perkančiajam subjektui jį gauti tiesiogiai naudojantis prieiga prie bet kurios iš valstybių narių nemokamos nacionalinės duomenų bazės?**

Taip

Ne

**Jei atitinkami dokumentai prieinami elektroniniu būdu, nurodykite:**

[https://draudejai.sodra.lt/draudeju\\_viesi\\_duomenys/](https://draudejai.sodra.lt/draudeju_viesi_duomenys/)

---

**Ar ekonominės veiklos vykdytojas pirkimo procedūroje dalyvauja kartu su kitais? Žymima TAIP, jei pasiūlymą teikia ūkio subjektų grupė (konsorciumas) pagal jungtinės veiklos sutartį**

Taip

Ne

---

**Jei pirkimas padalintas į dalis, nuoroda į pirkimo dalį (-is), dėl kurios (-ių) ekonominės veiklos vykdytojas nori dalyvauti konkurse:**

1,2

## **B. Informacija apie ekonominės veiklos vykdytojo teisinius atstovus #1**

- Šis skirsnis pildomas, jeigu tiekėjo vadovas įgalioja kitą asmenį pasirašyti pasiūlymą, bendrauti su pirkimo vykdytoju, įgalioja atstovauti ir pasirašyti EBVPD, bendrauti su pirkimo vykdytoju dėl EBVPD pateiktos informacijos, teikiamų kvalifikaciją ir pašalinimo pagrindų nebuvimą pagrindžiančių dokumentų, dėl pasiūlymo ir pan.

Jei taikytina, nurodykite asmens (-ų), įgalioto (-ų) atstovauti ekonominės veiklos vykdytojui šios pirkimo procedūros tikslais, vardą ir pavardę ir adresą:

**Vardas**

Daiva

**Pavardė**

Macijauskienė

**Gimimo data**

-

**Gimimo vieta**

-

**Gatvė ir namo numeris:**

Šiaulių 16 a.

**Pašto kodas:**

LT44353

**Miestas:**

Kaunas

**Šalis:**

Lietuva

**E. paštas:**

-

**Telefonas:**

-

**Pareigos arba statusas:**

-

**Prireikus pateikite išsamią informaciją apie atstovavimą (formą, aprėptį, paskirtį ir t. t.):**

-

### **C. Informacija apie rėmimąsi kitų subjektų pajėgumais**

**Ar siekdamas patenkinti IV dalyje nurodytus atrankos kriterijus ir V dalyje nurodytus kriterijus bei taisykles (jei tokių yra) ekonominės veiklos vykdytojas remiasi kitų subjektų pajėgumais?**

Taip

Ne

### **D. Informacija apie subrangovus, kurių pajėgumais ekonominės veiklos vykdytojas nesiremia**

- (Skirsnį reikia pildyti, tik jei šios informacijos aiškiai reikalauja perkančioji organizacija ar perkantysis subjektas.)

**Ar ekonominės veiklos vykdytojas ketina kurias nors sutarties dalis subrangos sutartimi pavesti atlikti trečiosioms šalims?**

Taip

Ne

- Jei perkančioji organizacija ar perkantysis subjektas aiškiai prašo šios informacijos, šalia informacijos pagal šį skirsnį, pateikite pagal šios dalies A ir B skirsnius ir III dalį reikalaujamą informaciją apie kiekvieną susijusį subrangovą (subrangovų kategorijas).

### **III dalis. Pašalinimo pagrindai**

#### **A. Su baudžiamaisiais nuosprendžiais susiję pagrindai**

##### **Direktyvos 2014/24/ES 57 straipsnio 1 dalyje nustatyti šie pašalinimo pagrindai**

##### **Dalyvavimas nusikalstamos organizacijos veikloje (VPĮ 46 str. 1 d. 1 p.)**

Ar pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo nuteistas galutiniu teismo sprendimu už dalyvavimą nusikalstamos organizacijos veikloje, o nuosprendis priimtas prieš ne daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsia? Kaip apibrėžta 2008 m. spalio 24 d. Tarybos pamatinio sprendimo 2008/841/TVR dėl kovos su organizuotu nusikalstamumu 2 straipsnyje (OL L 300, 2008 11 11, p. 42).

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

##### **Korupcija (VPĮ 46 str. 1 d. 2 p.)**

Ar pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo nuteistas galutiniu teismo sprendimu už korupciją, o nuosprendis priimtas prieš ne daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsia? Kaip apibrėžta Konvencijos dėl kovos su korupcija, susijusia

su Europos Bendrijų pareigūnais ar Europos Sąjungos valstybių narių pareigūnais, 3 straipsnyje (OL C 195, 1997 6 25, p. 1) ir 2003 m. liepos 22 d. Tarybos pamatinio sprendimo 2003/568/TVR dėl kovos su korupcija privačiame sektoriuje 2 straipsnio 1 dalyje (OL L 192, 2003 7 31, p. 54). Į pašalinimo pagrindus taip pat įtraukta korupcija, kaip apibrėžta perkančiosios organizacijos (perkančiojo subjekto) arba ekonominės veiklos vykdytojo nacionalinėje teisėje.

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

**Sukčiavimas (VPĮ 46 str. 1 d. 3 p.)**

Ar pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo nuteistas galutiniu teismo sprendimu už sukčiavimą, o nuosprendis priimtas prieš ne daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsia? Pagal Europos Bendrijų finansinių interesų apsaugos konvencijos 1 straipsnį (OL C 316, 1995 11 27, p. 48).

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

**Teroristiniai nusikaltimai arba su teroristine veikla susiję nusikaltimai (VPĮ 46 str. 1 d. 5 p.)**

Ar pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo nuteistas galutiniu teismo sprendimu už teroristinius nusikaltimus arba su teroristine veikla susijusius nusikaltimus, o nuosprendis priimtas prieš ne

daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsia? Kaip apibrėžta 2002 m. birželio 13 d. Tarybos pamatinio sprendimo dėl kovos su terorizmu 1 ir 3 straipsniuose (OL L 164, 2002 6 22, p. 3). Į pašalinimo pagrindus taip pat įtrauktas nusikalstamos veikos kurstymas, pagalba ar bendrininkavimas ją vykdant arba kėsintis ją įvykdyti, kaip nurodyta to pamatinio sprendimo 4 straipsnyje.

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

**Pinigų plovimas arba teroristų finansavimas (VPĮ 46 str. 1 d. 6 p.)**

Ar pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo nuteistas galutiniu teismo sprendimu už pinigų plovimą arba teroristų finansavimą, o nuosprendis priimtas prieš ne daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsia? Kaip apibrėžta 2005 m. spalio 26 d. Europos Parlamento ir Tarybos direktyvos 2005/60/EB dėl finansų sistemos apsaugos nuo jos panaudojimo pinigų plovimui ir teroristų finansavimui 1 straipsnyje (OL L 309, 2005 11 25, p. 15).

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

**Vaikų darbas ir kitos prekybos žmonėmis formos (VPĮ 46 str. 1 d. 7 p.)**

Ar pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo nuteistas galutiniu teismo sprendimu už vaikų darbą arba kitas prekybos

žmonėmis formos, o nuosprendis priimtas prieš ne daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsia? Kaip apibrėžta 2011 m. balandžio 5 d. Europos Parlamento ir Tarybos direktyvos 2011/36/ES dėl prekybos žmonėmis prevencijos, kovos su ja ir aukų apsaugos, pakeičiančios Tarybos pamatinį sprendimą 2002/629/TVR, 2 straipsnyje (OL L 101, 2011 4 15, p. 1).

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

## **B. Su mokesčių ar socialinio draudimo įmokų mokėjimu susiję pagrindai** **Direktyvos 2014/24/ES 57 straipsnio 2 dalyje nustatytos šios pašalinimo priemonės**

### **Mokesčių mokėjimas VPĮ 46 str. 3 d.**

Ar ekonominės veiklos vykdytojas pažeidė savo pareigas, susijusias su mokesčių mokėjimu, tiek šalyje, kurioje yra įsisteigęs, tiek perkančiosios organizacijos ar perkančiojo subjekto valstybėje narėje, jei tai nėra jo įsisteigimo šalis?

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

### **Socialinio draudimo įmokų mokėjimas VPĮ 46 str. 3 d.**

Ar ekonominės veiklos vykdytojas pažeidė savo pareigas, susijusias su socialinio draudimo įmokų mokėjimu, tiek šalyje, kurioje yra įsisteigęs, tiek perkančiosios organizacijos ar perkančiojo subjekto valstybėje narėje, jei tai nėra jo įsisteigimo šalis?

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

**URL**

[https://draudejai.sodra.lt/draudeju\\_viesi\\_duomenys/](https://draudejai.sodra.lt/draudeju_viesi_duomenys/)

**Kodas**

-

**Emitentas**

Valstybinio socialinio draudimo fondo valdyba prie Socialinės apsaugos ir darbo ministerijos

### **C. Su nemokumu, interesų konfliktu ar profesiniais nusižengimais susiję pagrindai**

**Direktyvos 2014/24/ES 57 straipsnio 4 dalyje nustatyti šie pašalinimo pagrindai**

**Su kitais ekonominės veiklos vykdytojais sudaryti susitarimai, kuriais siekta iškraipyti konkurenciją (VPĮ 46 str. 4 d. 1 p.)**

Ar ekonominės veiklos vykdytojas su kitais ekonominės veiklos vykdytojais yra sudaręs susitarimų, kuriais siekta iškraipyti konkurenciją?

Jūsų atsakymas

Taip

Ne

**Pripažinimas kaltu dėl sunkaus profesinio nusižengimo VPĮ 46 str. 4 d. 7 p., VPĮ 46 str. 6 d. 3 p.**

Ar ekonominės veiklos vykdytojas yra pripažintas kaltu dėl sunkaus profesinio nusižengimo kaip nurodyta žemiau?

**I. ar ekonominės veiklos vykdytojas yra padaręs profesinį pažeidimą, kai už finansinės atskaitomybės ir audito teisės aktų pažeidimus ekonominės veiklos vykdytojui ar jo vadovui paskirta administracinė nuobauda ar ekonominė sankcija, nustatytos Lietuvos Respublikos įstatymuose ar kitų valstybių teisės aktuose, ir nuo sprendimo, kuriuo buvo paskirta ši sankcija, įsiteisėjimo dienos arba nuo dienos, kai asmuo įvykdė administracinį nurodymą, praėjo mažiau kaip vieni metai?**

**II. Ar ekonominės veiklos vykdytojas yra padaręs kurį nors vieną iš žemiau nurodytų rimtų profesinių pažeidimų**(taikoma tik tada kai, ir tik tiek, kiek apibrėžta kituose pirkimo dokumentuose):

a) profesinės etikos pažeidimas, kai nuo ekonominės veiklos vykdytojo pripažinimo nesilaikančiu profesinės etikos normų momento praėjo mažiau kaip vieni metai;

b) konkurencijos, darbuotojų saugos ir sveikatos, informacijos apsaugos, intelektinės nuosavybės apsaugos pažeidimas, už kurį ekonominės veiklos vykdytojui ar jo vadovui yra paskirta administracinė nuobauda ar ekonominė sankcija, nustatytos Lietuvos Respublikos ar kitų valstybių įstatymuose, kai nuo sprendimo, kuriuo buvo paskirta ši sankcija, arba nuo dienos, kai asmuo įvykdė administracinį nurodymą, įsiteisėjimo dienos praėjo mažiau kaip vieni metai;

c) draudimo sudaryti draudžiamus susitarimus, įtvirtinto Lietuvos Respublikos konkurencijos įstatyme ar panašaus pobūdžio kitos valstybės teisės akte, pažeidimas, kai nuo sprendimo paskirti Konkurencijos įstatyme ar kitos valstybės teisės akte nustatytą ekonominę sankciją įsiteisėjimo dienos praėjo mažiau kaip 3 metai;

d) ekonominės veiklos vykdytojas, kuris yra fizinis asmuo, arba ekonominės veiklos vykdytojo, kuris yra juridinis asmuo, kita organizacija ar jos padalinys, vadovas, kitas valdymo ar priežiūros organo narys ar kitas asmuo, turintis (turintys) teisę atstovauti ekonominės veiklos vykdytojui ar jį kontroliuoti, jo vardu priimti sprendimą, sudaryti sandorį, arba dalyvis, turintis balsų daugumą juridinio asmens dalyvių susirinkime, yra pripažintas kaltu dėl tyčinio bankroto, kaip jis apibrėžtas Lietuvos Respublikos įmonių bankroto įstatyme ar panašaus pobūdžio kitų valstybių teisės aktuose, kai nuo teismo sprendimo įsiteisėjimo dienos praėjo mažiau kaip 3 metai?

Jūsų atsakymas

Taip

Ne

**Interesų konfliktas dėl dalyvavimo pirkimo procedūroje (VPĮ 46 str. 4 d. 2 p.)**

Ar ekonominės veiklos vykdytojas žino apie kokius nors [interesų konfliktus](#), kaip nurodyta nacionalinėje teisėje, atitinkamame skelbime ar pirkimo dokumentuose, kylančius dėl jo dalyvavimo pirkimo procedūroje?

Jūsų atsakymas

Taip

Ne

**Tiesioginis arba netiesioginis dalyvavimas rengiant šią pirkimo procedūrą (46 str. 4 d. 3 p.)**

Ar ekonominės veiklos vykdytojas arba su juo susijusi įmonė konsultavo perkančiąją organizaciją ar perkantįjį subjektą arba kitaip dalyvavo rengiant pirkimo procedūrą?

Jūsų atsakymas

Taip

Ne

**Sutarties nutraukimas anksčiau laiko, žala ar kitos panašios sankcijos (VPĮ 46 str. 4 d. 6 p.)**

Ar ekonominės veiklos vykdytojas turėjo tokios patirties: ankstesnė viešoji sutartis, ankstesnė sutartis su perkančiuoju subjektu arba ankstesnė koncesijos sutartis buvo nutraukta anksčiau laiko; arba buvo pareikalauta atlyginti su ankstesne sutartimi susijusią žalą ar skirtos kitos panašios sankcijos?

**Lietuvoje (be kita ko) - ar ekonominės veiklos vykdytojas yra įtrauktas į nepatikimų tiekėjų sąrašą ?**

Jūsų atsakymas

Taip

Ne

**Pripažinimas kaltu dėl faktų iškreipimo, informacijos nuslėpimo, negalėjimas pateikti reikalaujamų dokumentų ir su šia procedūra susijusios konfidencialios informacijos gavimas (46 str. 4 d. 4 p. ir 46 str. 4 d. 5 p.)**

Ar ekonominės veiklos vykdytojas yra susijęs su vienu iš šių atvejų, kai jis :

a) buvo labai iškreipęs faktus pateikdamas informaciją (**pateikęs melagingą informaciją**), reikalingą patikrinti, ar nėra pagrindų pašalinti, arba patikrinti atitiktį atrankos kriterijams;

b) slėpė tokią informaciją;

c) delsė pateikti patvirtinamuosius dokumentus, kurių reikalavo perkančioji organizacija ar perkantysis subjektas,

d) siekė daryti neteisėtą įtaką perkančiosios organizacijos ar perkančiojo subjekto sprendimų priėmimo procesui, kad gautų konfidencialios informacijos, dėl kurios per pirkimo procedūrą įgytų nepagrįstą pranašumą, arba tyčia teikti klaidinančios informacijos, kuri gali turėti esminės įtakos sprendimams dėl pašalinimo, atrankos ar sutarties skyrimo?

Jūsų atsakymas

Taip

Ne

#### D. Išimtinai nacionaliniai pašalinimo pagrindai

**Išimtinai nacionaliniai pašalinimo pagrindai, nurodyti atitinkamame skelbime ar pirkimo dokumentuose.**

**Išimtinai nacionaliniai pašalinimo pagrindai (VPĮ 46 str. 1 d. 4 p., 46 str. 4 d. 8 p.)**

Ar ekonominės veiklos vykdytojas yra susijęs su vienu iš šių atvejų, kai:

a) jis **neatitinka minimalių patikimo mokesčių mokėtojo kriterijų**, nustatytų Lietuvos Respublikos mokesčių administravimo įstatymo 40<sup>1</sup> straipsnio 1 dalyje ir dėl to laikomas padariusiu šiurkštų profesinį pažeidimą.

b) pats ekonominės veiklos vykdytojas ar bet kuris asmuo, kuris yra jo administracijos, valdymo ar priežiūros organo narys arba turi atstovavimo, sprendimo ar kontrolės įgaliojimus to ekonominės veiklos vykdytojo atžvilgiu, buvo **nuteistas galutiniu teismo sprendimu už nusikalstamą bankrotą**, o nuosprendis priimtas prieš ne daugiau kaip penkerius metus arba kai nuosprendyje aiškiai nustatytas pašalinimo laikotarpis tebesitęsias?

Jūsų atsakymas

Taip

Ne

---

Ar ši informacija ES valstybės narės duomenų bazėje nemokamai prieinama valdžios institucijoms?

Taip

Ne

**URL**

[http://www.vmi.lt/cms/informacija-apie-mokesciu-moketojus?fbclid=IwAR3\\_ZWzap0oP9j3fDM1JhXkS8LhLW\\_7I6KyA\\_h6gHzdEwsl7UbsG7ySKyPk](http://www.vmi.lt/cms/informacija-apie-mokesciu-moketojus?fbclid=IwAR3_ZWzap0oP9j3fDM1JhXkS8LhLW_7I6KyA_h6gHzdEwsl7UbsG7ySKyPk)

**Kodas**

-

**Emitentas**

Valstybinė mokesčių inspekcija

#### IV dalis. Atrankos kriterijai

##### α. Visų atrankos kriterijų bendra nuoroda

**Dėl atrankos kriterijų ekonominės veiklos vykdytojas pareiškia, kad**

## Jis atitinka visus reikalaujamus atrankos kriterijus

Jūsų atsakymas

Taip

Ne

## Baigti

### IV dalis. Baigiamieji pareiškimai

Ekonominės veiklos vykdytojai oficialiai pareiškia, kad II–V dalyse pateikta informacija yra tiksli ir teisinga ir kad ji pateikta visiškai suvokiant didelio faktų iškreipimo padarinius.

Ekonominės veiklos vykdytojai oficialiai pareiškia, kad pareikalavus gali nedelsdami pateikti nurodytus sertifikatus ir kitų formų įrodomuosius dokumentus, išskyrus tuos atvejus, kai:

- a) perkančioji organizacija ar perkantysis subjektas turi galimybę atitinkamus patvirtinamuosius dokumentus tiesiogiai gauti naudodamiesi prieiga prie bet kurios iš valstybių narių nemokamos nacionalinės duomenų bazės (su sąlyga, kad ekonominės veiklos vykdytojas pateikė reikalingą informaciją (interneto adresą, išduodančiąją instituciją ar įstaigą, tikslias dokumentų nuorodas), kuri perkančiajai organizacijai ar perkančiajam subjektui leidžia tai padaryti (pareikalavus dėl tokios prieigos turi būti pridėtas atitinkamas sutikimas), arba
- b) perkančioji organizacija ar perkantysis subjektas yra gavusi ir turi aktualius susijusius dokumentus iš ankstesnių (kitų) pirkimo procedūrų.

Ekonominės veiklos vykdytojai oficialiai sutinka perkančiajai organizacijai ar perkančiajam subjektui, nurodytam I dalyje, leisti susipažinti su dokumentais, kuriais patvirtinama informacija, pateikta šio Europos bendrojo viešųjų pirkimų dokumento III ir IV dalyse, kiek tai susiję su pirkimu, nurodytu I dalyje.

Data, vieta ir, jei reikia ar būtina, parašas (-ai):

#### **Data**

14-04-2020

#### **Vieta**

Kaunas

#### **Parašas**