Medtronic

The evidence points to Evolut™ TAVR

People who know,
think **Evolut™ First.**

01 Designed to be durable

02 Not all durability data is equal

03 Performance that matters

04 Supporting data

Designed to be durable.

Durability impacts mortality.

Valve design impacts durability.

Durability starts with design

Built on a proven foundation

With its supra-annular, self-expanding valve frame, Evolut™ TAVR is built on the original CoreValve™ platform which has consistently shown strong EOAs and low gradients over time.

How did we design for durability?

More surface

Taller leaflet mounting allows for a greater distance between the commissure and the edge of the leaflet, distributing stress over a greater distance.

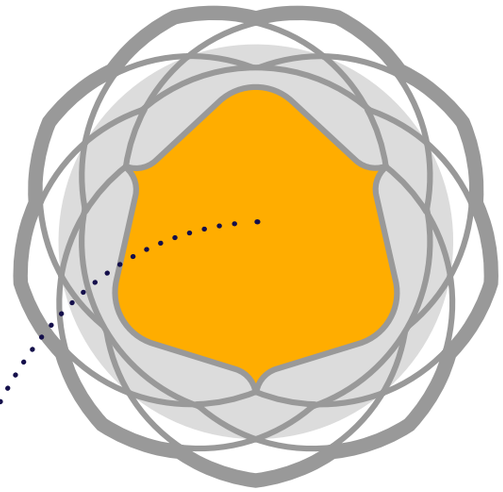
More height

By decoupling the native annular plane where the sealing occurs, from the working portion of the prosthetic leaflets, you can facilitate circularity and maximize leaflet coaptation.

More room

The tall valve keeps the working portion above and unconstrained by the native annulus, allowing for a large effective orifice area.

Supra-annular design benefits



Large EOAs mean less restriction of blood through the valve.

Less restriction leads to low gradients (mean systolic gradient).

Large EOAs have been correlated to less patient-prosthesis mismatch (PPM).

Less PPM and low gradients after aortic valve replacement have been linked to:

- Better survival[1,2]
- Less heart failure rehospitalization[2,3]
- Better valve durability[4]

CoreValve™/Evolut™ TAVR platform
Intermediate risk[5]
Average EOA at 5 years (cm^2)

Devices used:
83.8% CoreValve
16.2% Evolut™ R

2.2

Consistently strong EOAs

CoreValve/Evolut TAVR platform
Low risk[6]
Average EOA at 4 years (cm^2)

Devices used:
3.6% CoreValve
73% Evolut R
23.4% Evolut™ PRO

2.1

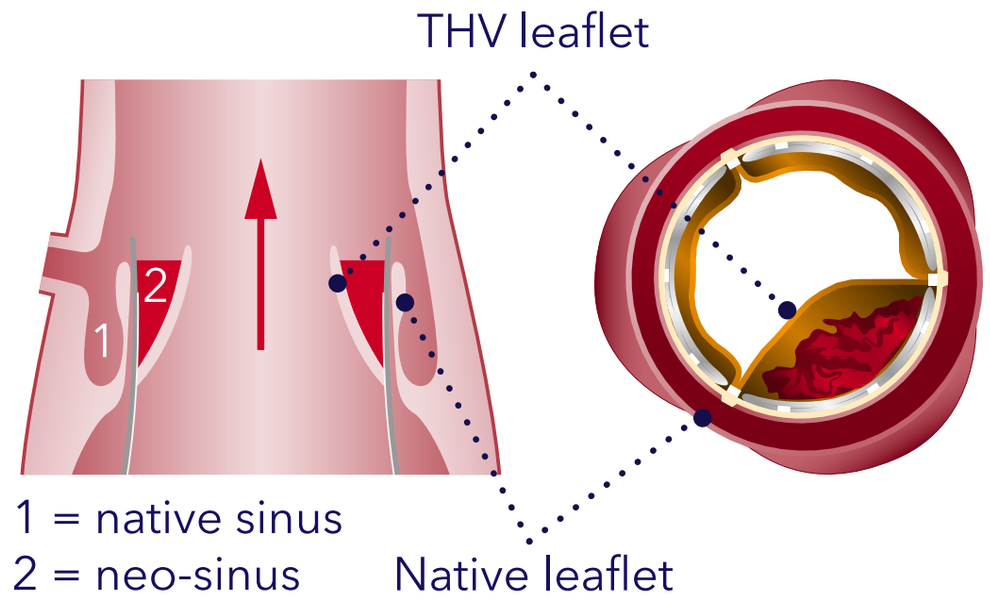
[1] Playford D, et al. *J Am Soc Echocardiogr*. 2020;33:1077–1086.e1.
[2] Herrmann HC, et al. *J Am Coll Cardiol*. 2018;72:2701–2711.
[3] Anand V, et al. *Am J Cardiol*. 2020;125:941–947.
[4] Flameng W, et al. *Circulation*. 2010;121:2123–2129.
[5] Van Mieghem, et al. 5-Year Clinical and Echocardiographic Outcomes from the Randomized SURTAVI Trial. Presented at TCT 2021.
[6] Reardon M, et al. Transcatheter Versus Surgical Aortic Valve Replacement in Aortic Stenosis Patients at Low Surgical Risk: 4-Year Outcomes from the Evolut Low Risk Trial. Presented at TCT; October 2023.

Supra-annular design benefits

Intra-annularity is a risk factor for thrombosis formation.[1,2] The Evolut™ TAVR system employs a supra-annular design.

The Evolut TAVR supra-annular design decreases the size and impact of a neo-sinus – allowing adequate washing behind the native leaflets.[1]

Design elements that produce blood flow stasis and extended blood residence time on the leaflets could increase risk of thrombosis, resulting in sub-optimal clinical results.[1]

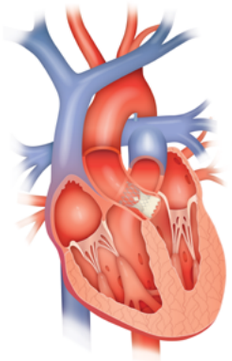


The intra-annular design creates a larger neo-sinus, a region between the native and transcatheter aortic valve leaflets where thrombus generally forms.

The larger neo-sinus is more prone to developing thrombus due to reduced blood velocity and impaired washout.

[1] Midha PA, et al. *Circulation*. 2017;136:1598-1609.
[2] Bogyi M, et al. *JACC Cardiovasc Interv*. 2021;14:2643-2656.

Subclinical leaflet thrombosis after TAVR: Risk factors, effect on outcome, and treatment options[1]



TAVR
(11,098 patients from 25 studies)

Potentially associated with

Presence of SLT†
(6% overall occurrence)

If untreated, associated with

Increased stroke risk
(RR 2.56)

OAC therapy

99% increase in odds for SLT resolution

Main risk factors:
- Intra-annular TAVR (RR 2.03 compared to supra-annular TAVR)
- SAPT/DAPT only (RR 0.42 with OAC)

RR: Relative risk
SAPT: Single antiplatelet therapy
DAPT: Dual antiplatelet therapy
OAC: Oral anticoagulation
SLT: Subclinical leaflet thrombosis

†At 30 days.
[1] Bogyi M, et al. *JACC Cardiovasc Interv.* 2021;14:2643-2656.

Not all durability data is equal.

Explore why the evidence points to Evolut™ TAVR.

Only CoreValve™ TAVR has shown a durability benefit over SAVR in multicentered, randomized clinical trials out to 5[1] and 10 years.[2]

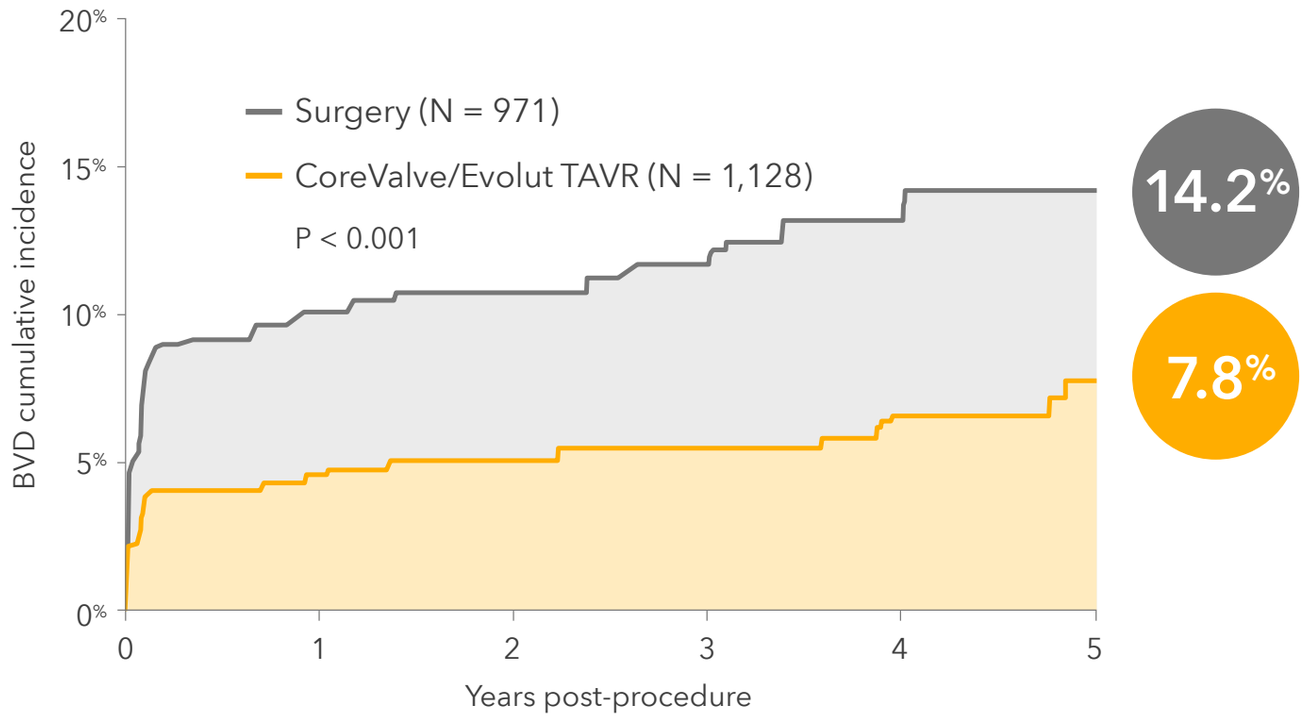
[1] O'Hair D, et al. *JAMA Cardiol*. 2023;8:111–119.
[2] Jørgensen T. Ten-year follow-up after transcatheter or surgical aortic valve implantation in severe aortic valve stenosis. Presented at ESC Congress; August 2023.

CoreValve™/Evolut™ TAVR is the first and only platform to demonstrate a durability and valve performance benefit over SAVR at five years in randomized clinical trials.[†1]

Devices used:
88% CoreValve
12% Evolut™ R

Bioprosthetic valve dysfunction[‡] out to 5 years[1]

Significantly better valve performance[‡] versus SAVR at 5 years



[†]In pooled analysis of intermediate- and high-risk patients.

[‡]Bioprosthetic Valve Dysfunction (BVD) was defined as[2,3]: SVD[4] (mean gradient ≥ 10 mm Hg increase from discharge/30 days AND ≥ 20 mm Hg at last echo or new onset/increase of ≥ moderate intraprosthetic aortic regurgitation), NSVD (30-day severe PPM at 30-day/discharge[2] or severe PVR through 5 years), clinical valve thrombosis, and endocarditis.

[1] Yakubov S, et al. Five-Year Incidence of Bioprosthetic Valve Dysfunction in Patients Randomized to Surgery or TAVR: Insights From the CoreValve US Pivotal and SURTAVI Trials. Presented at CRT; February 2023.

[2] Adapted from VARC-3 Writing Committee, et al. *Eur Heart J*. 2021;42:1825-1857.

[3] Capodanno D, et al. *Eur Heart J*. 2017;38:3382-3390.

[4] Adapted from VARC-3 Writing Committee, et al. and Capodanno D, et al.

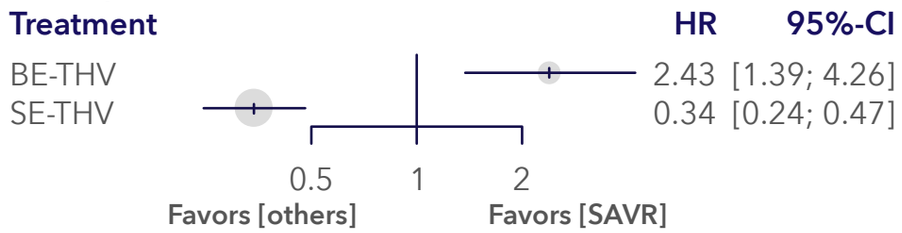
Valve durability for supra-annular, self-expandable TAV found to be statistically better at five years versus both SAVR and balloon-expandable TAV.[1]

5-year meta analysis[1]

Structural valve deterioration†

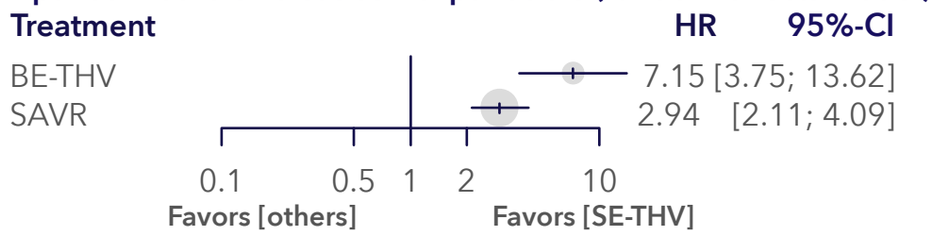
Only SE performs better than SAVR

Comparison: others versus SAVR (random effects model)



SE performs better than SAVR and BE

Comparison: others versus self-expandable (random effects model)



At five years, supra-annular, self-expandable (SE) valves demonstrated:

- Lowest risk of structural valve deterioration (SVD) compared with balloon-expandable (BE) valves and SAVR.
- Significantly stronger hemodynamics with larger EOAs and lower mean gradients versus BE valves.

Study design

- Meta-analysis
- 10 randomized controlled trials
- 9,388 patients
- Follow-up 1 to 6 years
- Multiple devices‡

†Based on the longest available follow-up for each of the 10 studies used for this meta-analysis. SVD was defined by the respective authors of each paper.

‡CoreValve™, Evolut™ R, Evolut™ PRO, Sapien™*, Sapien 3, Sapien XT, and ACURATE neo™*.

[1] Ueyama H, et al. *Am J Cardiol*. 2021;158:104-111.

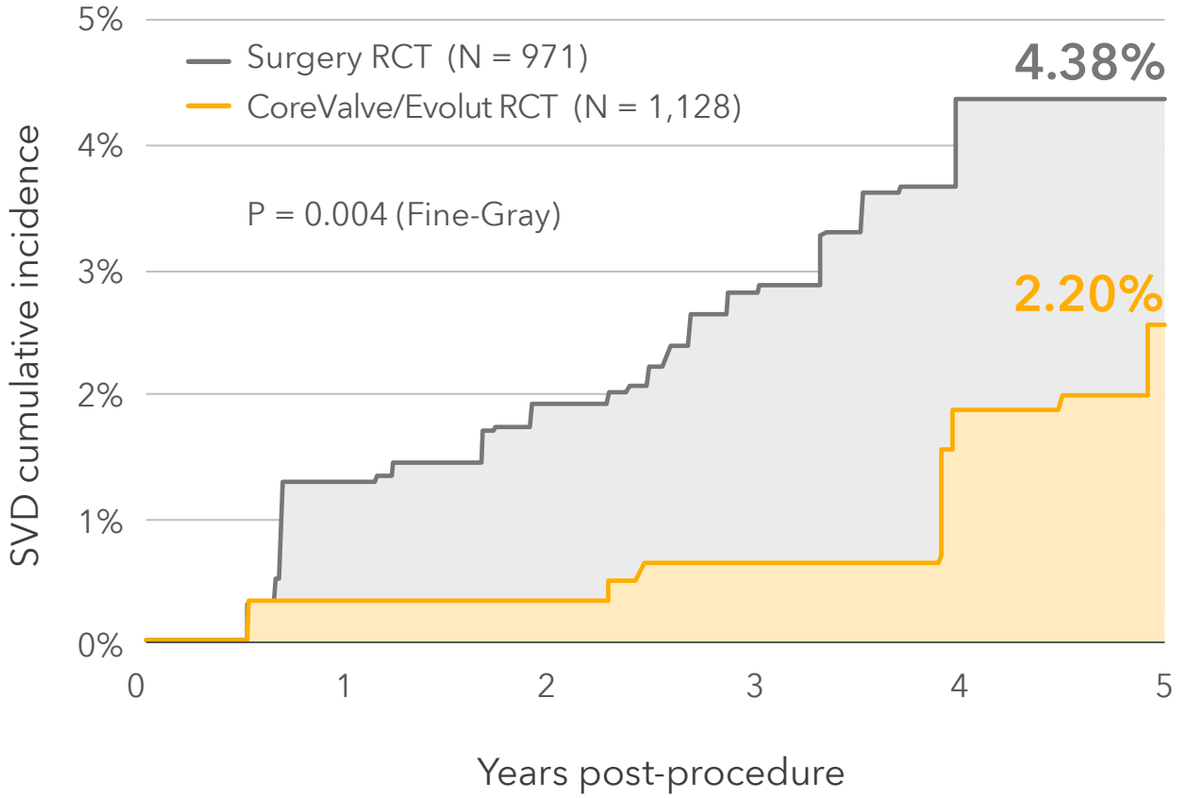
CoreValve™/Evolut™ is the first and only TAVR platform to demonstrate a significantly lower SVD than SAVR.

SVD definition

Devices used:
88.5% CoreValve
11.5% Evolut™ R

CoreValve/Evolut platform pooled analysis:

5-year SVD adjusted for competing risk of mortality[1]



[1] O'Hair D, et al. *JAMA Cardiol*. 2023;8:111–119.

Patients with SVD had a near **two-fold increased risk** for all-cause mortality and aortic valve re-hospitalization or worsening heart failure at five years.

SVD definition

RCT and Non-RCT cohorts:
97% CoreValve
3% Evolut R

CoreValve™ and Evolut™ platforms pooled analysis:

Worsened clinical outcomes in patients who develop SVD[1]

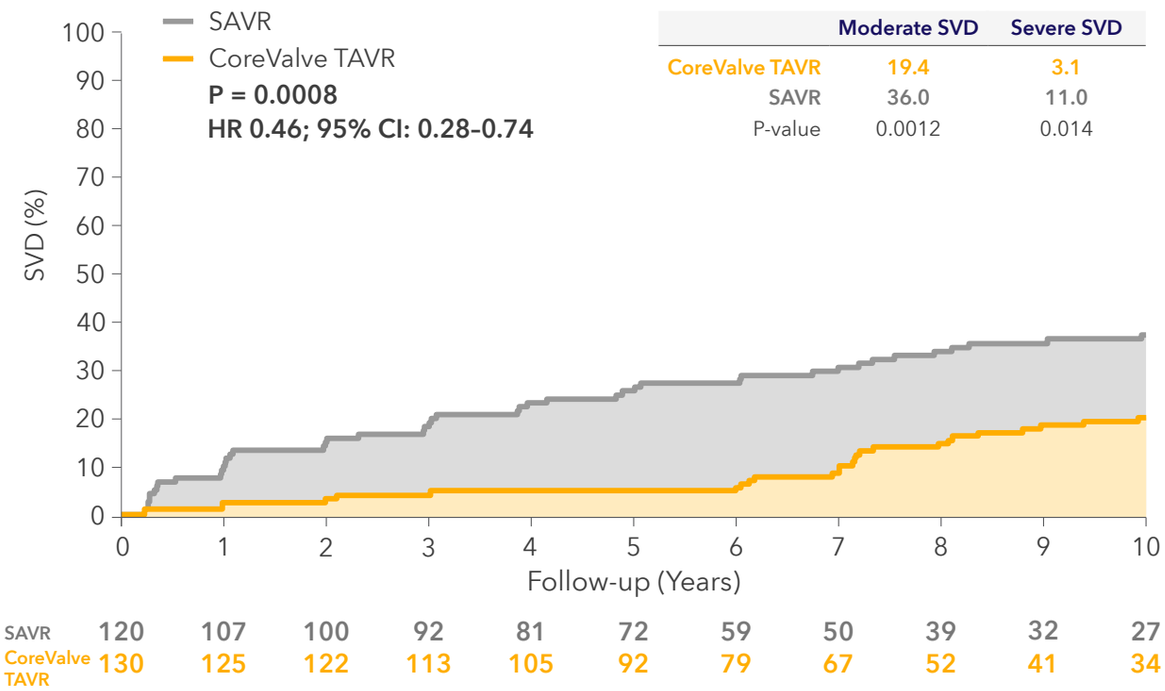
	HR (95% CI)	P value
Pooled surgery RCT and all CoreValve/Evolut (N = 4,762)		
All-cause mortality	2.03 (1.46, 2.82)	< 0.001
Cardiovascular mortality	1.86 (1.20, 2.90)	0.006
Aortic valve-related hospitalization	2.17 (1.23, 3.84)	0.008
Composite†	2.02 (1.42, 2.88)	< 0.001
Surgery RCT (N = 971)		
All-cause mortality	2.45 (1.40, 4.30)	0.002
Cardiovascular mortality	2.37 (1.10, 5.08)	0.003
Aortic valve-related hospitalization	2.20 (0.81, 5.98)	0.120
Composite†	2.73 (1.53, 4.88)	< 0.001
All CoreValve/Evolut TAVR (N = 3,791)		
All-cause mortality	2.34 (1.55, 3.53)	< 0.001
Cardiovascular mortality	2.17 (1.26, 3.76)	0.006
Aortic valve-related hospitalization	2.45 (1.22, 4.93)	0.010
Composite†	2.03 (1.29, 3.19)	0.002

†All-cause mortality or aortic valve-related hospitalization.

[1] O'Hair D, et al. *JAMA Cardiol*. 2023;8:111–119.

NOTION[1] 10 years

SVD out to 10 years[1]



	Moderate SVD	Severe SVD
CoreValve TAVR	19.4	3.1
SAVR	36.0	11.0
P-value	0.0012	0.014

37.7%

20.2%

The NOTION trial was a multicenter, randomized, head-to-head comparison of CoreValve TAVR versus SAVR followed out to 10 years in lower surgical risk patients ≥ 70 years of age who were eligible for surgery. TAVR had statistically lower rates of moderate or greater SVD out to 10 years versus surgery.‡

The NOTION 10-year data demonstrates excellent SVD rates in a lower surgical risk patient population. Perhaps most importantly, the data provides a signal of durability for the CoreValve platform versus SAVR.

The CoreValve™ platform demonstrates statistically better durability versus surgery at 10 years.†1

SVD definition

Device used:
100% CoreValve

†In patients at lower surgical risk over the age of 70.
‡Structural valve deterioration[2] was defined as moderate or severe hemodynamic SVD (Mean gradient ≥ 20 mm Hg or Mean gradient ≥ 10 mm Hg change from index discharge or moderate/severe intra-prosthetic aortic regurgitation [AR] – new or worsening from discharge).

[1] Jørgensen T. Ten-year follow-up after transcatheter or surgical aortic valve implantation in severe aortic valve stenosis. Presented at ESC Congress; August 2023.
[2] Capodanno D, et al. *Eur Heart J*. 2017;383:3382–3390.

Performance that matters.

1

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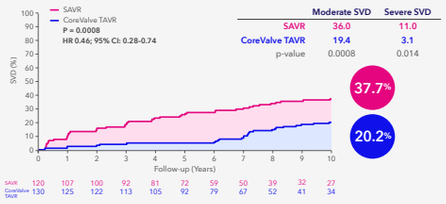
A decade of durability.

CoreValve™ TAVR platform demonstrates statistically better durability versus surgery at 10 years.†1

Statistically lower rates of moderate or greater structural valve deterioration (SVD) out to 10-years versus surgery.‡

SVD out to 10 years



	Moderate SVD	Severe SVD
SAVR	36.0	11.0
CoreValve TAVR	19.4	3.1
p-value	0.0008	0.014

37.7%

20.2%

Statistically lower bioprosthetic valve dysfunction (BVD) vs. SAVR at 10-years.‡

81.2% SAVR (N = 123)

67.8% CoreValve TAVR (N = 134)

P = 0.007

TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

†In patients at lower surgical risk over the age of 70. Devices used: CoreValve 100%.
‡Bioprosthetic Valve Dysfunction (BVD)† was defined as: moderate or severe hemodynamic SVD (Mean gradient ≥ 20 mm Hg or Mean gradient ≥ 10 mm Hg change from index discharge or moderate/severe intra-prosthetic aortic regurgitation (AR) (new or worsening from discharge), NSVD (moderate to severe patient-prosthesis mismatch or more than mild paravalvular leak), clinical valve thrombosis, and endocarditis.

Established failure rates

NOTION suggests the CoreValve™ platform fails at half the rate of surgery in low-risk patients.

2

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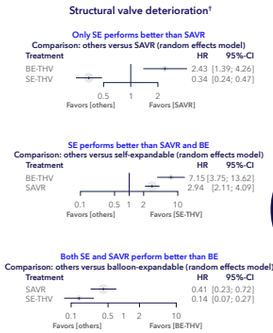
EVIDENCE UPDATE

Valve durability

Valve durability for supra-annular, self-expandable TAV found to be statistically better at five years versus both SAVR and balloon-expandable TAV

Structural valve deterioration†



SVD was less frequent in SE-THV compared with BE-THV and SAVR (HR 0.14, 95% CI 0.07 to 0.27; HR 0.34, 95% CI 0.24 to 0.47, respectively).

Study design

- Meta-analysis
- 10 randomized controlled trials
- 9,388 patients
- Follow-up 1 to 6 years
- Multiple devices‡

Key observations from the five-year meta-analysis:

At five years, supra-annular, self-expandable (SE) valves demonstrated:

- Lowest risk of structural valve deterioration (SVD) compared with balloon-expandable (BE) valves and SAVR.
- Significantly stronger hemodynamics with larger EOAs and lower mean gradients versus BE valves.

Authors noted that additional studies including newer generations of valves are warranted to address known THV-specific risks, such as AR and reintervention.

‡Based on the longest available follow-up for each of the 10 studies used for this meta-analysis. SVD was defined by the respective authors of each paper. "CoreValve™, Evolut™ R, Evolut™ PRO, Sapien™ 3, Sapien XT, and ACURATE neo™."

Established difference among platforms at five years

Drs. Ueyama and Attizzani established that self-expandable valves demonstrated the lowest risk of SVD compared to balloon-expandable valves and SAVR.

3

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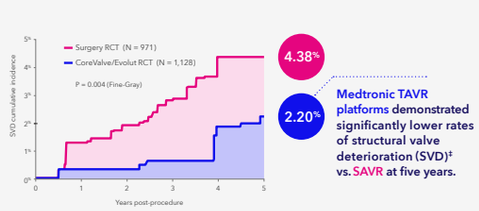
The best TAVR vs. SAVR durability data yet.

CoreValve™/Evolut™ is the first and only platform to demonstrate a durability benefit over SAVR at five years.†1



4.38%

2.20%

Medtronic TAVR platforms demonstrated significantly lower rates of structural valve deterioration (SVD)‡ vs. SAVR at five years.

TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

†In pooled analysis of intermediate and high-risk patients. Devices used: CoreValve 88%/Evolut R 12%.
‡Structural valve deterioration (SVD) was defined as an increase in mean gradient ≥ 10 mm Hg over five years with a mean gradient ≥ 20 mm Hg at last echo OR new onset/increase of central AR of ≥ moderate in severity.

Consequence of failure

O'Hair's pooled analysis shows the same statistical trend in durability of SEV over SAVR, as well as the consequence of developing SVD.

4

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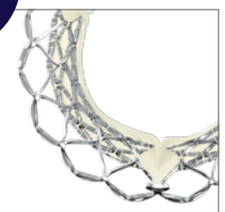
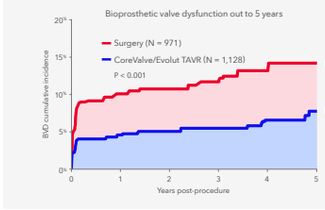
The best durability.



CoreValve™/Evolut™ TAVR is the first and only platform to demonstrate a durability benefit over SAVR at 5 years in randomized clinical trials.†1



14.2%

7.8%

Significantly better valve performance‡ versus SAVR at 5 years.

3x lower severe PPM versus SAVR at 30-day/discharge.

3.7% CoreValve/Evolut TAVR

11.8% SAVR

p < 0.001

TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

†In pooled analysis of intermediate- and high-risk patients. Devices used: CoreValve 88%/Evolut R 12%.
‡Bioprosthetic Valve Dysfunction (BVD) was defined as†1: SVD* (mean gradient ≥ 10 mm Hg increase from discharge/30 days AND ≥ 20 mm Hg at last echo or new onset/increase of ≥ moderate intraprosthetic aortic regurgitation), NSVD (30-day severe PPM at 30-day/discharge‡ or severe PVR through 5 years), clinical valve thrombosis, and endocarditis.

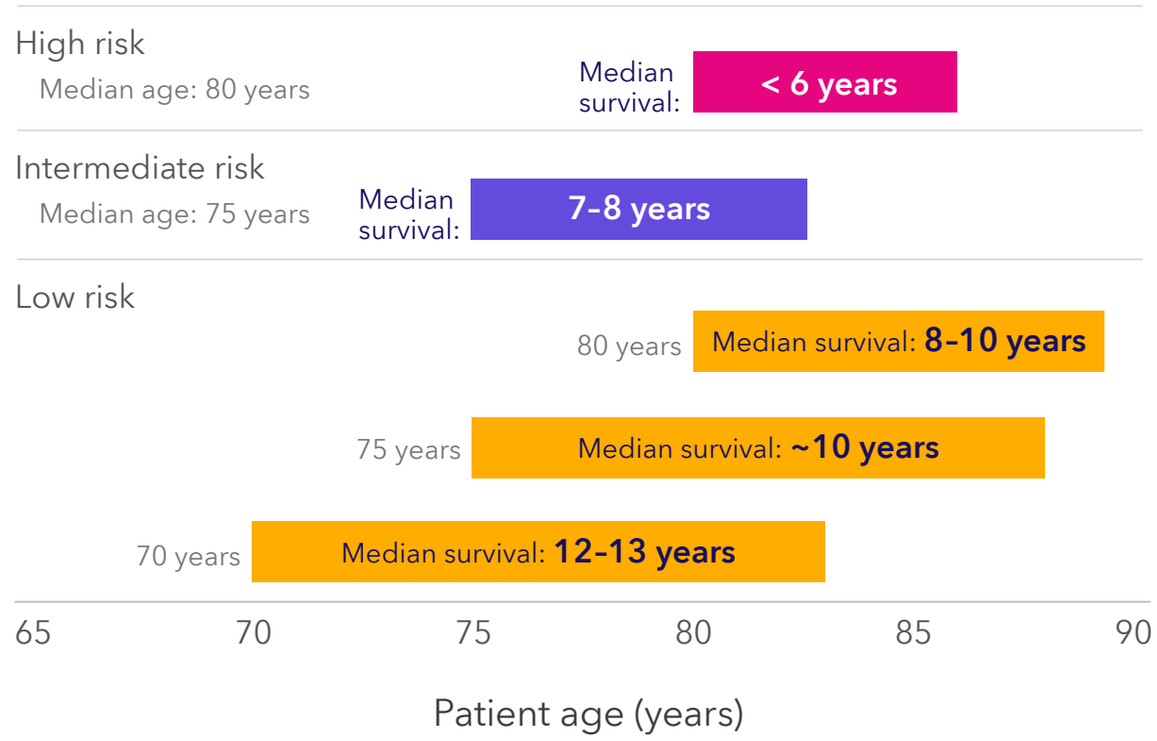
Established valve performance

The CoreValve/Evolut™ supra-annular, self-expanding bioprosthesis is the only TAVR platform to demonstrate significantly better valve performance, as assessed by BVD, compared with surgery in randomized clinical trials.

Longevity after surgical aortic valve replacement.

Stratification by age and surgical risk groups

Lifetime management of patients undergoing AVR[1]

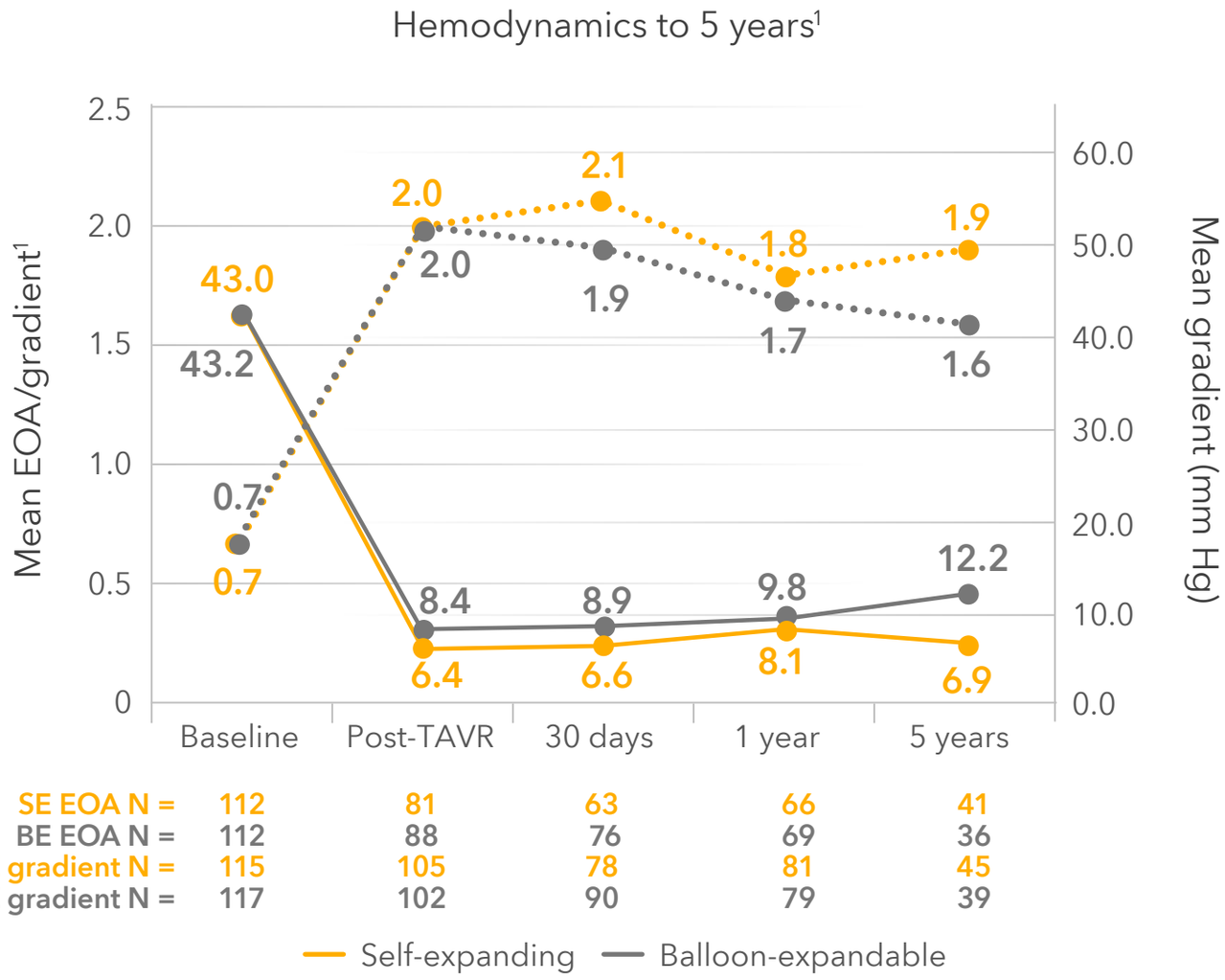


[1] Martinsson A, et al. *J Am Coll Cardiol*. 2021;78:2147-2157.

Supporting data

CoreValve™ TAV remained hemodynamically stable at five years.

CHOICE[1] 5 years



For EOAs:
Baseline: p = 0.71
Post-TAVR: p = 0.86
30 days: p = 0.13
1 year: p = 0.34
5 years: p = 0.02

For gradients:
Baseline: p = 0.90
Post-TAVR: p < 0.001
30 days: p < 0.001
1 year: p = 0.007
5 years: p = 0.001

In this prospective, randomized study, CoreValve TAV remained hemodynamically stable at 5 years whereas the SAPIEN™* TAV had a 20% decline in EOA and a 40% increase in gradient.

CoreValve also had a statistically significant advantage in terms of freedom from SVD over SAPIEN (0.0% vs. 6.6%; p = 0.018).

SVD definition

Device used:
100% CoreValve

[1] Abdel-Wahab M, et al. Five-year outcomes after TAVI with balloon-expandable vs. self-expanding valves: Results from the CHOICE randomised clinical trial. Presented at EuroPCR 2019. Paris, France.

Freedom from SVD:

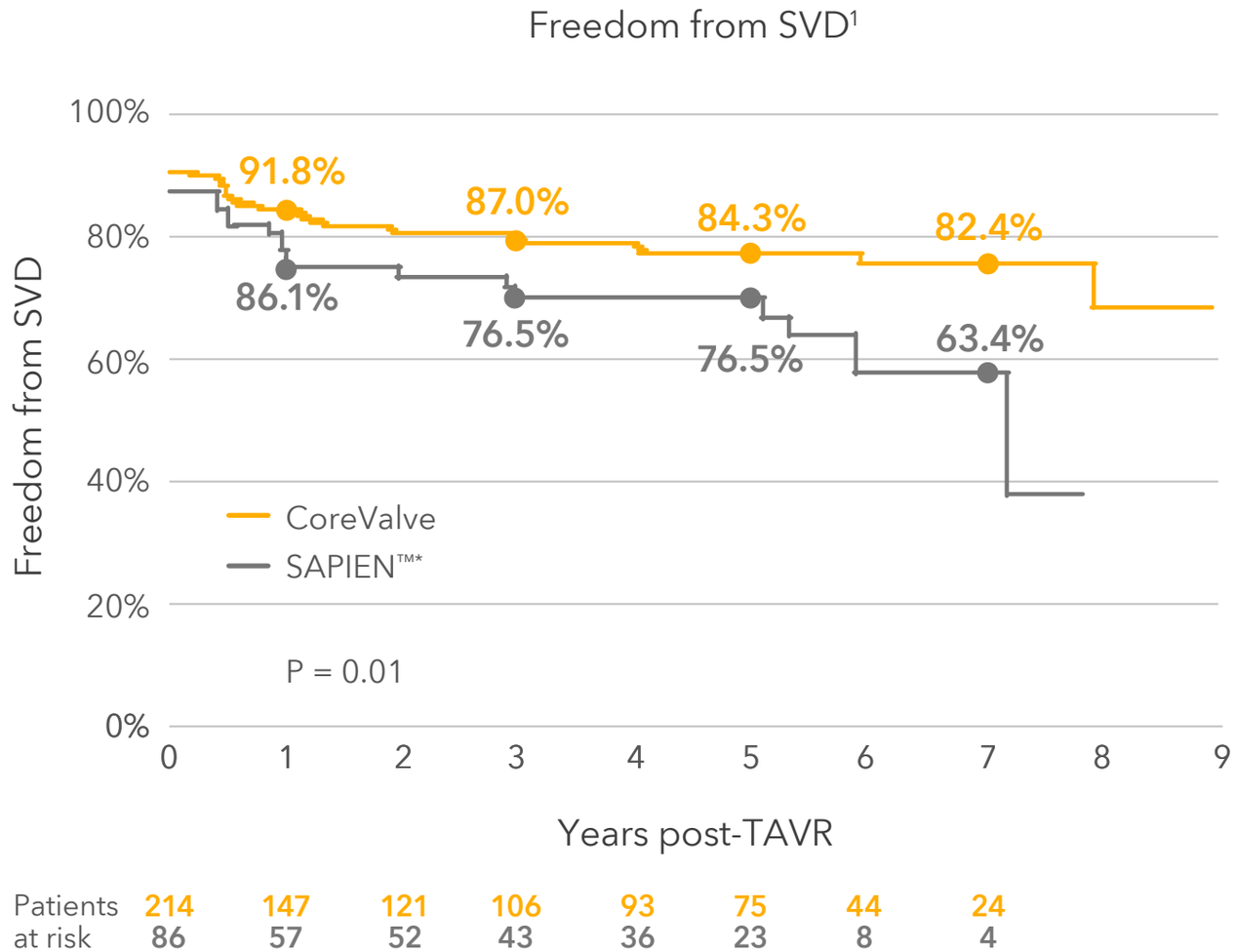
82.4%

for CoreValve™ TAV at seven years.

SVD definition

Device used:
100% CoreValve

DEUTSCH[1] 7 years



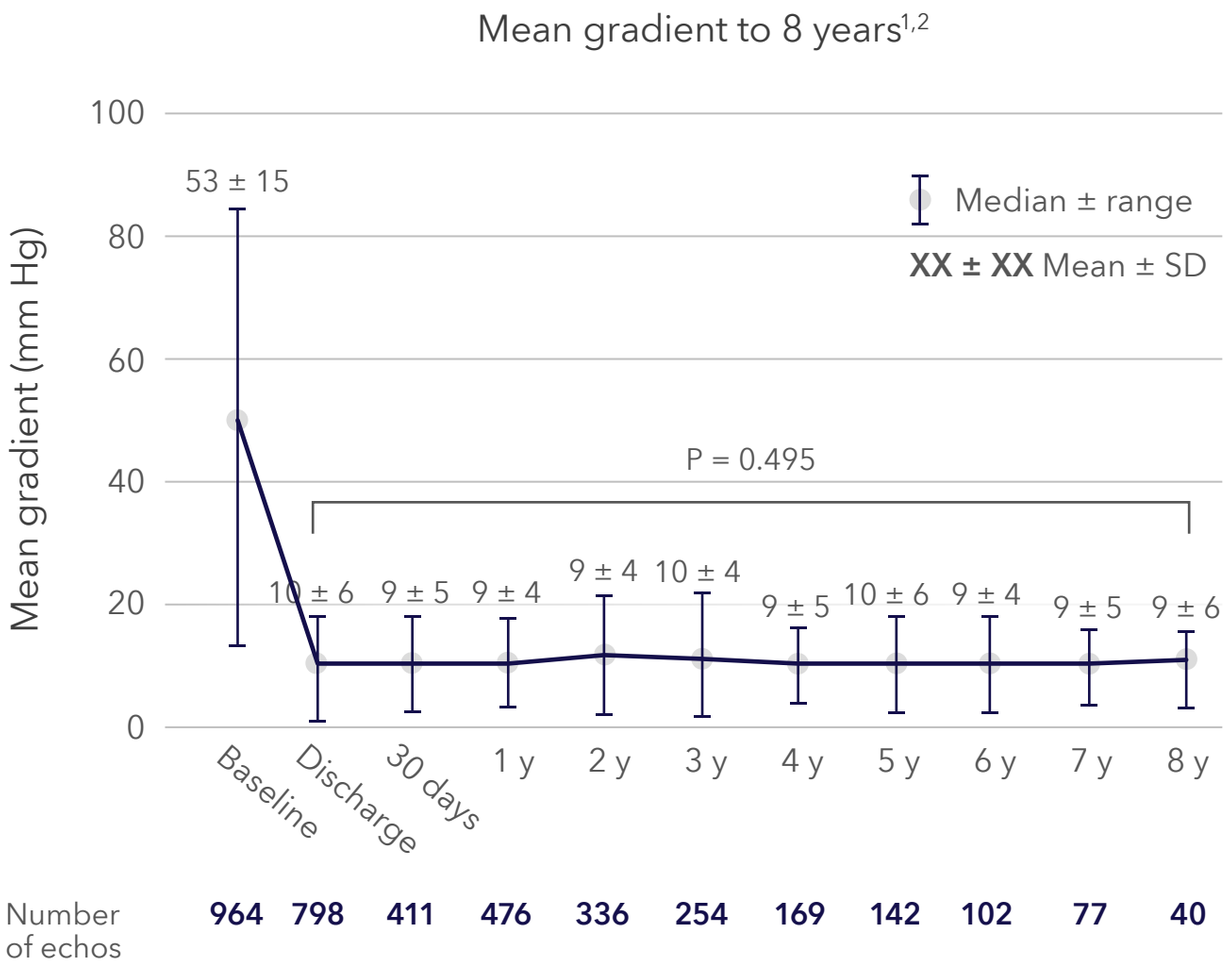
Retrospective analysis from a single-center registry

This chart clearly demonstrates significantly less SVD for CoreValve than SAPIEN out to 7 years. Freedom from SVD: 82.4% for CoreValve; 63.4% for SAPIEN.

When looking at freedom from SVD, at every time point (1, 3, 5, and 7 years), there was numerically less SVD with CoreValve than with SAPIEN.

[1] Deutsch MA, et al. *EuroIntervention*. 2018;14:41-49.

ITALIAN REGISTRY[1,2] 8 years



Long-term data on the self-expanding, supra-annular CoreValve™ platform.

Multicenter registry

Together with NOTION, this is the long-term data on the self-expanding, supra-annular CoreValve platform. Data demonstrates very low rates of moderate and severe hemodynamic SVD. The cumulative incidence of moderate and severe SVD at 8 years are 3.0% and 1.6%, respectively.

Additionally, the bioprosthetic valve failure (BVF) was also very low at 2.5% (includes any valve intervention, severe SVD, and any valve-related deaths), signaling durability for the CoreValve platform. The mean gradients remained low through 8 years.

SVD definition

Device used:
100% CoreValve

[1] Testa L, et al. Valve Performance and echocardiographic data throughout 8 years follow up after TAVR. Presented at EuroPCR 2019. Paris, France.
[2] Testa L, et al. *Eur Heart J*. 2020;41:1876-1886.

Indications
The Medtronic CoreValve™ Evolut™ R, Evolut™ PRO+, and Evolut™ FX Systems are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

The Medtronic CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems are indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (e.g., STS predicted risk of operative mortality score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

Contraindications
The CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems are contraindicated in patients who cannot tolerate Nitinol (titanium or nickel), gold (for Evolut FX Systems alone), an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

Warnings
General Implantation of the CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems should be performed only by physicians who have received Medtronic CoreValve Evolut R, Evolut PRO+, or Evolut FX training. This procedure should only be performed where emergency aortic valve surgery can be performed promptly. Mechanical failure of the delivery catheter system and/or accessories may result in patient complications. *Transcatheter aortic valve (bioprosthesis)* Accelerated deterioration due to calcific degeneration of the bioprostheses may occur in: children, adolescents, or young adults; patients with altered calcium metabolism (e.g., chronic renal failure or hyperthyroidism).

Precautions
General Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up. The safety and effectiveness of the CoreValve Evolut R, Evolut PRO+, and Evolut FX Systems have not been evaluated in the pediatric population. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in the following patient populations: Patients who do not meet the criteria for symptomatic severe native aortic stenosis as defined: (1) symptomatic severe high-gradient aortic stenosis – aortic valve area ≤ 1.0 cm^2 or aortic valve area index ≤ 0.6 cm^2/m^2, a mean aortic valve gradient ≥ 40 mm Hg, or a peak aortic-jet velocity ≥ 4.0 m/s; (2) symptomatic severe low-flow, low-gradient aortic stenosis – aortic valve area ≤ 1.0 cm^2 or aortic valve area index ≤ 0.6 cm^2/m^2, a mean aortic valve gradient < 40 mm Hg, and a peak aortic-jet velocity < 4.0 m/s; with untreated, clinically significant coronary artery disease requiring revascularization; with a preexisting prosthetic heart valve with a rigid support structure in either the mitral or pulmonic position if either the preexisting prosthetic heart valve could affect the implantation or function of the bioprosthesis or the implantation of the bioprosthesis could affect the function of the preexisting prosthetic heart valve; patients with liver failure (Child-Pugh Class C); with cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support; patients who are pregnant or breastfeeding. The safety and effectiveness of a CoreValve Evolut R, Evolut PRO+, or Evolut FX bioprosthesis implanted within a failed preexisting transcatheter bioprosthesis have not been demonstrated. Implanting a CoreValve Evolut R, Evolut PRO+, or Evolut FX bioprosthesis in a degenerated surgical bioprosthetic valve (transcatheter aortic valve in surgical aortic valve [TAV-in-SAV]) should be avoided in the following conditions: The degenerated surgical bioprosthetic valve presents with: a significant concomitant paravalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (e.g., wire form frame fracture); partially detached leaflet that in the aortic position may obstruct a coronary ostium; stent frame with a manufacturer-labeled inner diameter < 17 mm. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in patient populations presenting with the following: Blood dyscrasias as defined as leukopenia (WBC < 1,000 cells/mm^3), thrombocytopenia (platelet count < 50,000 cells/mm^3), history of bleeding diathesis or coagulopathy, or hypercoagulable states; congenital unicuspid valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation [3-4+]); moderate to severe (3-4+) or severe (4+) mitral or severe (4+) tricuspid regurgitation; hypertrophic obstructive cardiomyopathy; new or untreated echocardiographic evidence of intracardiac mass, thrombus, or vegetation; native aortic annulus size < 18 mm or > 30 mm per the baseline diagnostic imaging or surgical bioprosthetic aortic annulus size < 17 mm or > 30 mm; transarterial access unable to accommodate an 18 Fr introducer sheath or the 14 Fr equivalent EnVeo InLine™ Sheath when using models ENVEOR-US/D-EVPROP2329US or Evolut FX Delivery Catheter System with InLine™ Sheath when using model D-EVOLUTFX-2329 or transarterial access unable to accommodate a 20 Fr introducer sheath or the 16 Fr equivalent EnVeo InLine Sheath when using model ENVEOR-N-US or transarterial access unable to accommodate a 22 Fr introducer sheath or the 18 Fr equivalent Evolut PRO+ InLine Sheath when using model D-EVPROP34US or Evolut FX Delivery Catheter System with InLine Sheath when using model D-EVOLUTFX-34; prohibitive left ventricular outflow tract calcification; sinus of Valsalva anatomy that would prevent adequate coronary perfusion; significant aortopathy requiring ascending aortic replacement; moderate to severe mitral stenosis; severe ventricular dysfunction with left ventricular ejection fraction (LVEF) < 20%; symptomatic carotid or vertebral artery disease; and severe basal septal hypertrophy with an outflow gradient.

Before Use Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging. The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the devices is the responsibility of the physician. Refer to the Instructions for Use for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed below. Patients must present with transarterial access vessel diameters of ≥ 5 mm when using models ENVEOR-US/D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 5.5 mm when using model ENVEOR-N-US or ≥ 6 mm when using models D-EVPROP34US/D-EVOLUTFX-34, or patients must present with an ascending aortic (direct aortic) access site ≥ 60 mm from the basal plane for both systems. Implantation of the bioprosthesis should be avoided in patients with aortic root angulation (angle between plane of aortic valve annulus and horizontal plane/vertebrae) of > 30° for right subclavian/axillary access or > 70° for femoral and left subclavian/axillary access. For subclavian access, patients with a patent left internal mammary artery (LIMA) graft must present with access vessel diameters that are either ≥ 5.5 mm when using models ENVEOR-L-US/D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6 mm when using model ENVEOR-N-US or ≥ 6.5 mm when using models D-EVPROP34US/D-EVOLUTFX-34. Use caution when using the subclavian/axillary approach in patients with a patent LIMA graft or patent RIMA graft. For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft. For transfemoral access, use caution in patients who present with multiplanar curvature of the aorta, acute angulation of the aortic arch, an ascending aortic aneurysm, or severe calcification in the aorta and/or vasculature. If ≥ 2 of these factors are present, consider an alternative access route to prevent vascular complications. Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established.

During Use If a misload is detected during fluoroscopic inspection, do not attempt to reload the bioprosthesis. Discard the entire system. Inflow crown overlap that has not ended before the 4th node within the capsule increases the risk of an infold upon deployment in constrained anatomies, particularly with moderate-severe levels of calcification and/or bicuspid condition. Do not attempt to direct load the valve. After the procedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis. After the procedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment. Excessive contrast media may cause renal failure. Prior to the procedure, measure the patient's creatinine level. During the procedure, monitor contrast media usage. Conduct the procedure under fluoroscopy. Fluoroscopic procedures are associated with the risk of radiation damage to the skin, which may be painful, disfiguring, and long-term. The safety and efficacy of a CoreValve Evolut R, Evolut PRO+, or Evolut FX bioprosthesis implanted within a transcatheter bioprosthesis have not been demonstrated.

Potential adverse events
Potential risks associated with the implantation of the CoreValve Evolut R, Evolut PRO+, or Evolut FX transcatheter aortic valve may include, but are not limited to, the following: • death • myocardial infarction, cardiac arrest, cardiogenic shock, or cardiac tamponade • coronary occlusion, obstruction, or vessel spasm (including acute coronary closure) • cardiovascular injury (including rupture, perforation, tissue erosion, or dissection of vessels, ascending aorta trauma, ventricle, myocardium, or valvular structures that may require intervention) • emergent surgical or transcatheter intervention (e.g., coronary artery bypass, heart valve replacement, valve explant, percutaneous coronary intervention [PCI], balloon valvuloplasty) • prosthetic valve dysfunction (regurgitation or stenosis) due to fracture; bending (out-of-round configuration) of the valve frame; underexpansion of the valve frame; calcification; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (prosthesis-patient mismatch); malposition (either too high or too low)/malplacement • prosthetic valve migration/embolization • prosthetic valve endocarditis • prosthetic valve thrombosis • delivery catheter system malfunction resulting in the need for additional recrossing of the aortic valve and prolonged procedural time • delivery catheter system component migration/embolization • stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits • individual organ (e.g., cardiac, respiratory, renal [including acute kidney failure]) or multi-organ insufficiency or failure • major or minor bleeding that may require transfusion or intervention (including life-threatening or disabling bleeding) • vascular access-related complications (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, or stenosis) • mitral valve regurgitation or injury • conduction system disturbances (e.g., atrioventricular node block, left bundle-branch block, asystole), which may require a permanent pacemaker • infection (including septicemia) • hypotension or hypertension • hemolysis • peripheral ischemia • General surgical risks applicable to transcatheter aortic valve implantation: • bowel ischemia • abnormal lab values (including electrolyte imbalance) • allergic reaction to antiplatelet agents, contrast medium, or anesthesia • exposure to radiation through fluoroscopy and angiography • permanent disability.

Please reference the CoreValve Evolut R, Evolut PRO+, and Evolut FX Instructions for Use for more information regarding indications, warnings, precautions, and potential adverse events.

Caution: Federal Law (USA) restricts these devices to the sale by or on the order of a physician.

The commercial name of the Evolut™ R device is Medtronic CoreValve™ Evolut™ R System, the commercial name of the Evolut™ PRO+ device is Medtronic Evolut™ PRO+ System, and the commercial name of the Evolut™ FX device is Medtronic Evolut™ FX System.

Medtronic

710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA

Toll-free: 800.328.2518
Tel: +1.763.514.4000

LifeLine
CardioVascular Technical Support
Toll-free: 877.526.7890
Tel: +1.763.526.7890
rs.structuralheart@medtronic.com

medtronic.com

UC202300043b EN
10/2023

CoreValve
is the first
only TAVR
to demons
significantl
SVD than S

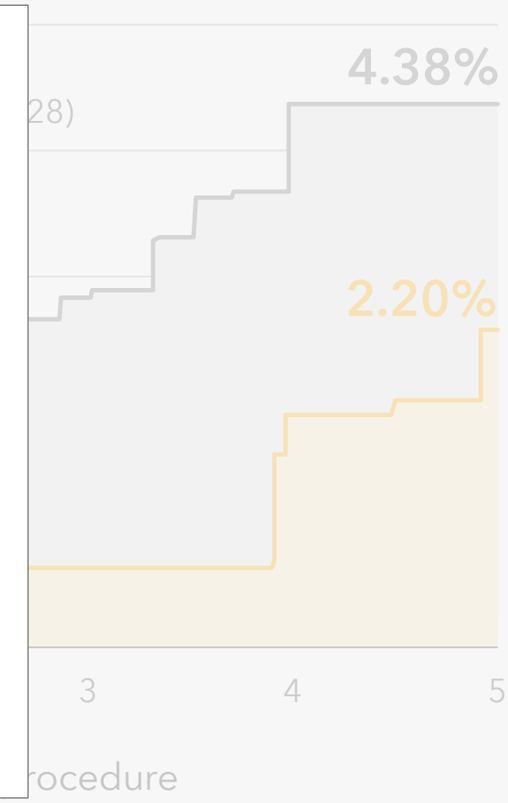
SVD definition[1]

SVD was defined as ≥ moderate hemodynamic valve deterioration (HVD): Increase in mean gradient ≥ 10 mm Hg from discharge/30-day echo to last available echo AND mean gradient ≥ 20 mm Hg at last available echo OR new onset/increase of intra-prosthetic aortic regurgitation (AR) ≥ moderate.

[1] Adapted from VARC-3 Writing Committee, et al. *Eur Heart J.* 2021;42:1825-1857.

CoreValve/Evolut platform pooled analysis:

5-year SVD adjusted for competing risk of mortality[1]



rocedure

[1] O'Hair D, et al. *JAMA Cardiol.* 2023;8:111–119.

SVD definition

Devices used:
88.5% CoreValve
11.5% Evolut™ R

Patients wit
had a near t
increased ri
all-cause m
and aortic v
re-hospitaliz
or worsenin
failure at five years.

SVD definition

RCT and Non-RCT cohorts:
97% CoreValve
3% Evolut R

CoreValve™ and Evolut™ platforms pooled analysis:

Worsened clinical outcomes in patients who develop SVD[1]

	HR (95% CI)	P value
2)		
	2.03 (1.46, 2.82)	< 0.001
	1.86 (1.20, 2.90)	0.006
	2.17 (1.23, 3.84)	0.008
	2.02 (1.42, 2.88)	< 0.001
	2.45 (1.40, 4.30)	0.002
	2.37 (1.10, 5.08)	0.003
	2.20 (0.81, 5.98)	0.120
	2.73 (1.53, 4.88)	< 0.001
	2.34 (1.55, 3.53)	< 0.001
	2.17 (1.26, 3.76)	0.006
	2.45 (1.22, 4.93)	0.010
	2.03 (1.29, 3.19)	0.002

0.10 1.00 10.00
Lower risk with SVD ← → Higher risk with SVD

†All-cause mortality or aortic valve-related hospitalization.

[1] O'Hair D, et al. *JAMA Cardiol*. 2023;8:111–119.

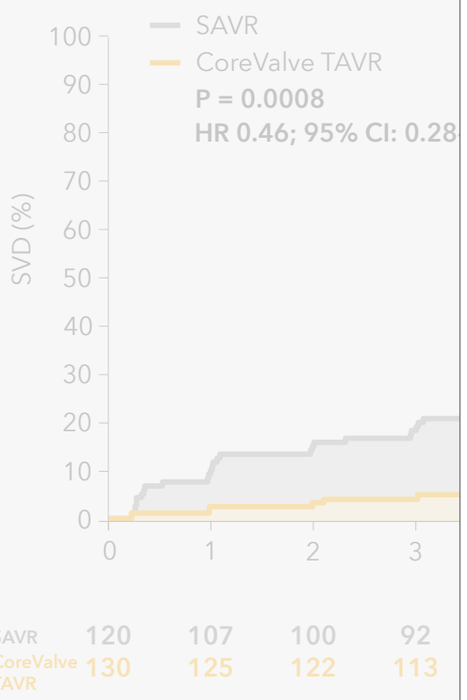
SVD definition[1]

SVD was defined as ≥ moderate hemodynamic valve deterioration (HVD): Increase in mean gradient ≥ 10 mm Hg from discharge/30-day echo to last available echo AND mean gradient ≥ 20 mm Hg at last available echo OR new onset/increase of intra-prosthetic aortic regurgitation (AR) ≥ moderate.

[1] Adapted from VARC-3 Writing Committee, et al. *Eur Heart J*. 2021;42:1825-1857.

NOTION[1] 10 years

SVD out to 10 years[1]



SVD definition[1]

- Moderate or greater hemodynamic SVD
- Mean gradient ≥ 20 mm Hg OR
- Mean gradient ≥ 10 mm Hg change from baseline OR
- Moderate/severe intra-prosthetic aortic regurgitation (AR) (new or worsening from baseline)

[1] Capodanno D, et al. *Eur Heart J*. 2017;38:3382-3390.

The CoreValve™ rm onstrates tically r durability s surgery years.†1

The NOTION trial was a multicenter, randomized, head-to-head comparison of CoreValve TAVR versus SAVR followed out to 10 years in lower surgical risk patients ≥ 70 years of age who were eligible for surgery. TAVR had statistically lower rates of moderate or greater SVD out to 10 years versus surgery.‡

The NOTION 10-year data demonstrates excellent SVD rates in a lower surgical risk patient population. Perhaps most importantly, the data provides a signal of durability for the CoreValve platform versus SAVR.

SVD definition

Device used:
100% CoreValve

†In patients at lower surgical risk over the age of 70.
‡Structural valve deterioration[2] was defined as moderate or severe hemodynamic SVD (Mean gradient ≥ 20 mm Hg or Mean gradient ≥ 10 mm Hg change from index discharge or moderate/severe intra-prosthetic aortic regurgitation [AR] – new or worsening from discharge).
[1] Jørgensen T. Ten-year follow-up after transcatheter or surgical aortic valve implantation in severe aortic valve stenosis. Presented at ESC Congress; August 2023.
[2] Capodanno D, et al. *Eur Heart J*. 2017;383:3382–3390.

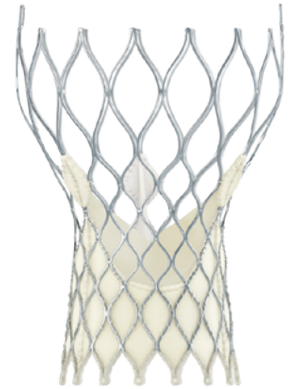
Performance that matters.

1

Medtronic

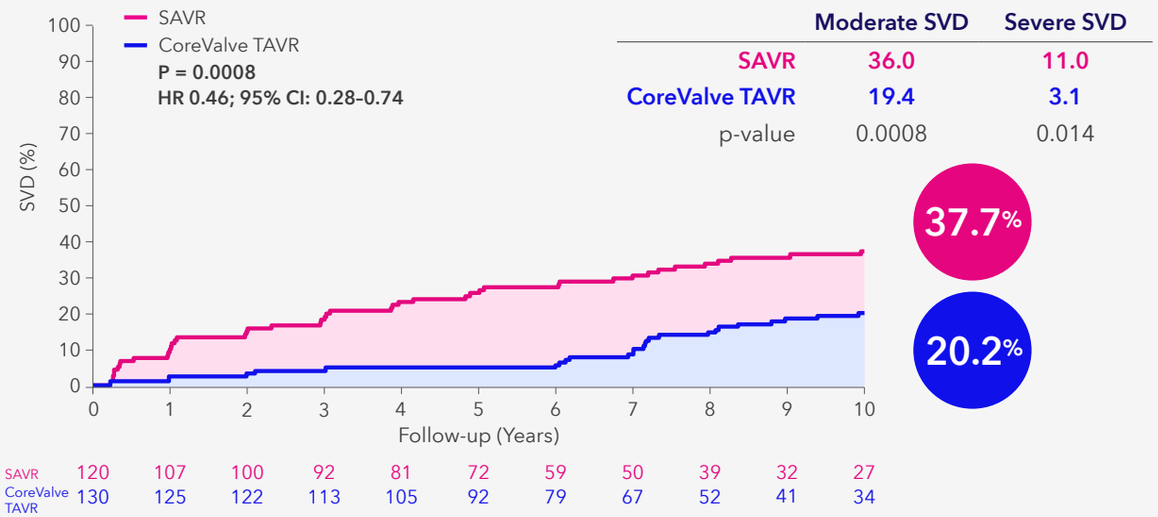
A decade of durability.

CoreValve™ TAVR platform demonstrates statistically better durability versus surgery at 10 years.[†1]

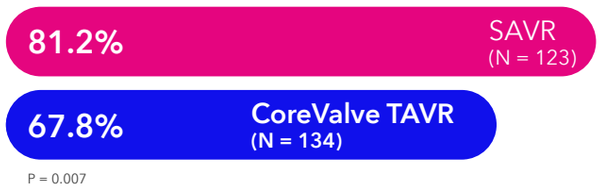


Statistically lower rates of moderate or greater structural valve deterioration (SVD) out to 10-years versus surgery.[‡]

SVD out to 10 years



Statistically lower bioprosthetic valve dysfunction (BVD) vs. SAVR at 10-years.[‡]

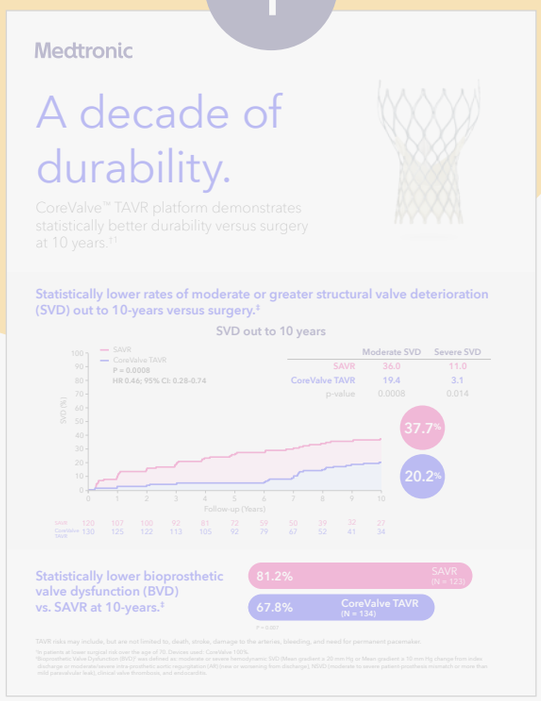


TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

[†]In patients at lower surgical risk over the age of 70. Devices used: CoreValve 100%.
[‡]Bioprosthetic Valve Dysfunction (BVD)[2] was defined as: moderate or severe hemodynamic SVD (Mean gradient ≥ 20 mm Hg or Mean gradient ≥ 10 mm Hg change from index discharge or moderate/severe intra-prosthetic aortic regurgitation (AR) (new or worsening from discharge), NSVD (moderate to severe patient-prosthesis mismatch or more than mild paravalvular leak), clinical valve thrombosis, and endocarditis.

Performance that matters.

1



Established failure rates

NOTION suggests the CoreValve™ platform fails at half the rate of surgery in low-risk patients.

Medtronic

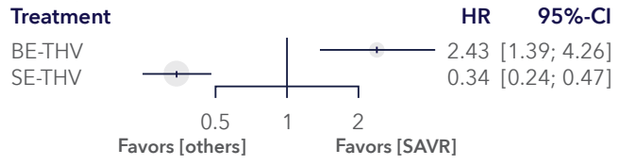
EVIDENCE UPDATE

Valve durability

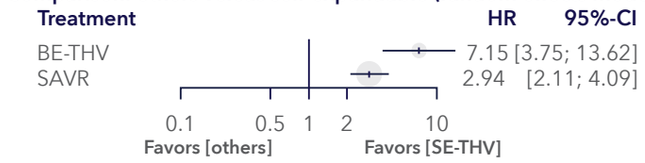
Valve durability for supra-annular, self-expandable TAV found to be statistically better at five years versus both SAVR and balloon-expandable TAV

Structural valve deterioration†

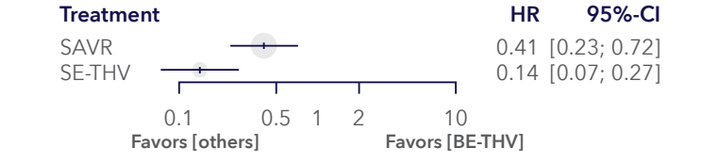
Only SE performs better than SAVR
Comparison: others versus SAVR (random effects model)



SE performs better than SAVR and BE
Comparison: others versus self-expandable (random effects model)



Both SE and SAVR perform better than BE
Comparison: others versus balloon-expandable (random effects model)



Study design

- Meta-analysis
- 10 randomized controlled trials
- 9,388 patients
- Follow-up 1 to 6 years
- Multiple devices‡

Key observations from the five-year meta-analysis:

At five years, supra-annular, self-expandable (SE) valves demonstrated:

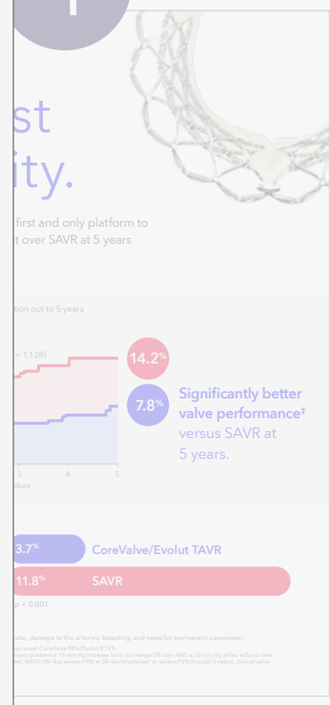
- Lowest risk of structural valve deterioration (SVD) compared with balloon-expandable (BE) valves and SAVR.
- Significantly stronger hemodynamics with larger EOAs and lower mean gradients versus BE valves.

Authors noted that additional studies including newer generations of valves are warranted to address known THV-specific risks, such as AR and reintervention.

SVD was less frequent in SE-THV compared with BE-THV and SAVR (HR 0.14, 95% CI 0.07 to 0.27; HR 0.34, 95% CI 0.24 to 0.47, respectively).

†Based on the longest available follow-up for each of the 10 studies used for this meta-analysis. SVD was defined by the respective authors of each paper.
‡CoreValve™, Evolut™ R, Evolut™ PRO, Sapien™*, Sapien 3, Sapien XT, and ACURATE neo™*.

4

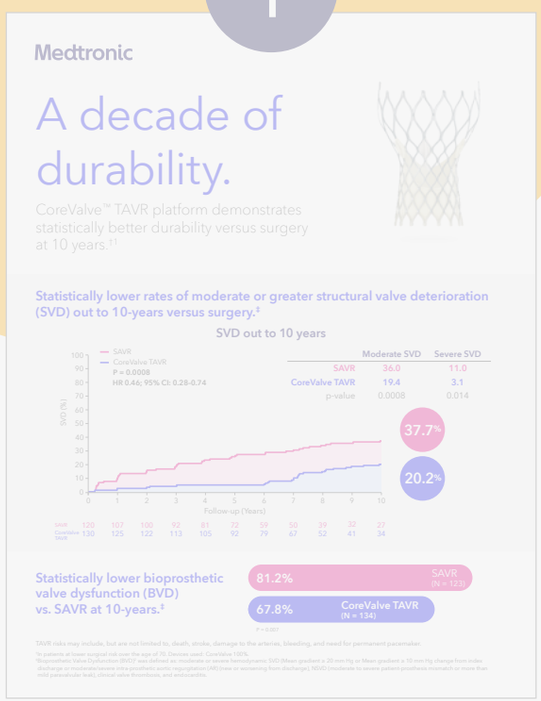


valve performance

ve/Evolut™
r, self-expanding
s is the only TAVR
demonstrate
better valve
, as assessed by
red with surgery
d clinical trials.

Performance that matters.

1

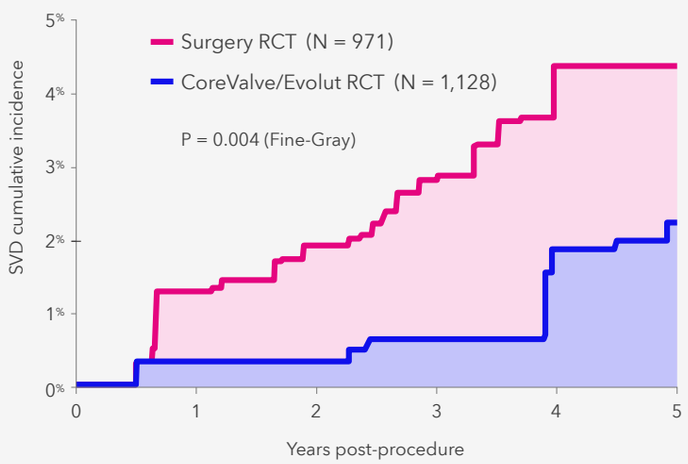


Established failure rates
NOTION suggests the CoreValve™ platform fails at half the rate of surgery in low-risk patients.

Medtronic

The best TAVR vs. SAVR durability data yet.

CoreValve™/Evolut™ is the first and only platform to demonstrate a durability benefit over SAVR at five years.†1



4.38%

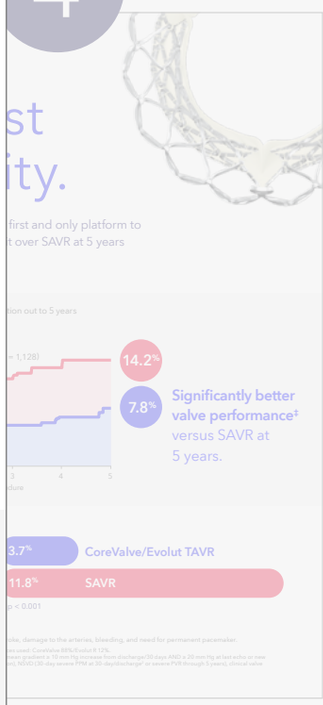
2.20%

Medtronic TAVR platforms demonstrated significantly lower rates of structural valve deterioration (SVD)‡ vs. SAVR at five years.

TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

†In pooled analysis of intermediate and high-risk patients. Devices used: CoreValve 88%/Evolut R 12%.
‡Structural valve deterioration (SVD) was defined as an increase in mean gradient ≥ 10 mm Hg over five years with a mean gradient ≥ 20 mm Hg at last echo OR new onset/increase of central AR of ≥ moderate in severity.

4



valve performance
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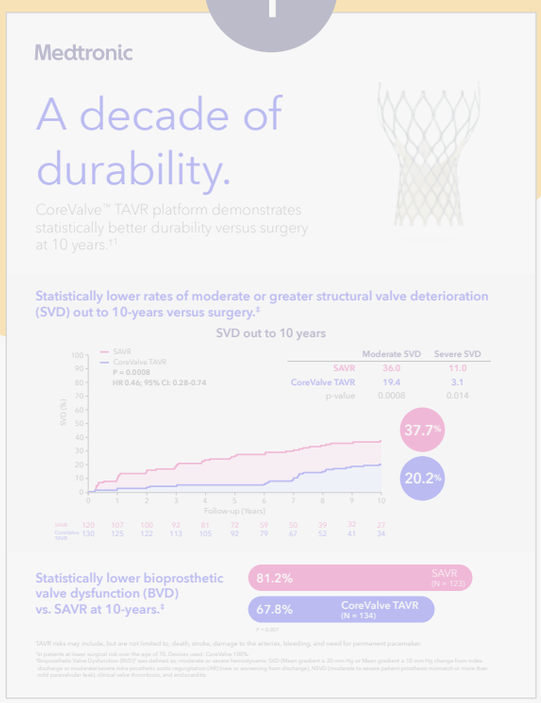
Performance that matters.

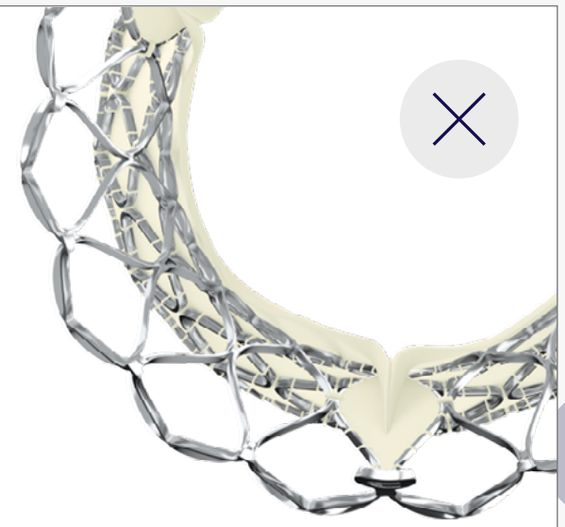
1



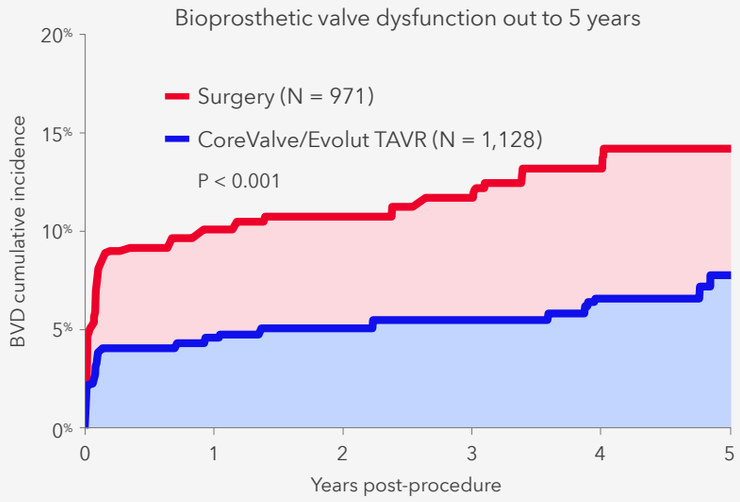
Established failure rates
NOTION suggests the CoreValve™ platform fails at half the rate of surgery in low-risk patients.

Medtronic

The best durability.



CoreValve™/Evolut™ TAVR is the first and only platform to demonstrate a durability benefit over SAVR at 5 years in randomized clinical trials.†1



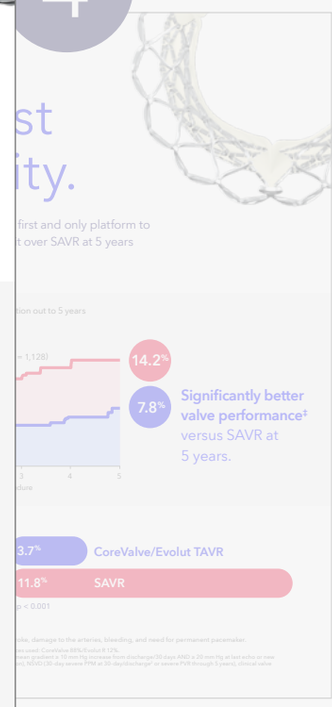
Significantly better valve performance‡ versus SAVR at 5 years.

3x lower severe PPM versus SAVR at 30-day/discharge.

TAVR risks may include, but are not limited to, death, stroke, damage to the arteries, bleeding, and need for permanent pacemaker.

†In pooled analysis of intermediate- and high-risk patients. Devices used: CoreValve 88%/Evolut R 12%.
‡Bioprosthetic Valve Dysfunction (BVD) was defined as[2,3]: SVD[4] (mean gradient ≥ 10 mm Hg increase from discharge/30 days AND ≥ 20 mm Hg at last echo or new onset/increase of ≥ moderate intraprosthetic aortic regurgitation), NSVD (30-day severe PPM at 30-day/discharge[2] or severe PVR through 5 years), clinical valve thrombosis, and endocarditis.

4



valve performance
ve/Evolut™
r, self-expanding
s is the only TAVR
demonstrate
better valve
, as assessed by
red with surgery
d clinical trials.

CoreValve™ TAV remains hemodynamically stable at five years.

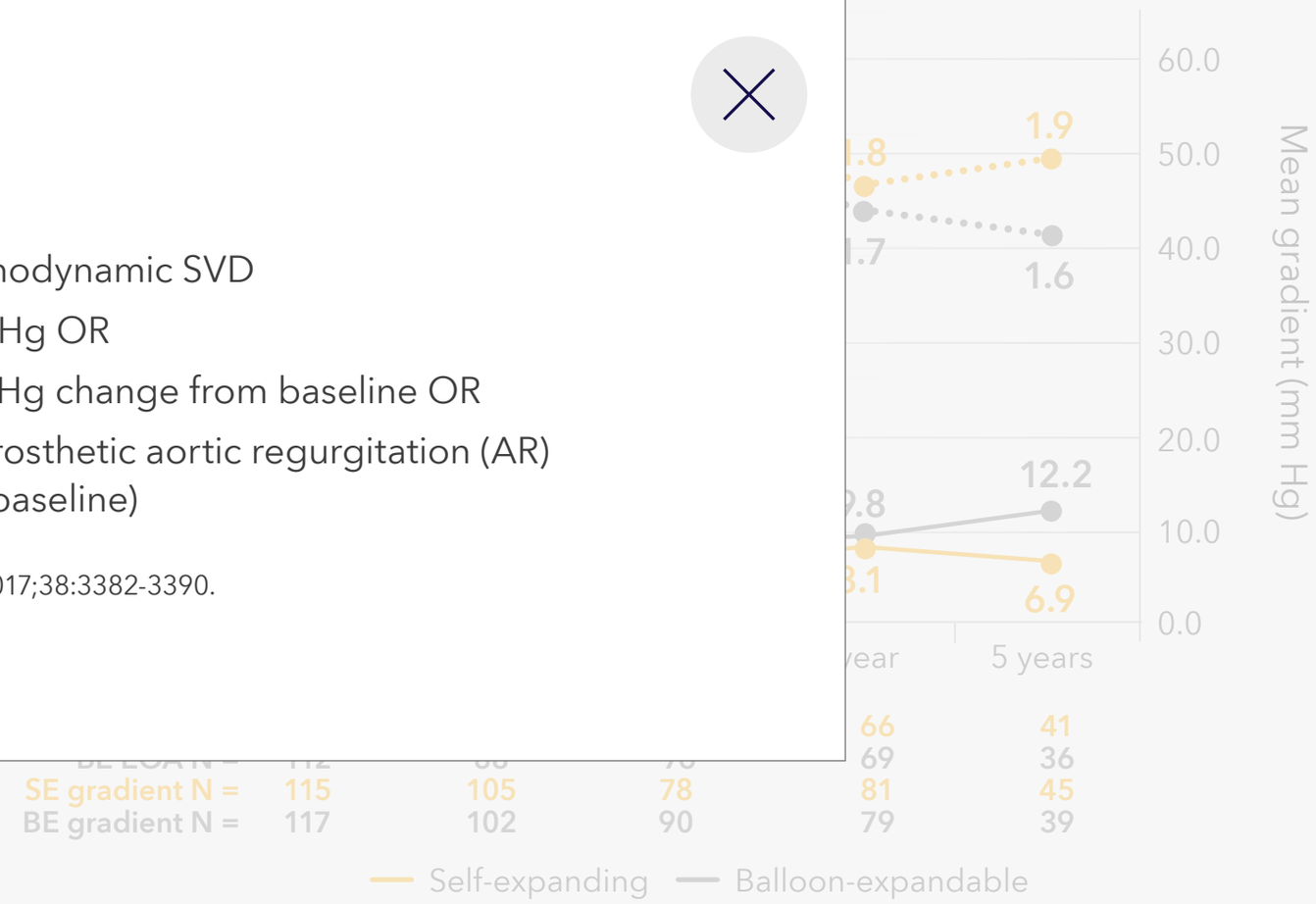
SVD definition[1]

- Moderate or greater hemodynamic SVD
- Mean gradient ≥ 20 mm Hg OR
- Mean gradient ≥ 10 mm Hg change from baseline OR
- Moderate/severe intra-prosthetic aortic regurgitation (AR) (new or worsening from baseline)

[1] Capodanno D, et al. *Eur Heart J*. 2017;38:3382-3390.

CHOICE[1] 5 years

Hemodynamics to 5 years[1]



For EOAs:
Baseline: p = 0.71
Post-TAVR: p = 0.86
30 days: p = 0.13
1 year: p = 0.34
5 years: p = 0.02

For gradients:
Baseline: p = 0.90
Post-TAVR: p < 0.001
30 days: p < 0.001
1 year: p = 0.007
5 years: p = 0.001

In this prospective, randomized study, CoreValve TAV remained hemodynamically stable at 5 years whereas the SAPIEN™* TAV had a 20% decline in EOA and a 40% increase in gradient.

CoreValve also had a statistically significant advantage in terms of freedom from SVD over SAPIEN (0.0% vs. 6.6%; p = 0.018).

SVD definition

Device used:
100% CoreValve

[1] Abdel-Wahab M, et al. Five-year outcomes after TAVI with balloon-expandable vs. self-expanding valves: Results from the CHOICE randomised clinical trial. Presented at EuroPCR 2019. Paris, France.

Freedom from

82.4

for CoreValve™

at seven years

SVD definition[1]

- Moderate or greater hemodynamic SVD
- Mean gradient ≥ 20 mm Hg OR
- Mean gradient ≥ 10 mm Hg change from baseline OR
- Moderate/severe intra-prosthetic aortic regurgitation (AR) (new or worsening from baseline)

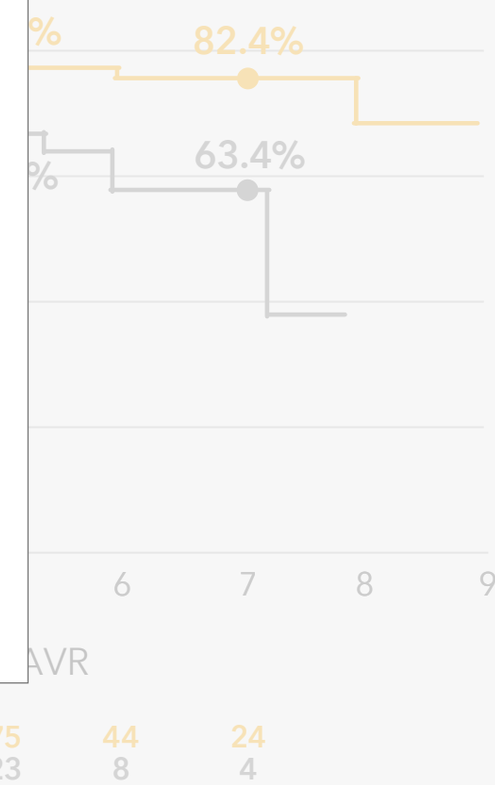
[1] Capodanno D, et al. *Eur Heart J*. 2017;38:3382-3390.

SVD definition

Device used:
100% CoreValve

DEUTSCH[1] 7 years

Freedom from SVD[1]



Retrospective analysis from a single-center registry

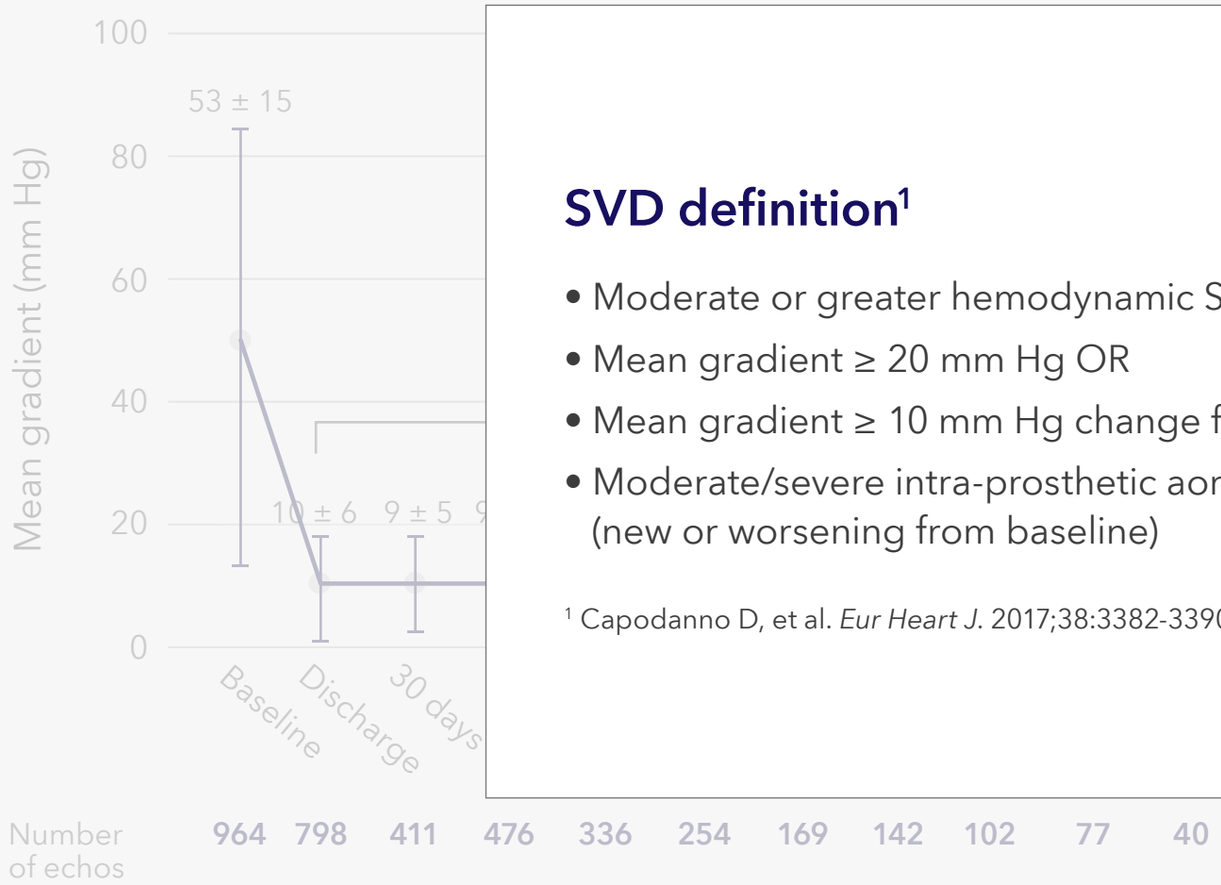
This chart clearly demonstrates significantly less SVD for CoreValve than SAPIEN out to 7 years. Freedom from SVD: 82.4% for CoreValve; 63.4% for SAPIEN.

When looking at freedom from SVD, at every time point (1, 3, 5, and 7 years), there was numerically less SVD with CoreValve than with SAPIEN.

[1] Deutsch MA, et al. *EuroIntervention*. 2018;14:41-49.

ITALIAN REGISTRY[1,2] 8 years

Mean gradient to 8 years[1,2]



Multicenter registry

Together with NOTION, this is the long-term data on the self-expanding, supra-annular CoreValve platform. Data demonstrates very low rates of moderate and severe hemodynamic SVD. The cumulative incidence of moderate and severe SVD at 8 years are 3.0% and 1.6%, respectively.

Additionally, the bioprosthetic valve failure (BVF) was also very low at 2.5% (includes any valve intervention, severe SVD, and any valve-related deaths), signaling durability for the CoreValve platform. The mean gradients remained low through 8 years.

[1] Testa L, et al. Valve Performance and echocardiographic data throughout 8 years follow up after TAVR. Presented at EuroPCR 2019. Paris, France.
[2] Testa L, et al. *Eur Heart J*. 2020;41:1876-1886.

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rm.

SVD definition

Device used:
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