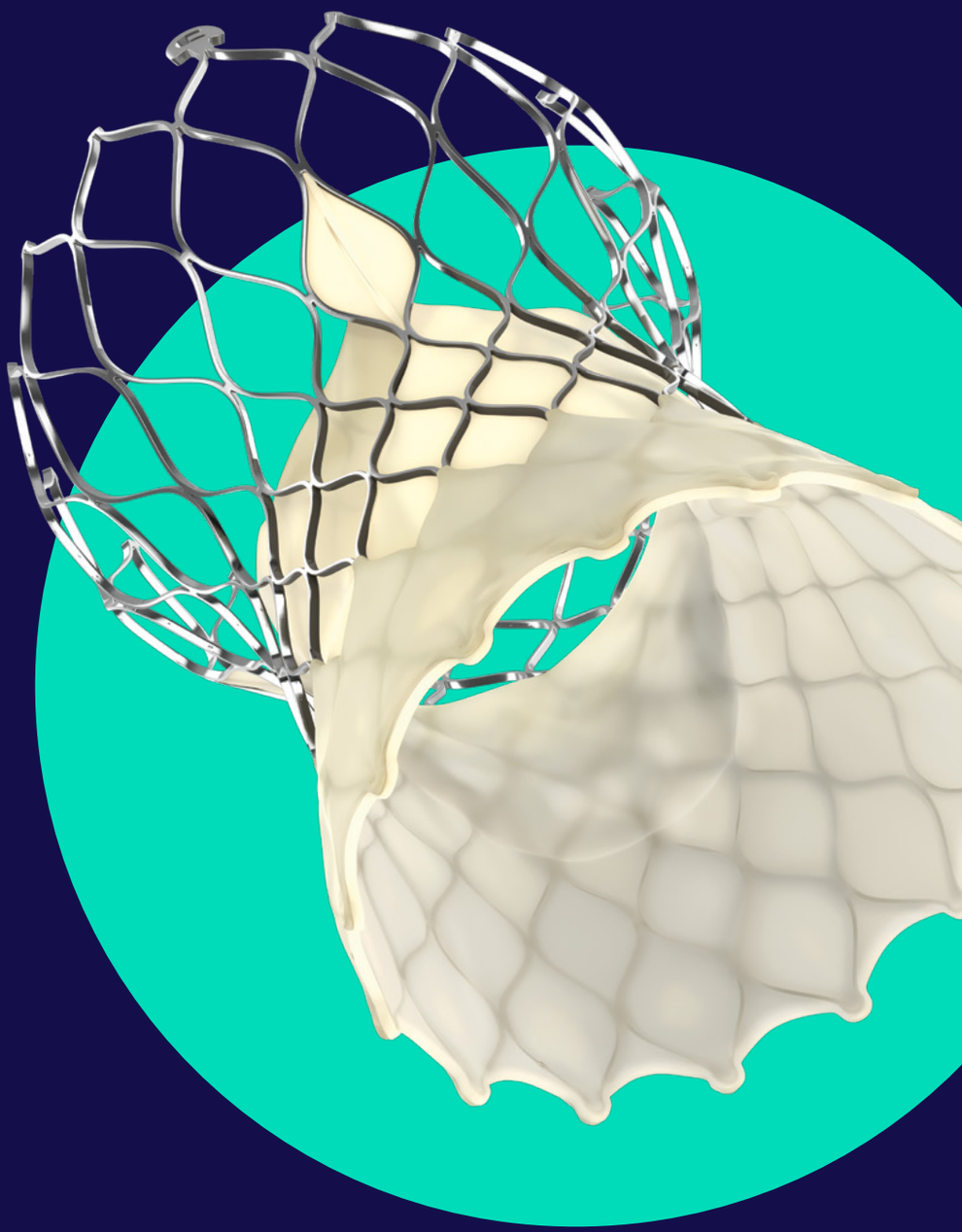
Medtronic

Designed to be durable.



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

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™ TAVI 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.

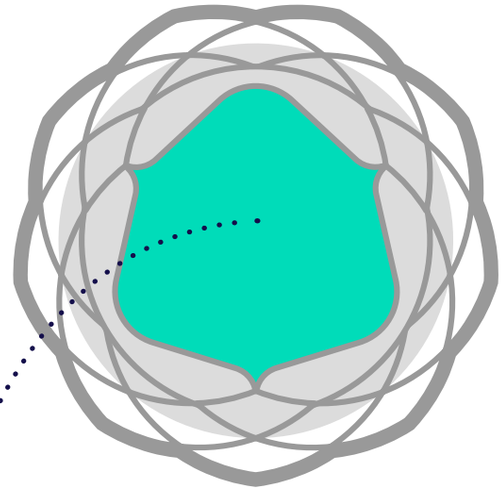
More height

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[4,5]

CoreValve™/Evolut™ TAVI platform
Intermediate risk[6]
Average EOA at 5 years (cm^2)

Devices used:
83.8% CoreValve
16.2% Evolut™ R

2.2

Consistently strong EOAs

CoreValve/Evolut TAVI platform
Low risk[7]
Average EOA at 2 years (cm^2)

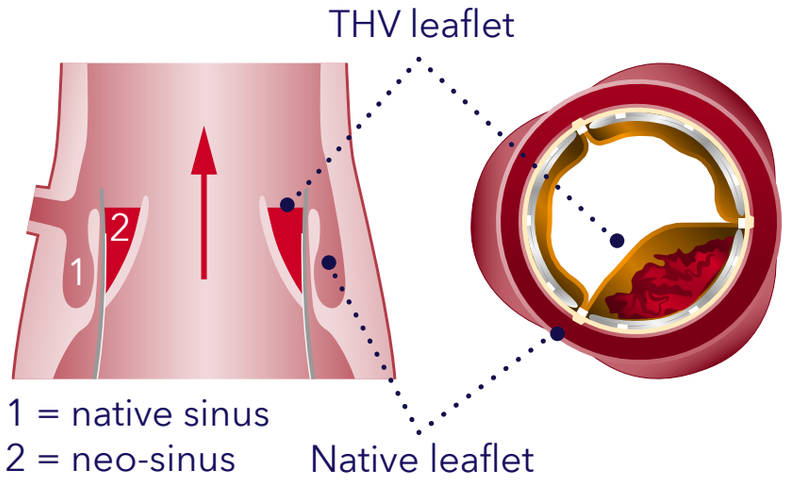
Devices used:
3.6% CoreValve
74.1% Evolut R
22.3% Evolut™ PRO

2.2

[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] O'Hair D. Presented at American College of Cardiology 70th Annual Scientific Session & Expo. May 2021.
[5] Søndergaard L, et al. *J Am Coll Cardiol.* 2019;73:546–553.
[6] Van Mieghem, et al. 5-Year Clinical and Echocardiographic Outcomes from the Randomized SURTAVI Trial. Presented at TCT 2021.
[7] Forrest JK, on behalf of the Evolut Low Risk Investigators. The Evolut Low Risk Trial Complete 2-year Follow-up. Presented at EuroPCR 2021.

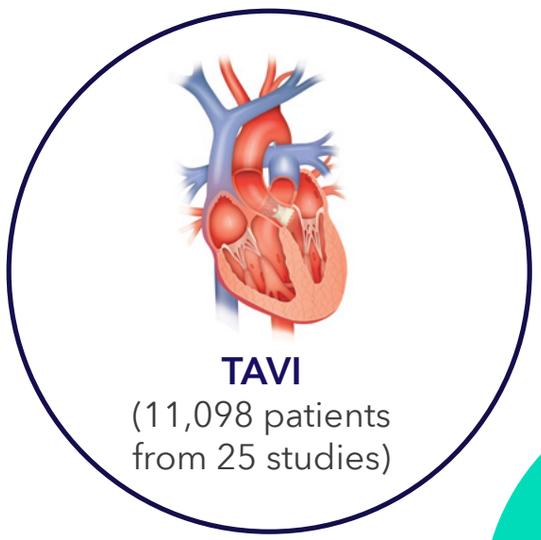
Supra-annular design benefits

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



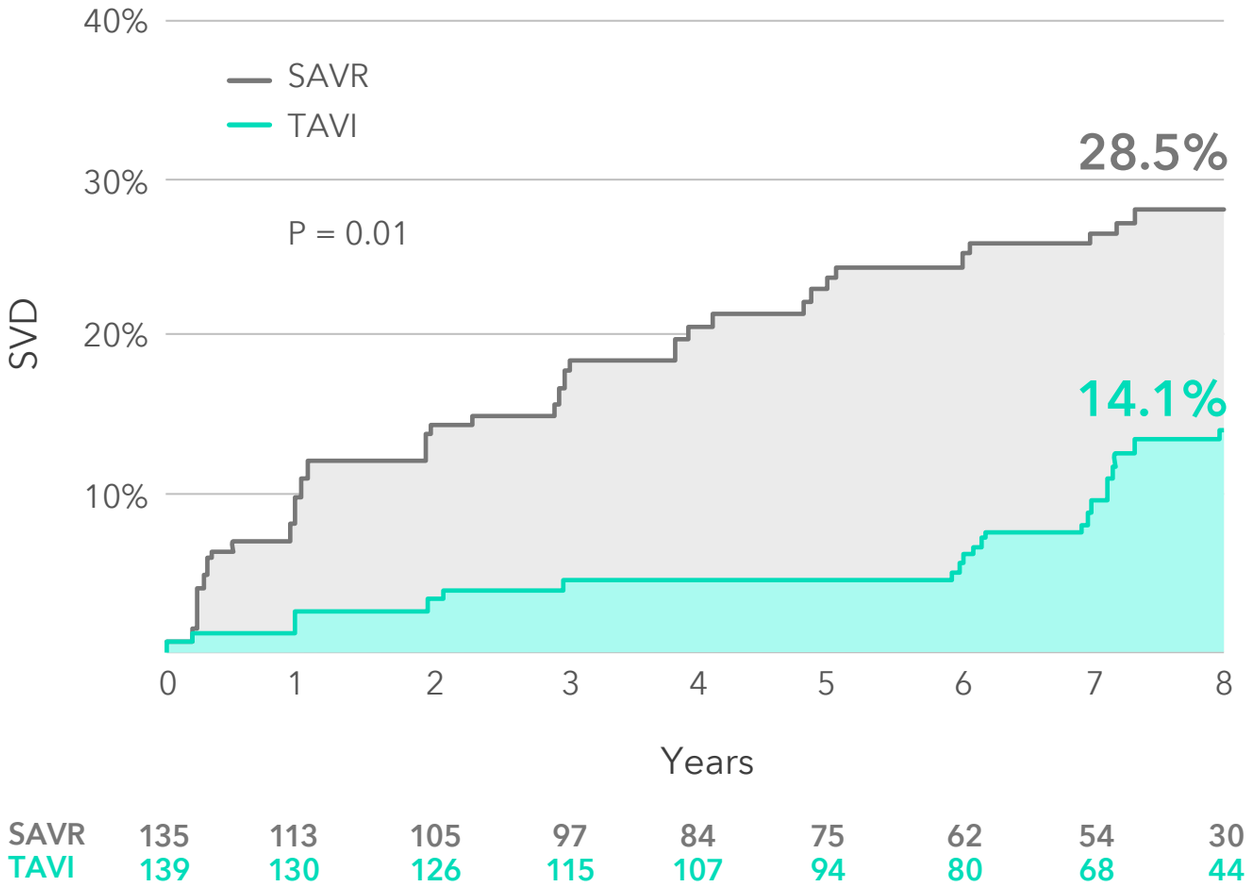
Subclinical leaflet thrombosis after TAVI: risk factors, effect on outcome, and treatment options[2]

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



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

NOTION[1] 8 years



The NOTION trial is a multicenter, randomized, head-to-head comparison of CoreValve TAVI versus SAVR followed out to 8 years in lower surgical risk patients ≥ 70 years of age who are eligible for surgery. TAVI had significantly less hemodynamic SVD out to 8 years.

The NOTION 8-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.

[1] Søndergaard L. Long-term follow-up of transcatheter and surgical bioprosthetic aortic valves in patients with severe aortic stenosis and lower surgical risk. Presented at PCR Valvese-Course. November 24, 2020.

The CoreValve™ platform was more durable than SAVR at eight years.

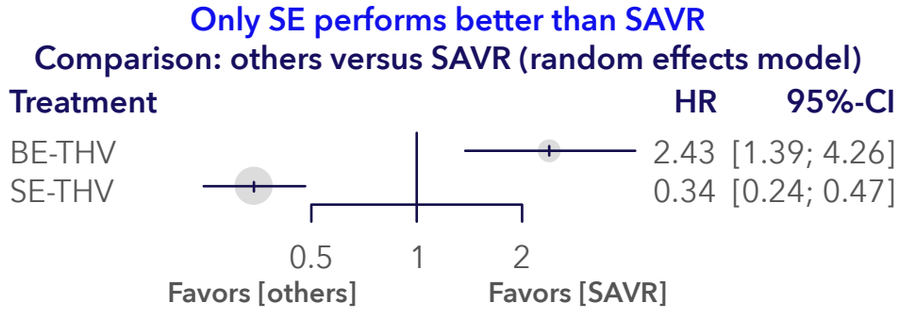
SVD definition

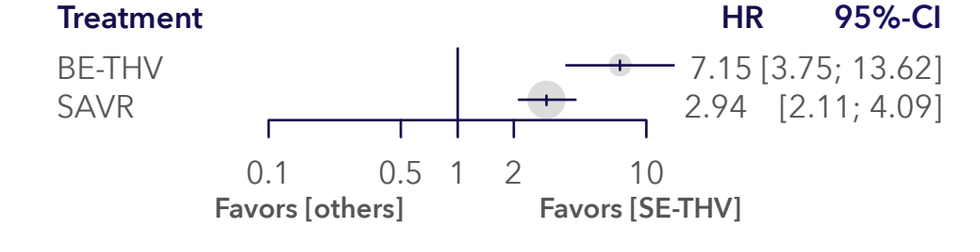
Device used:
100% CoreValve

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

Dr. Attizzani 5-year meta analysis[1]

Structural valve deterioration[†]





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.

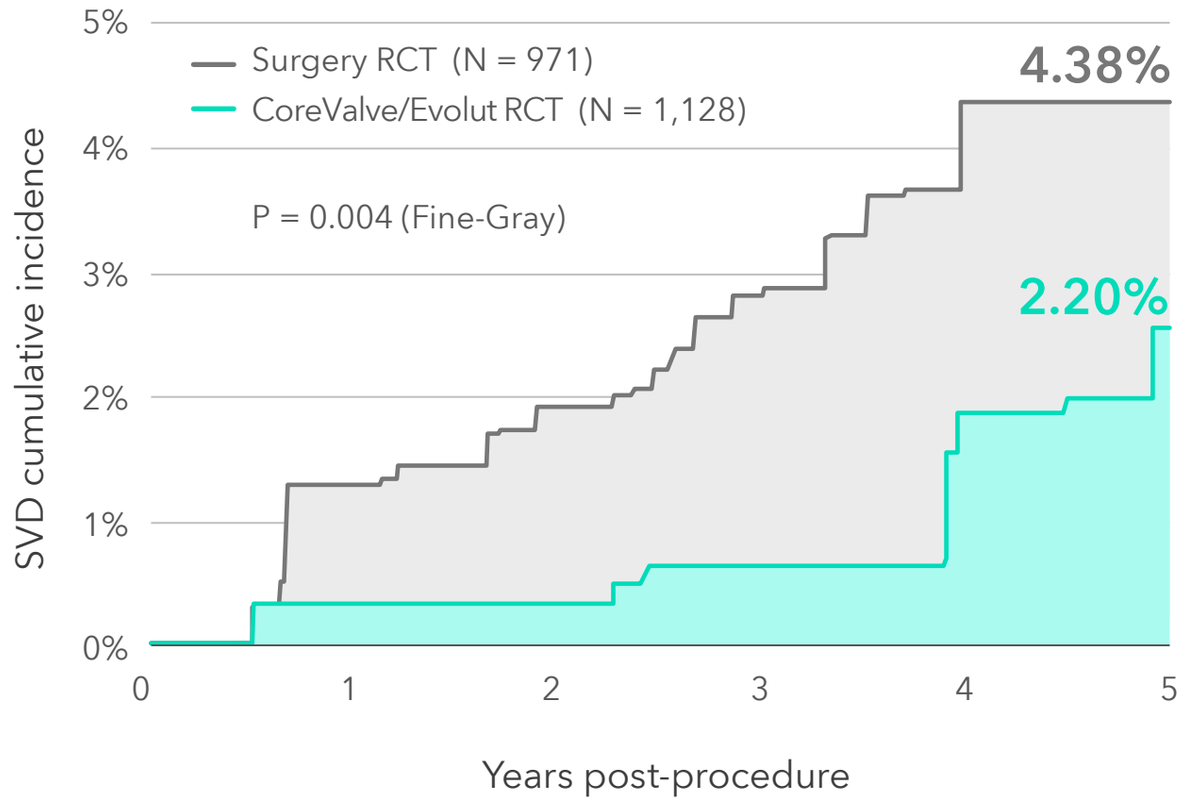
CoreValve™ and Evolut™ are the first and only TAVI platforms to demonstrate a lower SVD than SAVR.

SVD definition

Devices used:
88.5% CoreValve
11.5% Evolut™ R

CoreValve and Evolut pooled analysis:

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



[1] Reardon et al. 5-Year Incidence, Timing and Predictors of Structural Valve Deterioration of Transcatheter and Surgical Aortic Bioprostheses: Insights from the CoreValve US Pivotal and SURTAVI Trials. Presented at ACC 2022. Updated data on file.

Patients with SVD had a near **two-fold increased risk** for all-cause mortality (P < 0.001) and hospitalization for AV disease or worsening heart failure (P = 0.01) at five years.

SVD definition

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

CoreValve™ and Evolut™ pooled analysis:

Worsened clinical outcomes in patients who develop SVD[1]

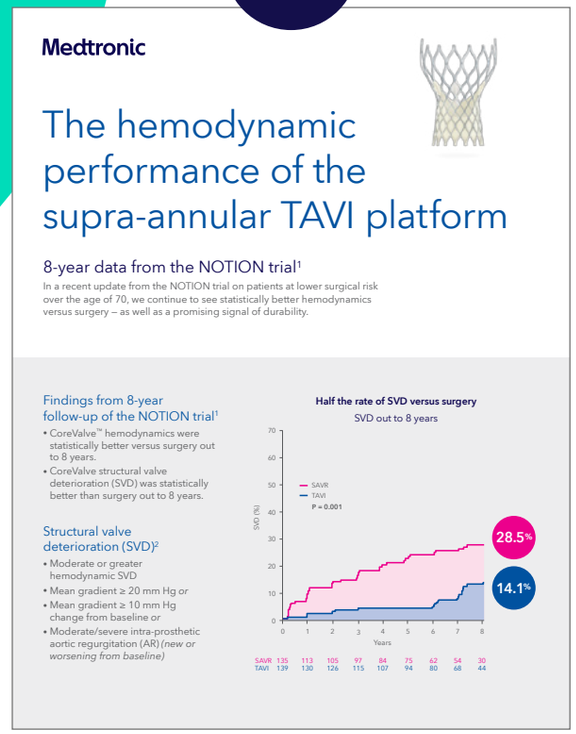
	HR (95% CI)	P value
Pooled surgery RCT and all CoreValve/Evolut (N = 4,762)		
All-cause mortality	2.03 (1.46, 2.82)	< 0.001
Cardiovascular mortality	1.86 (1.20, 2.90)	0.006
Aortic valve-related hospitalization	2.17 (1.23, 3.84)	0.008
Composite†	2.02 (1.42, 2.88)	< 0.001
Surgery RCT (N = 971)		
All-cause 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 TAVI (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] Reardon, et al. 5-Year Incidence, Timing and Predictors of Structural Valve Deterioration of Transcatheter and Surgical Aortic Bioprostheses: Insights from the CoreValve US Pivotal and SURTAVI Trials. Presented at ACC 2022. Updated data on file.

Designed to be durable.

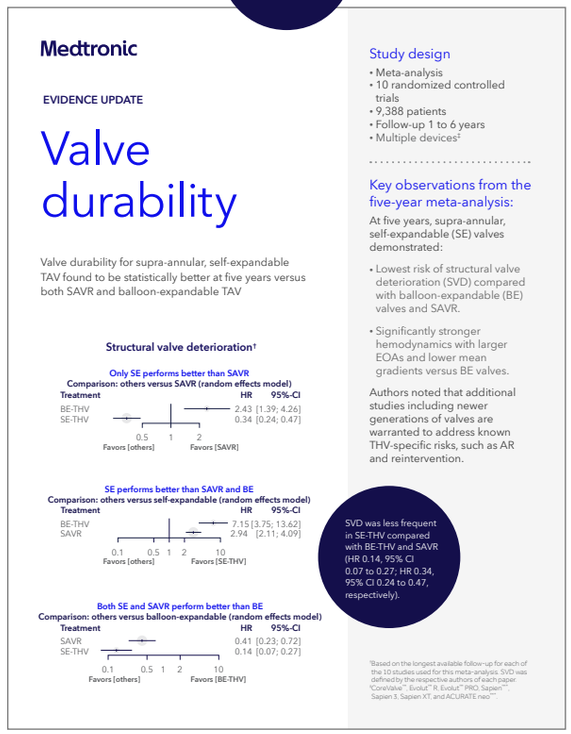
1



Established failure rates

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

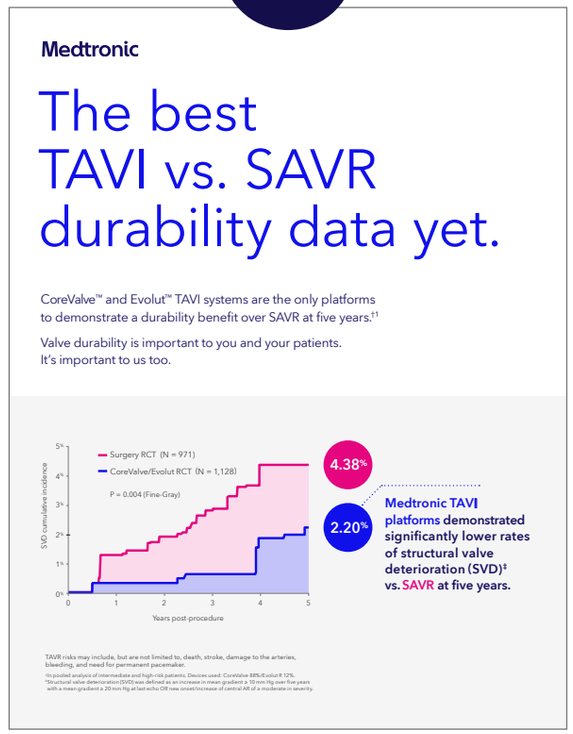
2



Established difference among platforms at five years

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

3



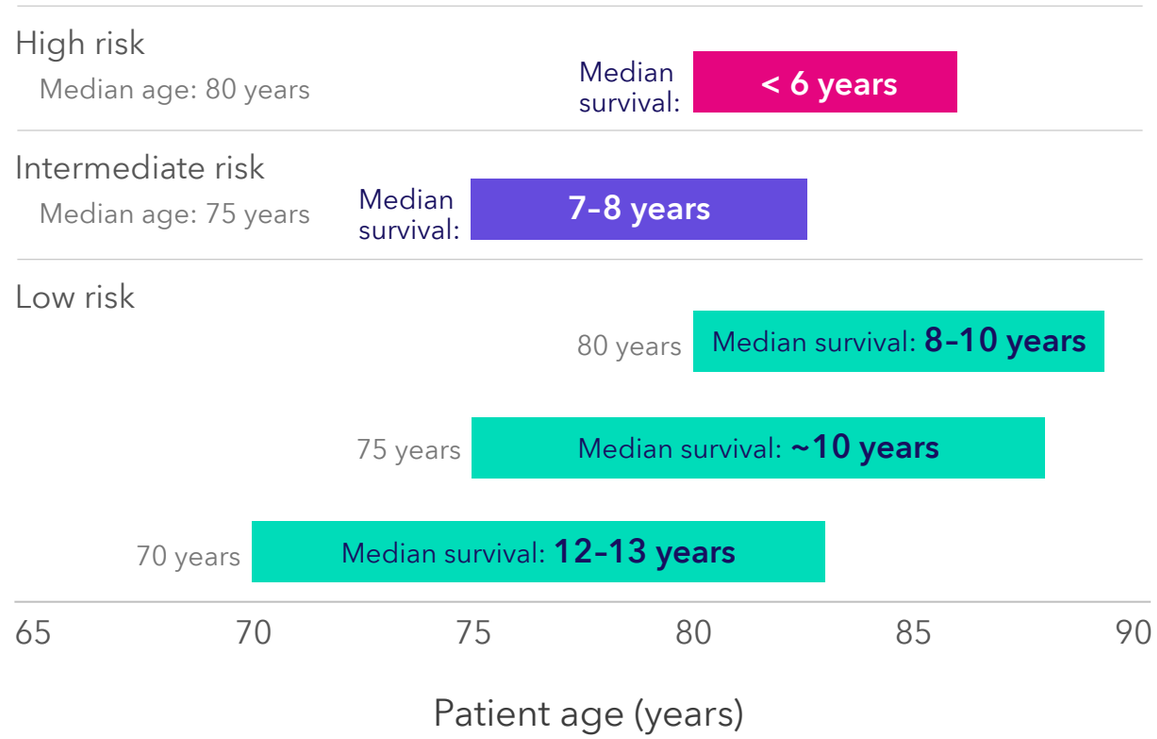
Consequence of failure

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

Longevity after surgical aortic valve replacement.

Stratification by age and surgical risk groups

Lifetime management of patients undergoing AVR[1]

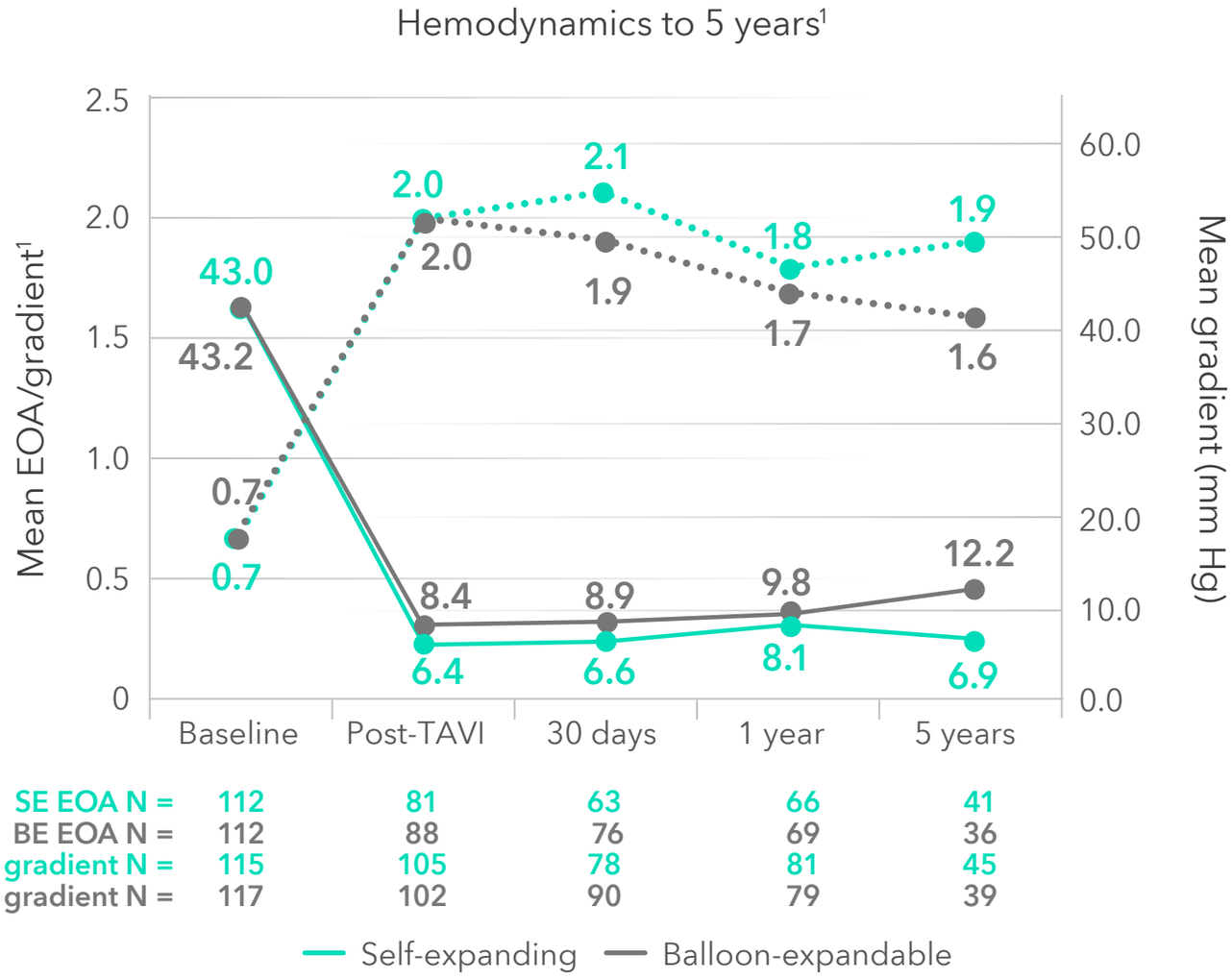


[1] Martinsson A, et al. *J Am Coll Cardiol*. 2021;78:2147-2157.

Supporting data

CoreValve™ TAV remained hemodynamically stable at five years.

CHOICE[1] 5 years



For EOAs:
Baseline: p = 0.71
Post-TAVI: 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-TAVI: 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:

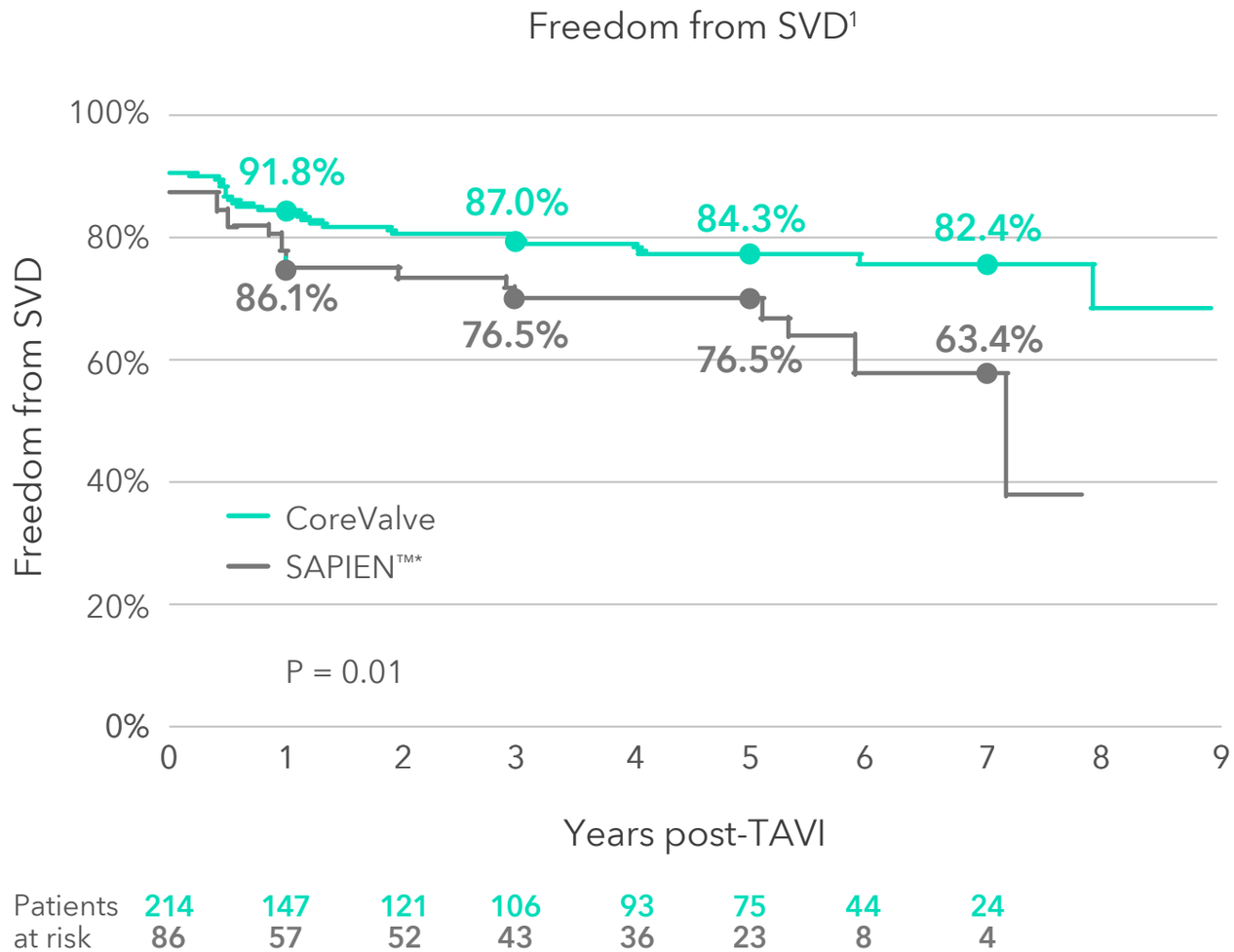
82.4%

for CoreValve™ TAV
at seven years.

SVD definition

Device used:
100% CoreValve

DEUTSCH[1] 7 years



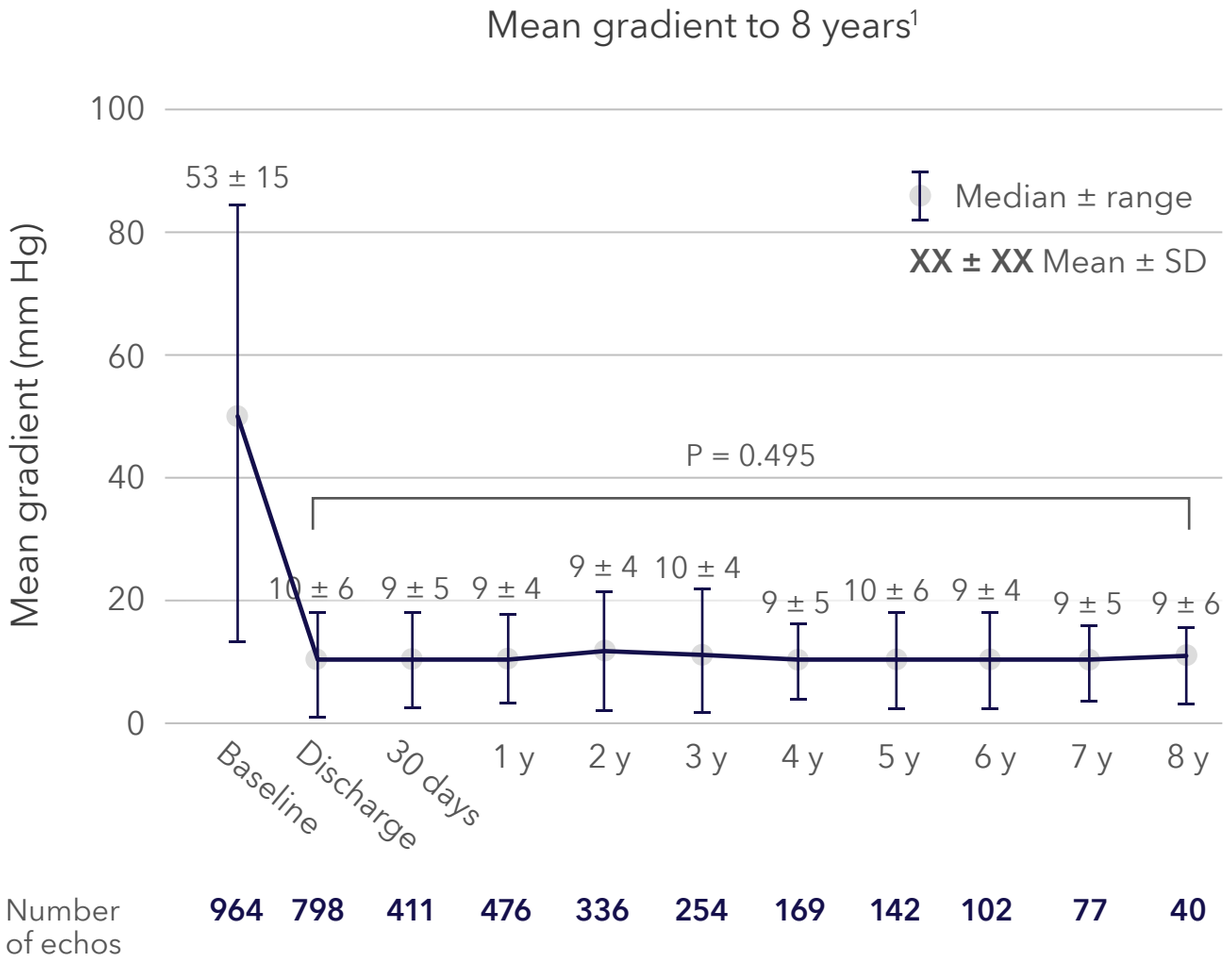
Retrospective analysis from a single-center registry

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] 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.

See the CoreValve™ Evolut™ R, the CoreValve™ Evolut™ PRO and the Evolut™ PRO+ device manuals for detailed information regarding the instructions for use, the implant procedure, indications, contraindications, warnings, precautions, and potential adverse events. For further information, contact your local Medtronic representative and/or consult the Medtronic website at medtronic.eu.

For applicable products, consult instructions for use on manuals.medtronic.com. Manuals can be viewed using a current version of any major internet browser.

For best results, use Adobe Acrobat® Reader with the browser.

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

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Evolut™ first

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The hemodynamic performance of the supra-annular TAVI platform

8-year data from the NOTION trial[1]

In a recent update from the NOTION trial on patients at lower surgical risk over the age of 70, we continue to see statistically better hemodynamics versus surgery – as well as a promising signal of durability.

Findings from 8-year follow-up of the NOTION trial[1]

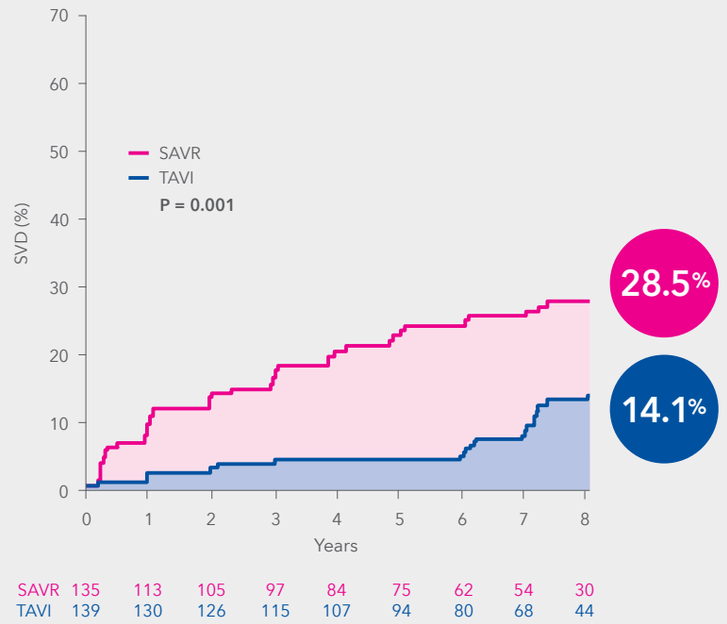
- CoreValve™ hemodynamics were statistically better versus surgery out to 8 years.
- CoreValve structural valve deterioration (SVD) was statistically better than surgery out to 8 years.

Structural valve deterioration (SVD)[2]

- 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)*

Half the rate of SVD versus surgery

SVD out to 8 years



Designed to be durable.

Evolut™ first

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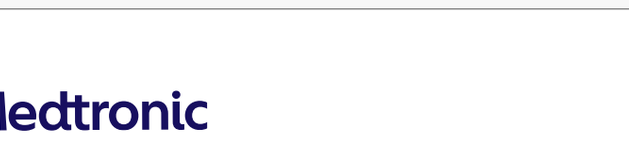
EVIDENCE UPDATE

Valve durability

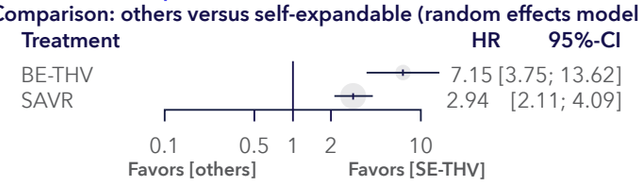
Valve durability for supra-annular, self-expandable TAV found to be statistically better at five years versus both SAVR and balloon-expandable TAV

Structural valve deterioration†

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™*.

Designed to be durable.

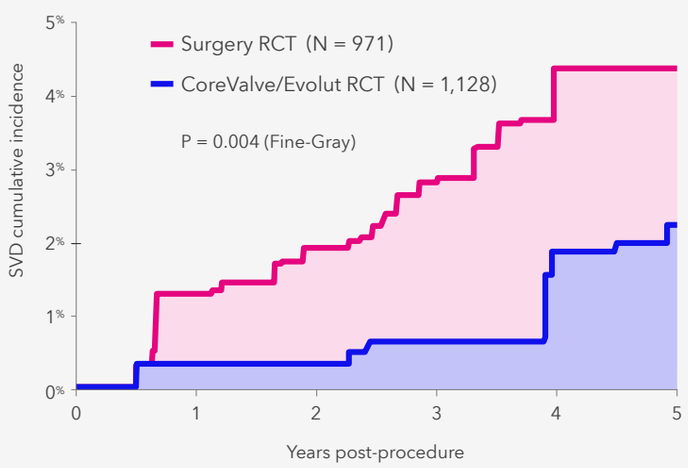
Evolut™ first

Medtronic

The best TAVI vs. SAVR durability data yet.

CoreValve™ and Evolut™ TAVI systems are the only platforms to demonstrate a durability benefit over SAVR at five years.[†1]

Valve durability is important to you and your patients. It's important to us too.



4.38%

2.20%

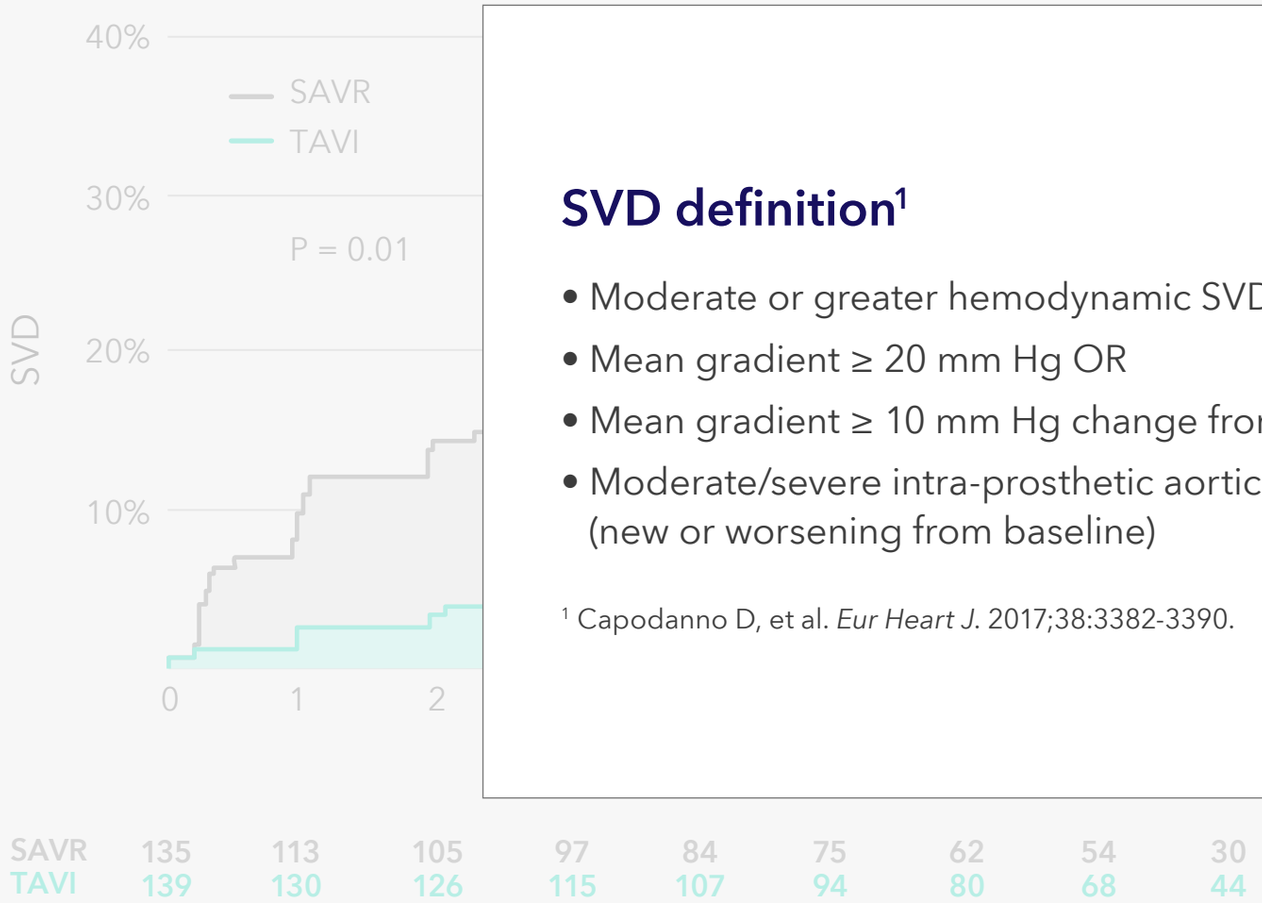
Medtronic TAVI platforms demonstrated significantly lower rates of structural valve deterioration (SVD)[‡] vs. SAVR at five years.

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.

NOTION[1] 8 years

SVD out to 8 years[1]



SAVR	135	113	105	97	84	75	62	54	30
TAVI	139	130	126	115	107	94	80	68	44

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The NOTION 8-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.

[1] Søndergaard L. Long-term follow-up of transcatheter and surgical bioprosthetic aortic valves in patients with severe aortic stenosis and lower surgical risk. Presented at PCR Valvese-Course; November 24, 2020.

oreValve™
rm was
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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

CoreValve™
and Evolut
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TAVI platfo
to demons
a lower SV
than SAVR.

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.

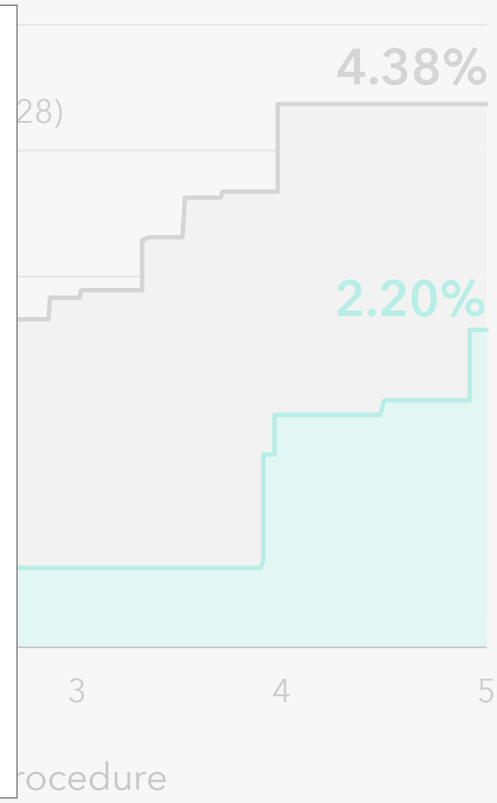
[1] Adapted from VARC-3 Writing Committee, et al. *Eur Heart J.* 2021;42:1825-1857.

SVD definition

Devices used:
88.5% CoreValve
11.5% Evolut R

CoreValve and Evolut pooled analysis:

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



[1] Reardon et al. 5-Year Incidence, Timing and Predictors of Structural Valve Deterioration of Transcatheter and Surgical Aortic Bioprostheses: Insights from the CoreValve US Pivotal and SURTAVI Trials. Presented at ACC 2022. Updated data on file.

Patients with S
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CoreValve™ and Evolut™ 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

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.

SVD definition

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

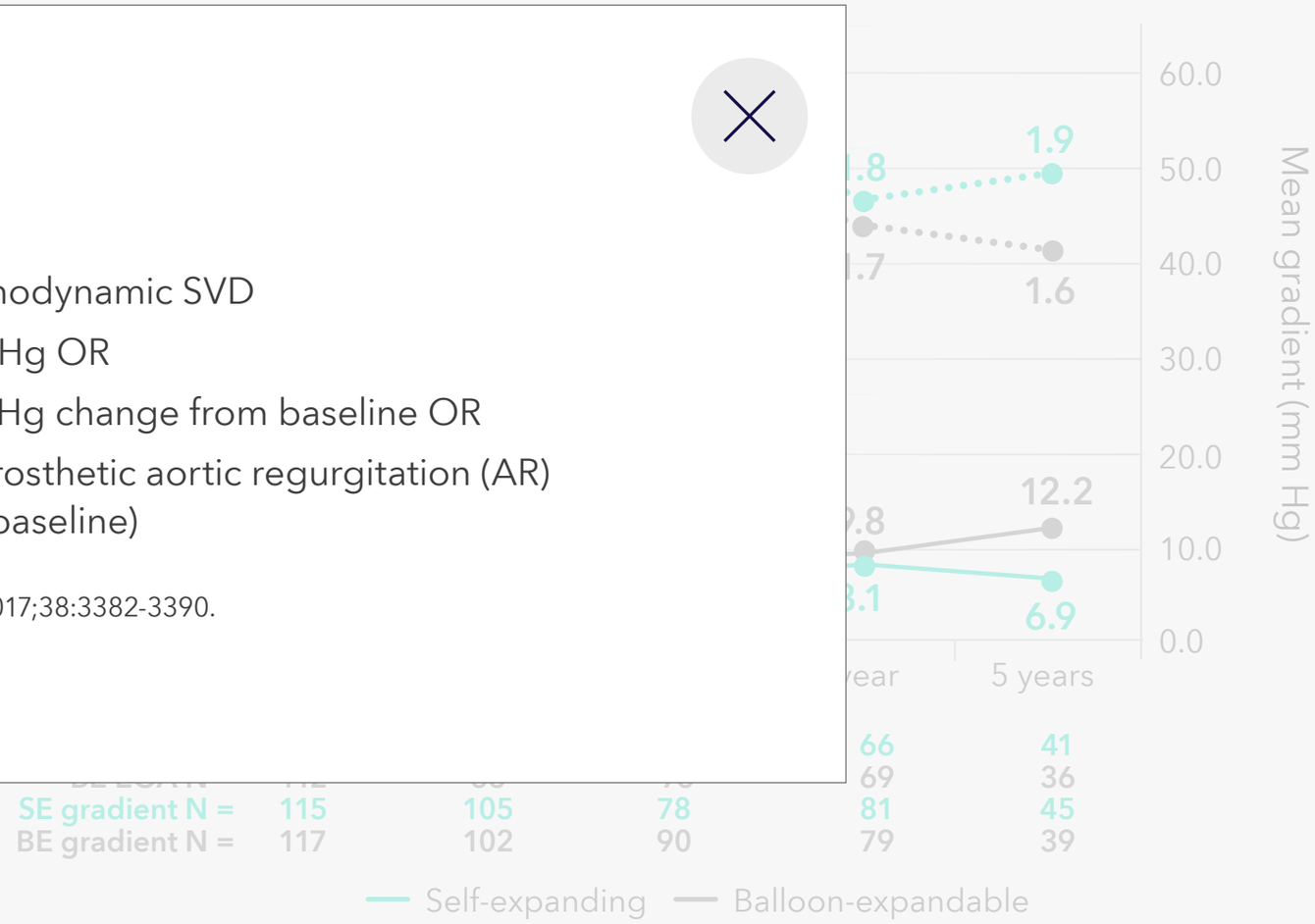
†All-cause mortality or aortic valve-related hospitalization.

[1] Reardon, et al. 5-Year Incidence, Timing and Predictors of Structural Valve Deterioration of Transcatheter and Surgical Aortic Bioprostheses: Insights from the CoreValve US Pivotal and SURTAVI Trials. Presented at ACC 2022. Updated data on file.

CoreValve™ TAV remain hemodyna stable at five years.

CHOICE[1] 5 years

Hemodynamics to 5 years[1]



For EOAs:
Baseline: p = 0.71
Post-TAVI: 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-TAVI: 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.

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.

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)

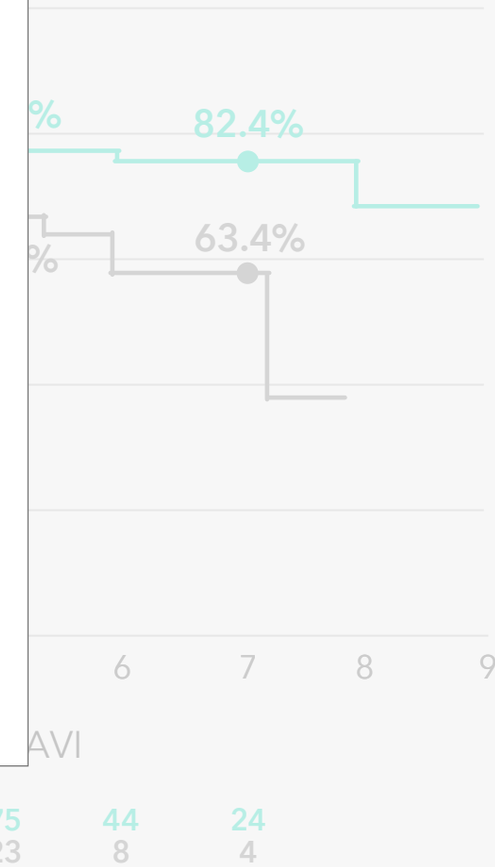
[1] Capodanno D, et al. *Eur Heart J*. 2017;38:3382-3390.

SVD definition

Device used:
100% CoreValve

DEUTSCH[1] 7 years

Freedom from SVD[1]



Patients at risk	214	147	121	106	93	75	44	24
	86	57	52	43	36	23	8	4

Retrospective analysis from a single-center registry

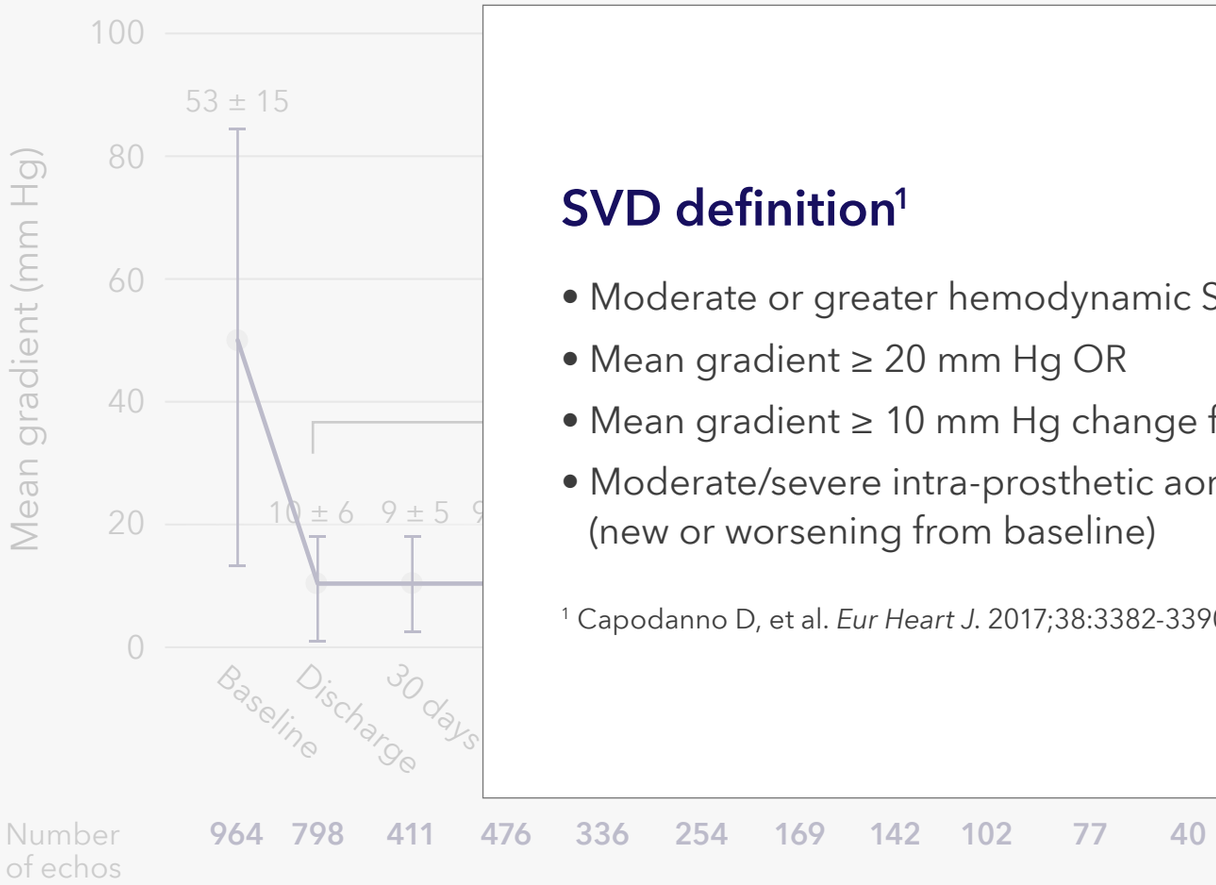
This chart clearly demonstrates significantly less SVD for CoreValve than SAPIEN out to 7 years. Freedom from SVD: 82.4% for CoreValve; 63.4% for SAPIEN.

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] 8 years

Mean gradient to 8 years[1]



SVD definition[1]

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

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Multicenter registry

Together with NOTION, this is the longest-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.