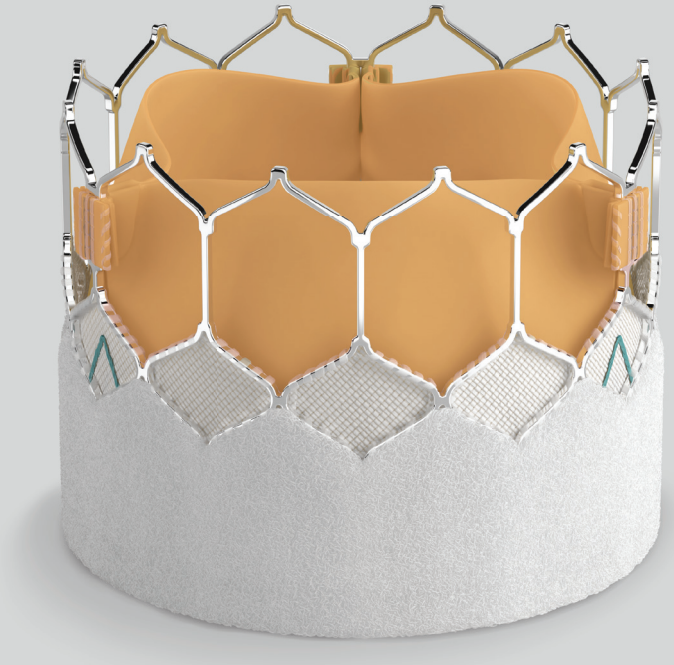
SAPIEN 3 Ultra RESILIA Transcatheter Heart Valve System

Value Analysis



Edwards

The Edwards SAPIEN 3 Ultra RESILIA transcatheter heart valve is transforming the therapy of aortic valve replacement

Disease overview

Severe aortic stenosis (AS) is a common disease and the majority of severe, symptomatic AS (sSAS) patients face a poor prognosis without treatment. Aortic valve replacement is the only effective treatment for severe, symptomatic AS. Both surgical and transcatheter options are available for many patients; a multi-disciplinary Heart Team will work with the patients and their family to determine the best choice for them.

Procedure therapy

Transcatheter aortic valve replacement (TAVI) is a less invasive procedure that does not require open heart surgery. The TAVI procedure can be performed through multiple approaches. The most common approach is the transfemoral approach.

Clinical study overview

The Edwards SAPIEN valve platform is the most widely studied transcatheter platform worldwide with over 25,000 patients enrolled in clinical studies and registries.

The PARTNER Trials, sponsored by Edwards Lifesciences, represent the largest, most rigorous comparative body of evidence in the history of aortic valve replacement. The PARTNER 3 Trial is an important randomized controlled trial (RCT) that compared TAVI, using the SAPIEN 3 valve, to surgical aortic valve replacement (SAVR) in low-risk patients. The SAPIEN 3 Ultra RESILIA valve, approved in 2022, is the most recently approved iteration of the SAPIEN 3 valve from Edwards Lifesciences.

The SAPIEN 3 Ultra RESILIA valve

The SAPIEN 3 Ultra RESILIA valve features bovine pericardial tissue treated with the proprietary RESILIA tissue treatment, the same trusted tissue that is featured today in the most widely implanted surgical aortic valve in the US. The frame of the SAPIEN 3 Ultra RESILIA valve is made from cobalt chromium alloy for high radial strength and fatigue resistance. The valve also features an inner and outer PET skirt designed to reduce paravalvular leak after implantation. Building on the SAPIEN 3 and SAPIEN 3 Ultra valves, the SAPIEN 3 Ultra RESILIA valve is designed with the future needs of patients in mind.

SAPIEN 3 Ultra RESILIA Valve

The SAPIEN 3 Ultra RESILIA valve is approved for use in severe, symptomatic aortic stenosis patients who are deemed to be appropriate for transcatheter heart valve replacement therapy.

Clinical, economic, and humanistic outcomes

In low-risk patients, TAVI with the SAPIEN 3 valve demonstrated 8.5% composite death, stroke, or rehospitalization* at one year compared with SAVR at 15.1%.

PARTNER 3 Trial Low-risk Data

1.0% **Death or Disabling Stroke at 1 Year†1**

TAVI Superior to Surgery[1]

For composite endpoint of death, stroke, or rehospitalization*

* Rehospitalization defined as valve-related or procedure-related and including heart failure.

† The PARTNER 3 Trial showed TAVI with SAPIEN 3 valve was superior to SAVR for the composite endpoint of death, stroke, or rehospitalization at one year. 1.0% death or disabling stroke was also an observed outcome in the PARTNER 3 Trial.

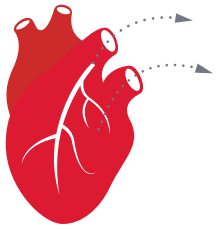
1. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve replacement with a Balloon-Expandable valve in low-risk patients. N Engl J Med. 2019;380(18):1695–1705.

Table of contents

Severe aortic stenosis is life-threatening and treatment is critical[1]

What is aortic stenosis (AS)?

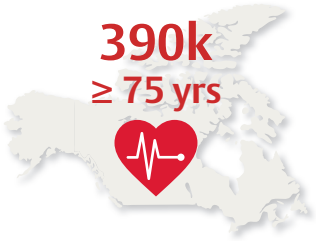
Aortic stenosis is a narrowing of the aortic valve opening, which restricts normal blood flow. As a result, the heart needs to work harder and may not pump enough oxygen-rich blood to the body.[2]



Over time, the leaflets become stiff, resulting in limitation of the normal opening during systole, causing stress and increasing the risk of heart failure.

Aortic stenosis is one of the most common and most serious valve disease problems[2]

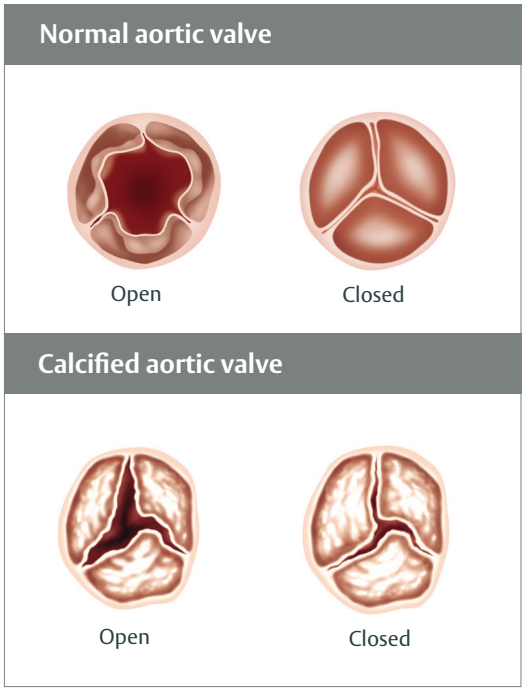
Approximately 390,000 people or 12.4% of the population over the age of 75 in Canada suffers from AS and this number is expected to increase as the aging population grows.[3,4]



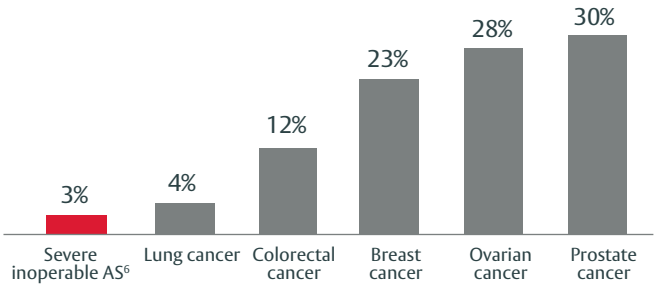
After the onset of symptoms, patients with **severe aortic stenosis have a survival rate as low as 50% at 1 year[5] and 20% at 5 years** without aortic valve replacement.[1]

Severe aortic stenosis has a worse prognosis than many metastatic cancers.[6]

Healthy and diseased aortic valves



5-year survival rate of distant metastatic lung cancer, colorectal cancer, breast cancer, ovarian cancer, prostate cancer, and severe, inoperable AS



1. Otto CM. Timing of aortic valve surgery. Heart. 2000;84:211-218.
2. http://www.heart.org/HEARTORG/Conditions/More/HeartValveProlemsandDisease/Problem-Aortic-Valve-Stenosis_UCM_450437_Article.jsp#.Vt4
3. Osnabrugge, Ruben L.J., et al. Aortic Stenosis in the Elderly Disease Prevalence and Number Candidates for Transcatheter Aortic Valve Replacement: A Meta Analysisand Modeling Study. J Am Coll Cardiol. 2013;62:1002-1012.
4. Statistics Canada. Population estimates on July 1st, by age and sex. 2022. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501
5. Leon, MB, et. al. Transcatheter Aortic-Valve Implantation for AS in Patients Who Cannot Undergo Surgery. N Engl J Med. 2010;363:1597-1607.
6. Using constant hazard ratio. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic.

Effective treatment of sSAS requires aortic valve replacement

How is aortic stenosis diagnosed?

Severe aortic stenosis is diagnosed several ways, including transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), cardiac catheterization, or cardiac magnetic resonance (CMR).

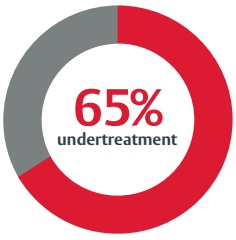
Aortic valve replacement (AVR) is the only effective treatment option for sSAS

There are two treatment options for patients with sSAS: TAVI and SAVR.

TAVI is a less invasive procedure that does not require open heart surgery. TAVI uses a catheter to replace the heart valve instead of opening the chest. The PARTNER 3 Trial has proven TAVI to be superior to surgery in low-risk patients for the primary endpoint of a composite of all-cause mortality, stroke, or rehospitalization* at 1 year, as well as 6 pre-specified secondary endpoints.[1]

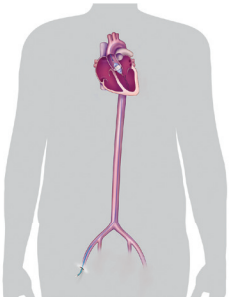
SAVR with a bioprosthetic or mechanical valve is an option for some patients. In this procedure, the heart valve is replaced through an open surgical incision in the chest.

Regardless of the procedure, AS remains an undertreated disease. Approximately 2/3 of sSAS patients remain untreated in the US.[2] In a UK study, 11.3% of people over the age of 65 who were registered in primary care centres (n - 2,500) had moderate to severe heart valve disease, but more than half of them had not been previously diagnosed.[3] Canada continues to struggle with inadequate access to primary care in many provinces and territories, likely creating a barrier to detection of heart valve disease.[4,5]



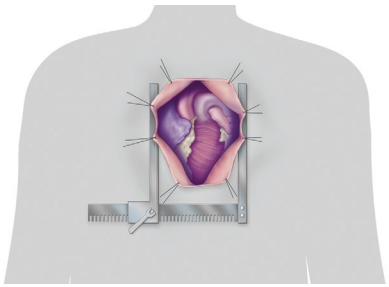
~2/3
of diagnosed sSAS patients remain untreated

Transcatheter aortic valve implantation (TAVI)



TAVI uses a catheter to insert a new valve within the native diseased aortic valve.

Surgical aortic valve replacement (SAVR)



SAVR through open heart surgery allows a new valve to be inserted within the native diseased aortic valve.

* Rehospitalization defined as valve-related or procedure-related and including heart failure.

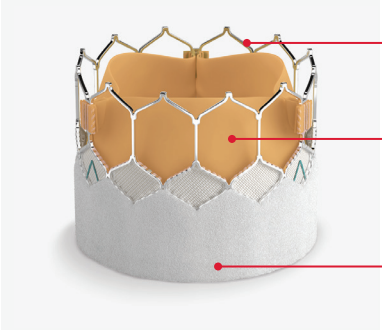
1. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380(18):1695-1705.
2. Brennan, M. Addressing the Undertreatment of Aortic Stenosis, Duke University School of Medicine. Presentation to American Association of Thoracic Surgery, 2019.
3. d'Arcy JL, Coffey S, Loudon MA, et al. 2016. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. Eur Heart J 37(47): 3515-22
4. Heart Valve Voice Canada. Working together to create a better patient journey. Feb 2022.
5. Peckham A, Ho J, Marchildon G. 2018. Policy Innovations in Primary Care Across Canada: A Rapid Review Prepared for the Canadian Foundation for Healthcare Improvement. Toronto: North American Observatory on Health Systems and Policies

The Edwards SAPIEN 3 Ultra RESILIA transcatheter heart valve was designed with patient needs in mind

SAPIEN 3 Ultra RESILIA valve

The SAPIEN 3 Ultra RESILIA valve is comprised of a balloon-expandable, radiopaque, cobalt-chromium frame, trileaflet bovine pericardial tissue, and polyethylene terephthalate (PET) fabric skirt. The valve leaflets are treated with the proprietary RESILIA technology. The valve design facilitates future coronary access*[1] through its low frame height, open-cell geometry, and intra-annular design for possible future interventions.

SAPIEN 3 Ultra RESILIA valve design



Cobalt-chromium frame
Designed for low delivery profile and high radial strength; facilitates future coronary access

Bovine pericardial tissue leaflets with RESILIA
Matched trileaflet design; RESILIA tissue treatment designed to enhance bioprosthetic valve durability

Inner and outer skirt
Engineered to reduce paravalvular leak (PVL) with maximized contact and sealing with the annulus

RESILIA tissue

40+ years of expertise in developing next-generation tissue solutions.

Neutralogic Fixation → XenoLogix Treatment → ThermaFix Process → RESILIA Tissue

RESILIA tissue valves are the first and only class of THV valves to deliver the combination of:

- Advanced calcium-blocking technology†[2]
- Potential to improve valve longevity and reduce reintervention†‡[2]
- The only THV with dry tissue storage, removing the need for glutaraldehyde storage

Complete range of valve sizes

Valve size	20 mm	23 mm	26 mm	29 mm
Native annulus size by TEE	16 – 19 mm	18 – 22 mm	21 – 25 mm	24 – 28 mm
Native annulus area (CT)	273 – 345 mm^2	338 – 430 mm^2	430 – 546 mm^2	540 – 683 mm^2
Area-derived diameter (CT)	18.6 – 21 mm	20.7 – 23.4 mm	23.4 – 26.4 mm	26.2 – 29.5 mm

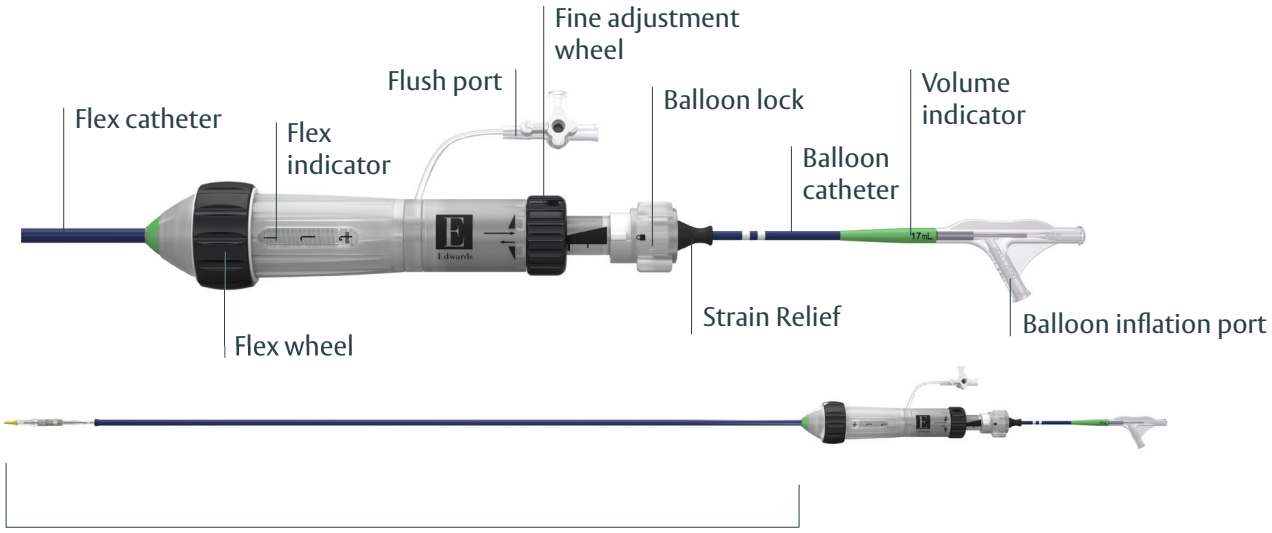
TEE: Transesophageal echocardiography
CT: Computed tomography

* 100% successful post-TAVI coronary access (68/68 patients)
† No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.
‡ RESILIA tissue tested against tissue from commercially available bovine pericardial valves from Edwards Lifesciences in a juvenile sheep model.
1. Tarantini G, et al. Coronary Access After TAVI with Commissural Alignment: The ALIGN-ACCESS Study. Cardiovascular Interventions.2022.
2. Flameng et al. A randomized assessment of an advanced tissue preservation technology in the juvenile sheep model. J Thorac Cardiovasc Surg. 2015;149:340–5.

The Edwards Commander delivery system is used for delivery of the Edwards SAPIEN 3 Ultra RESILIA valve

The Edwards Commander delivery system has several features designed for predictability and control during THV procedures. The Commander delivery system offers dual articulation for tracking and coaxiality and a balloon-expansion platform that delivers stable, precise deployment of the THV valve.

Edwards Commander delivery system



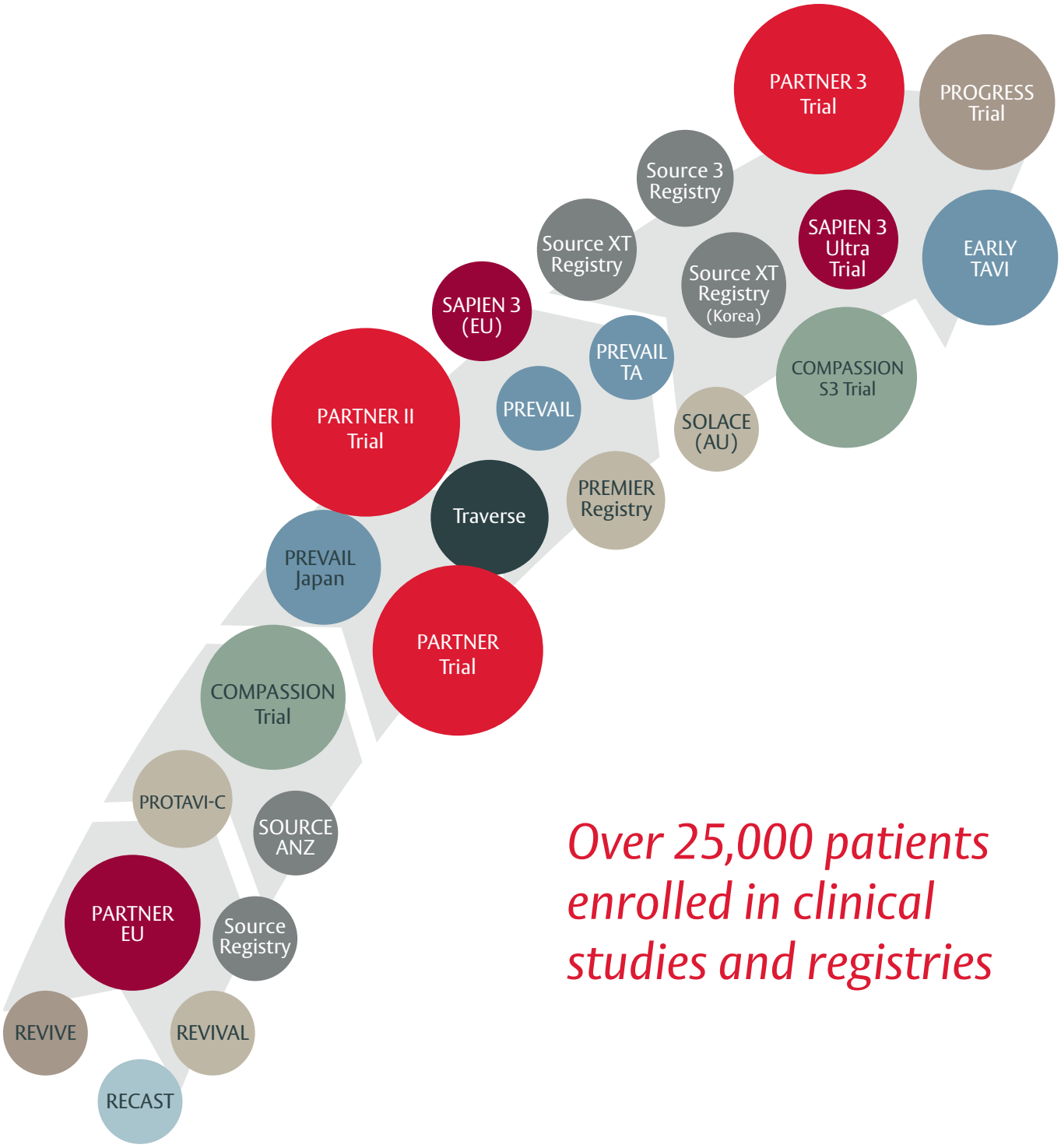
Edwards THV system price includes accessories

The Edwards transcatheter heart valve system kit includes the valve and the accessories required.

Device	Description
Edwards THV	SAPIEN 3 Ultra RESILIA valve
Delivery system	Edwards Commander delivery system
Crimper	Edwards Crimper
Sheath	Edwards eSheath+ introducer set
Inflation device	Inflation syringe (1 syringe)

The Edwards SAPIEN valve platform is the most clinically-studied transcatheter valve platform worldwide

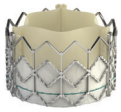
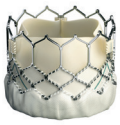
The SAPIEN valve clinical portfolio includes a full spectrum of clinical studies and registries from concept to long-term follow-up. Thousands of patients have received Edwards transcatheter heart valves through an extensive series of ongoing global studies that provide an evolving body of rigorous clinical evidence. To date, clinical studies have been conducted in over 25 countries.

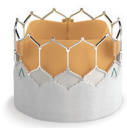


Over 25,000 patients enrolled in clinical studies and registries

The PARTNER Trials represent the largest, most rigorous comparative body of evidence in the history of aortic valve replacement

The PARTNER Trials are a series of landmark clinical trials sponsored by Edwards Lifesciences. Since 2007, thousands of patients in the United States and around the globe have participated in these trials, critical for establishing the clinical value of SAPIEN TAVI technology for treatment of severe, symptomatic aortic stenosis.

Product	Clinical study name	Clinical study date # of TAVI patients	Clinical study population†	HC approval date (device first issue date)	HC approved indication(s)
SAPIEN valve 	**PARTNER IB Trial**	**2007 - 2009** 179 patients	Inoperable	2011-06-22[1]	Discontinued
	PARTNER IA Trial	**2007 - 2009** 348 patients	High-risk		
SAPIEN XT valve 	**PARTNER IIB Trial**	**2011 - 2013** 282 patients	High-risk	2013-10-09[2]	Patients with symptomatic severe calcific aortic stenosis requiring aortic valve replacement (AVR), who have an estimated operative/procedural mortality risk ≥ 10% as assessed by a risk tool such as the Logistic EuroSCORE or STS-PROM.
	PARTNER IIA Trial	**2011 - 2013** 994 patients	Intermediate- risk		
SAPIEN 3 valve 	**PARTNER II S3 High-risk Trial**	**2013 - 2014** 583 patients	Inoperable and high-risk	2019-12-12[2]	Patients with heart disease due to native calcific aortic stenosis at any or all levels of surgical risk for open heart surgery. Patients with symptomatic heart disease due to a failing aortic bioprosthetic valve or a failing mitral surgical bioprosthetic valve who are judged by a heart team to be at high or greater risk for open surgical therapy.
	PARTNER II S3i Trial	**2014** 1,077 patients	Intermediate- risk		
	PARTNER 3 Trial	**2016 - 2017** 496 patients	Low-risk		

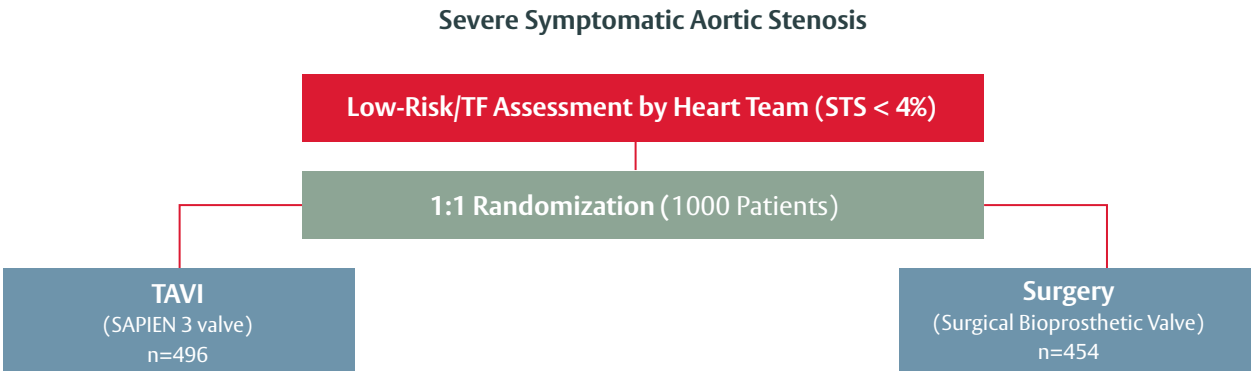
	Product	HC approval date (device first issue date)	HC approved indication(s)
SAPIEN 3 technology advancements	**SAPIEN 3 Ultra valve** 	2019-12-17[2]	Patients with heart disease due to native calcific aortic stenosis at any or all levels of surgical risk for open heart surgery. Patients with symptomatic heart disease due to a failing aortic bioprosthetic valve or a failing mitral surgical bioprosthetic valve who are judged by a heart team to be at high or greater risk for open surgical therapy.
	SAPIEN 3 Ultra RESILIA valve 	2023-07-06[2]	

Edwards data on file
† Surgical risk level noted in table only applicable for native aortic indication
1. Government of Canada: Archived Medical Device Licence Listing. Sept 2023.
2. Government of Canada: Active Medical Device Licence Listing. Sept 2023.

The PARTNER 3 Trial evaluated TAVI in low-risk patients

Study design

The PARTNER 3 Trial compared treatment with the SAPIEN 3 valve to surgery in low-risk patients with severe, symptomatic aortic stenosis. The primary endpoint was a composite of all-cause mortality, stroke, or rehospitalization* at 1 year. TAVI with the SAPIEN 3 valve achieved superiority, with a 46% reduction in the event rate for the primary endpoint of the trial. The study proved that TAVI with the SAPIEN 3 valve is superior to surgery on the primary endpoint and 6 additional pre-specified secondary endpoints.



Follow-up
30 days, 6 months, and annually through 10 years

Primary Endpoint
Composite of all-cause mortality, stroke, or rehospitalization* at 1 year post-procedure

Baseline patient characteristics of As-Treated (AT) populations

	PARTNER IA Trial High-risk[1] (n=657)	PARTNER IIA Trial Intermediate-risk[2] (n=1,938)	PARTNER 3 Trial Low-risk[3] (n=950)
Mean age	84	82	73
STS score	11.8	5.8	1.9
NYHA Class III/IV	94.5%	76.7%	27.7%
KCCQ Score	41.8	54.1	70.2
CAD	75.9%	67.8%	27.8%
Previous CABG	43.3%	24.6%	2.4%
COPD	43.7%	30.8%	5.6%
Permanent pacemaker	21.2%	11.8%	2.6%

Patients in the PARTNER 3 Trial are approximately 10 years younger with less comorbidities than those in previous PARTNER Trials

* Rehospitalization defined as valve-related, procedure-related or heart-failure-related.

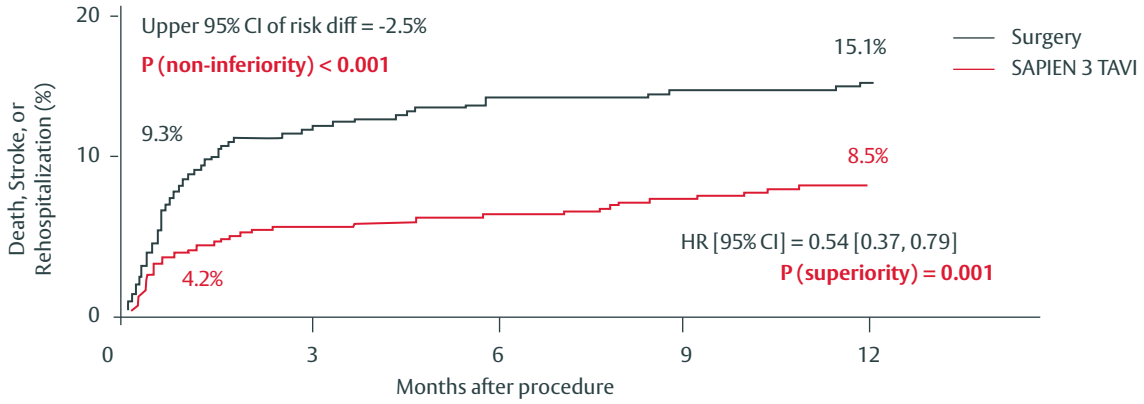
1. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011;364(23):2187-2198.
2. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016;374(17):1609-1620.
3. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380(18):1695-1705.

The Edwards SAPIEN 3 valve is the only valve proven superior to surgery for the outcomes that matter*

In a population of severe, symptomatic aortic stenosis patients who were at low surgical risk, TAVI compared to surgery demonstrated superiority in the primary endpoint and 6 pre-specified secondary endpoints, after first achieving non-inferiority.

The composite primary endpoint included death, stroke, or rehospitalization† and showed a significant reduction of 46% at both 30 days and 1 year compared to surgery. Multiple sensitivity analyses confirmed the robustness of the primary endpoint findings.

Secondary endpoints adjusted for multiple comparisons indicated that TAVI reduced new-onset atrial fibrillation, index hospitalization days, and a measure of poor treatment outcome (death or low KCCQ score at 30 days).



No. at risk:						
Surgery	454	408	390	381	377	374
SAPIEN 3 TAVI	495	475	467	462	456	451

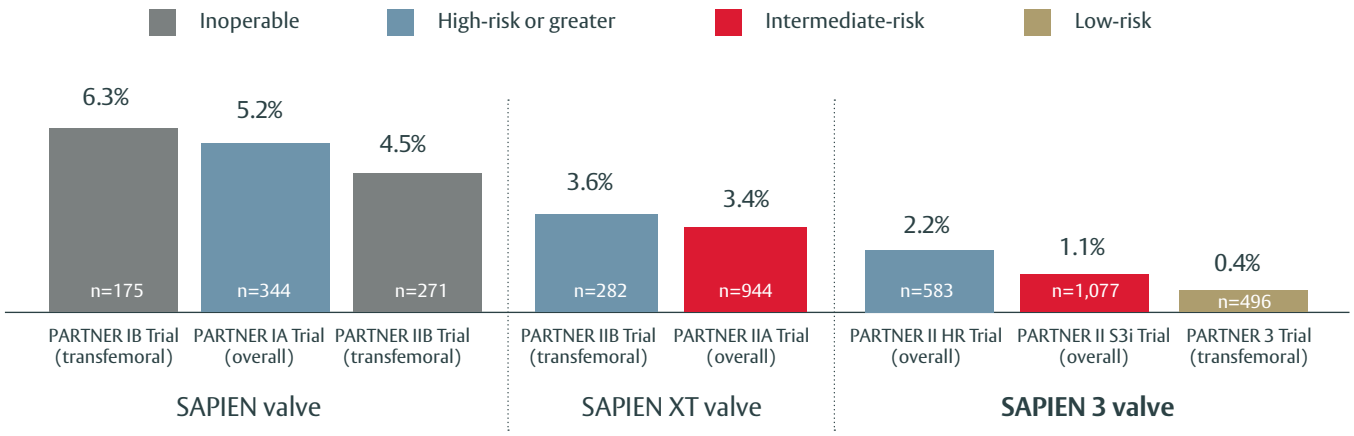
8.5% TAVI | **15.1%** SAVR

Death, stroke, or rehospitalization† at 1 year

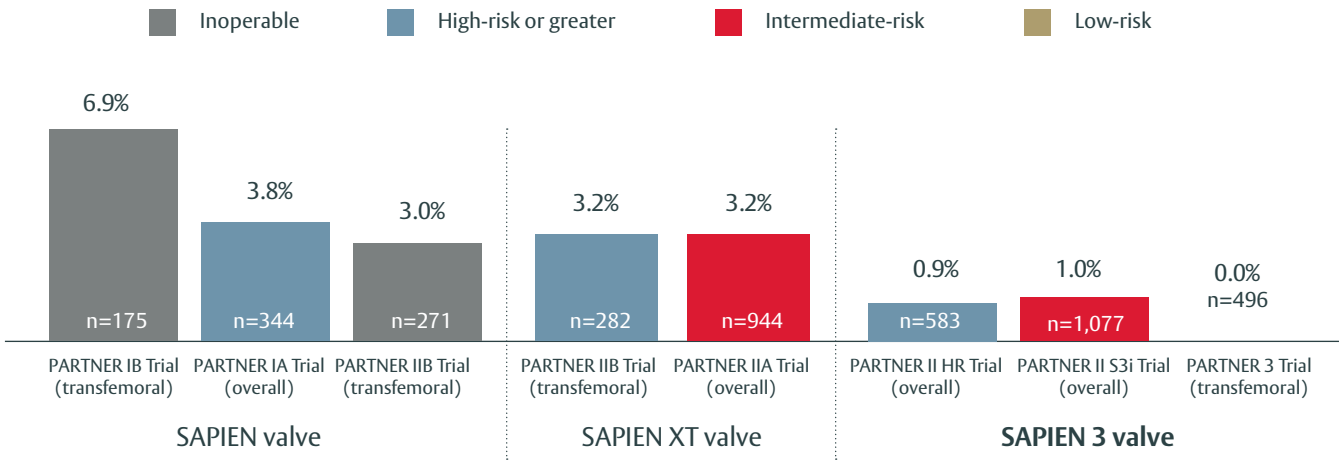
*The PARTNER 3 trial showed TAVI with SAPIEN 3 valve was superior to SAVR for the composite endpoint of death, stroke, or rehospitalization at one year. 1.0% death or disabling stroke was also an observed outcome in the PARTNER 3 Trial.
† Rehospitalization defined as valve-related or procedure-related and including heart failure.

The SAPIEN 3 valve builds on the clinical results of previous Edwards transcatheter valves

PARTNER Trial, PARTNER II Trial, and PARTNER 3 Trial 30-day mortality



PARTNER Trial, PARTNER II Trial, and PARTNER 3 Trial 30-day major[1] or disabling[2] stroke

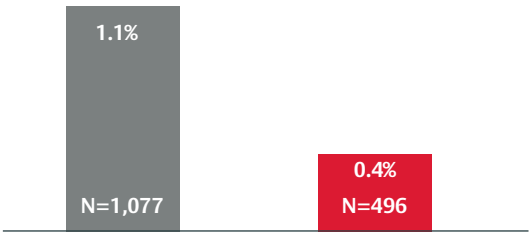


1. PARTNER Trial distinguished stroke severity through a CEC-adjudicated retrospective analysis of neurologic events. A major stroke was defined as a stroke associated with a modified Rankin Scale score of 2 or greater at 30 days or longer after the event.
2. PARTNER II Trial defined disabling stroke as a modified Rankin Scale score of 2 or more at either 30 days or 90 days after the index clinical event.

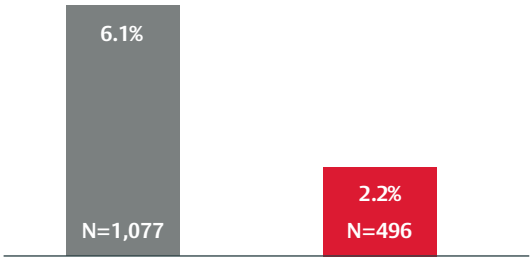
Improved outcomes in low-risk patients may further enhance economic value

In addition to clinical value, today's healthcare environment also demands economic value be taken into consideration. Improvements are demonstrated in several fundamental areas that drive economic value.

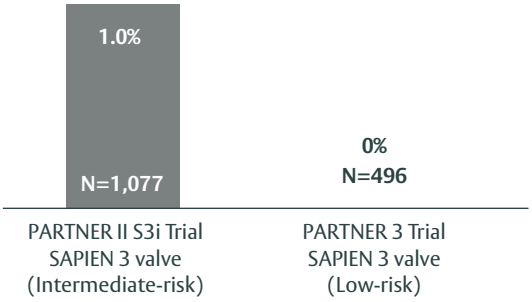
All-cause mortality at 30 days



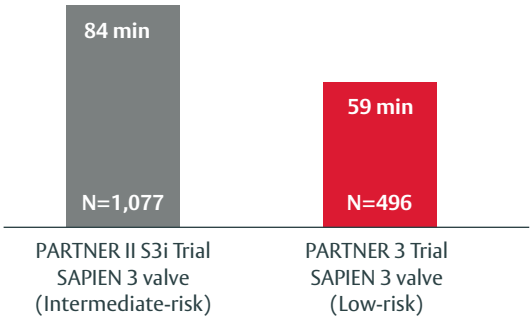
Major vascular complication at 30 days



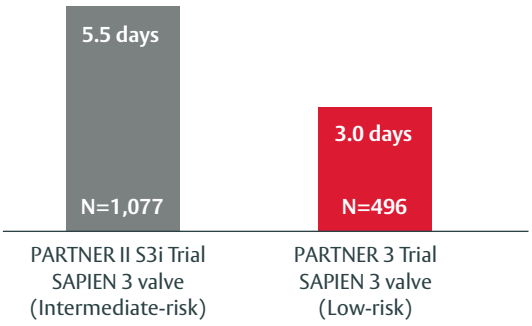
Disabling stroke at 30 days



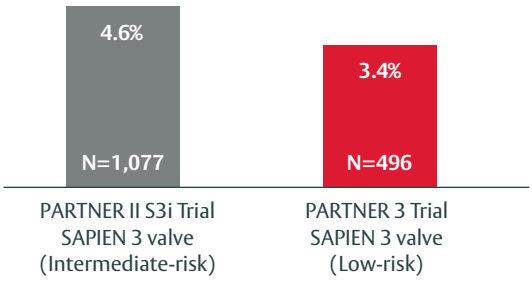
Total procedure time (min)



Mean length of stay (LOS)



Readmissions at 30 days*



* Readmission defined as valve related or procedure related and including heart failure.

1. Thourani V, Kodali S, Makkar R, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. Lancet. 2016;387(10034):2218-25.
2. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380(18):1695-1705.

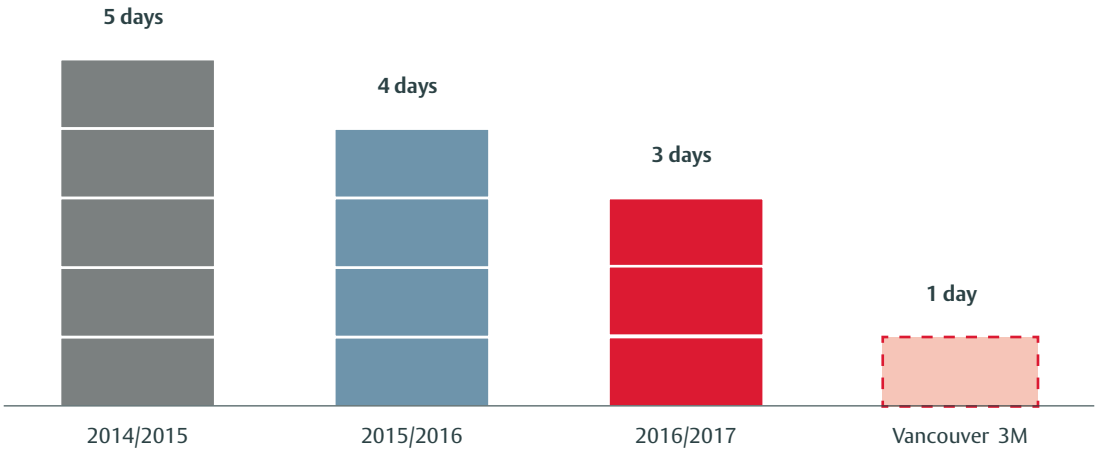
Length of Stay Reductions among Canadian TAVI patients

Length of stay (LOS) has been shown to be a cost driver for TAVI procedures. Patients undergoing TAVI who were discharged within 2 days of their procedure had a substantially lower cost compared with those with longer admissions.[3]

LOS continues to trend downwards through innovative clinical approaches

- Vancouver 3M (multidisciplinary, multimodality, but minimalist) clinical pathway study[4] found: 80% of patients could be discharged after 1 day and 90% could be discharged within 2 days
- At Health Sciences North in Sudbury, Ontario the median post-TAVI hospital length of stay decreased from 5 to 1 day after 3M clinical pathway implementation.[5]

Canadian real-world data shows significant reductions in LOS among TAVI patients[1,2]

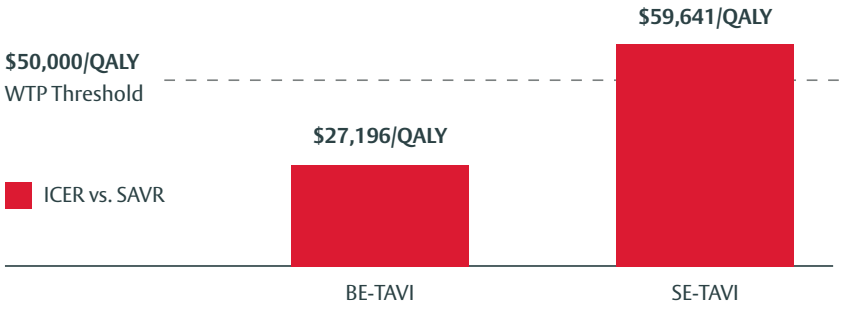


1. CCS. National Quality Report: Transcatheter Aortic Valve Implantation. 2019.
2. INESSS. Profil évolutif de l'utilisation et des résultats cliniques de l'implantation valvulaire aortique par cathéter (TAVI) et par voie chirurgicale (RVA) au Québec : évaluation en contexte réel de soins de 2013 à 2019. 2021.
3. Harindra et al. Drivers of healthcare costs associated with the episode of care for surgical aortic valve replacement versus transcatheter aortic valve implantation. 2016.
4. Wood et al. The Vancouver 3M (Multidisciplinary, Multimodality, But Minimalist) Clinical Pathway Facilitates Safe Next-Day Discharge Home at Low-, Medium-, and High-Volume Transfemoral Transcatheter Aortic Valve Replacement Centers: The 3M TAVR Study. 2019.
5. Hanna et al. The Safety of Early Discharge Following Transcatheter Aortic Valve Implantation Among Patients in Northern Ontario and Rural Areas Utilizing the Vancouver 3M TAVI Study Clinical Pathway. 2022.

The cost-effectiveness of TAVI

The cost-effectiveness of TAVI is influenced by the type of TAVI system utilized by the interventional cardiologist.[1]

A Canadian cost effectiveness analysis comparing TAVI vs. SAVR in low surgical risk patients with sSAS[2] demonstrated that BE-TAVI was less costly and more effective than SE-TAVI. In most cases, BE-TAVI was the preferred treatment option for sSAS patients at low risk.

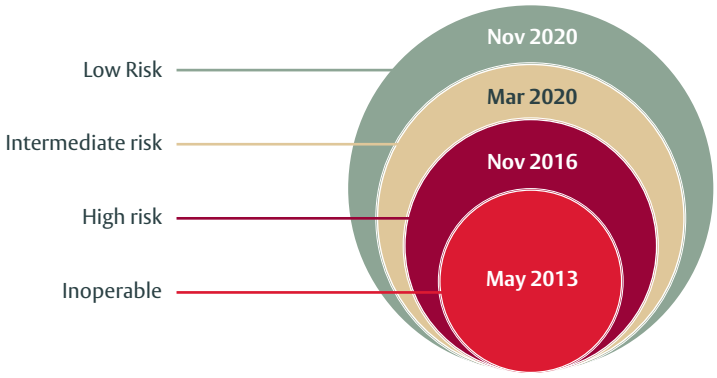


WTP = willingness to pay
TAVI = transcatheter aortic valve implantation
SAVR = surgical aortic valve replacement;
BE-TAVI = balloon expandable-TAVI
SE-TAVI = self-expandable-TAVI
ICER = incremental cost effectiveness ratio
QALY = quality adjusted life year
LOS = length of stay

Notably, the cost-effectiveness analysis assumed a LOS of 5 days. The average real-world Canadian LOS was reported to be 3 days in 2016/17 and has continued to trend downwards. As a result, it is likely that the cost effectiveness of BE-TAVI has further improved.

TAVI Cost Effectiveness Assessments

Clinical and cost effectiveness of TAVI has been assessed extensively by the Ontario Health Technology Advisory Committee (OHTAC) who have issued positive recommendations on the funding of TAVI for patients with severe aortic stenosis at **all surgical risk levels**.



In 2023, TAVI procedure should be funded for patients with severe aortic stenosis at all surgical risk levels

1. CADTH. Transcatheter Aortic Valve Implantation for Patients with Severe Symptomatic Aortic Stenosis. 2021.
2. Tam et al. The cost-effectiveness of transcatheter aortic valve replacement in low surgical risk patients with severe aortic stenosis. 2021.
3. OHTAC. Transcatheter Aortic Valve Implantation in Patients With Severe Aortic Valve Stenosis at Low Surgical Risk. 2020.
4. OHTAC. Transcatheter Aortic Valve Implantation in Patients With Severe, Symptomatic Aortic Valve Stenosis at Intermediate Surgical Risk. 2020.
5. OHTAC. Transcatheter Aortic Valve Implantation for Treatment of Aortic Valve Stenosis. 2016.
6. OHTAC. Transcatheter Aortic Valve Implantation for Treatment of Aortic Valve Stenosis: An Evidence Update. 2013.

Canadian Health Technology Assessments

HTA Agency	Title; date of publication	Key Findings
CADTH[1]	Transcatheter Aortic Valve Implantation for Patients with Severe Symptomatic Aortic Stenosis; July 2021.	The cost-effectiveness of TAVI compared to SAVR was examined in patients with severe symptomatic aortic stenosis at high, intermediate, and low surgical risk. The cost-effectiveness was influenced by the type of TAVI system used, the cost of treatment-associated expenses (such as post-operative follow-up costs and hospitalization costs), and the characteristics of patients selected for treatment.
OHTAC[2]	Transcatheter Aortic Valve Implantation in Patients With Severe Aortic Valve Stenosis at Low Surgical Risk; November 2020.	Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding transcatheter aortic valve implantation in adults with severe aortic valve stenosis who are at low surgical risk
OHTAC[3]	Transcatheter Aortic Valve Implantation in Patients With Severe, Symptomatic Aortic Valve Stenosis at Intermediate Surgical Risk; March 2020.	The Quality business unit at Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding transcatheter aortic valve implantation (TAVI) in patients with severe, symptomatic aortic valve stenosis who are at intermediate surgical risk.

INESSS[4]	Quality Standards for Transcatheter Aortic Valve Implantation (TAVI) in Québec; November 2017.	In the context of limited resources, it is up to the multidisciplinary team to use its judgment when making recommendations and give priority to patients for whom TAVI remains the only treatment option. It is advisable to avoid performing TAVI on patients who are not likely to see an improvement in their life expectancy and quality of life. This refers to patients for whom, even if the procedure is successful:
		• life expectancy is less than one year;
		• it is anticipated that there is a low probability of improving quality of life and/or life expectancy.
		
		Based on all the information gathered, the multidisciplinary TAVI team should:
		• determine the risk-benefit ratio for each treatment option;
		• document the surgical risk (low, intermediate, high, prohibitive);
		• propose one of the following three treatment options:
		  • surgical aortic valve replacement
		  • transcatheter aortic valve implantation;
		  • medical treatment.

OHTAC[5]	Transcatheter Aortic Valve Implantation for Treatment of Aortic Valve Stenosis; November 2016.	The Ontario Health Technology Advisory Committee recommends that transcatheter aortic valve implantation be publicly funded in patients with severe symptomatic degenerative aortic valve stenosis: • Who are not candidates for surgical aortic valve replacement or • Who have an estimated risk of mortality of 8% or greater within 30 days of surgery, as determined by a multidisciplinary cardiac team after evaluating the patient's Society of Thoracic Surgeons risk assessment score and other patient characteristics. The Ontario Health Technology Advisory Committee recommends that transcatheter aortic valve implantation be offered only in selected hospitals, as determined by the Cardiac Care Network of Ontario.

1. CADTH. Transcatheter Aortic Valve Implantation for Patients with Severe Symptomatic Aortic Stenosis. 2021.
2. OHTAC. Transcatheter Aortic Valve Implantation in Patients With Severe Aortic Valve Stenosis at Low Surgical Risk. 2020.
3. OHTAC. Transcatheter Aortic Valve Implantation in Patients With Severe, Symptomatic Aortic Valve Stenosis at Intermediate Surgical Risk. 2020.
4. INESSS. Quality Standards for Transcatheter Aortic Valve Implantation (TAVI) in Québec. 2017.
5. OHTAC. Transcatheter Aortic Valve Implantation for Treatment of Aortic Valve Stenosis. 2016.

Minimizing post-TAVI permanent pacemaker implantation (PPI) may yield substantial cost-savings to hospitals

The use of a self-expanding valve is a predictor for PPI in TAVI patients

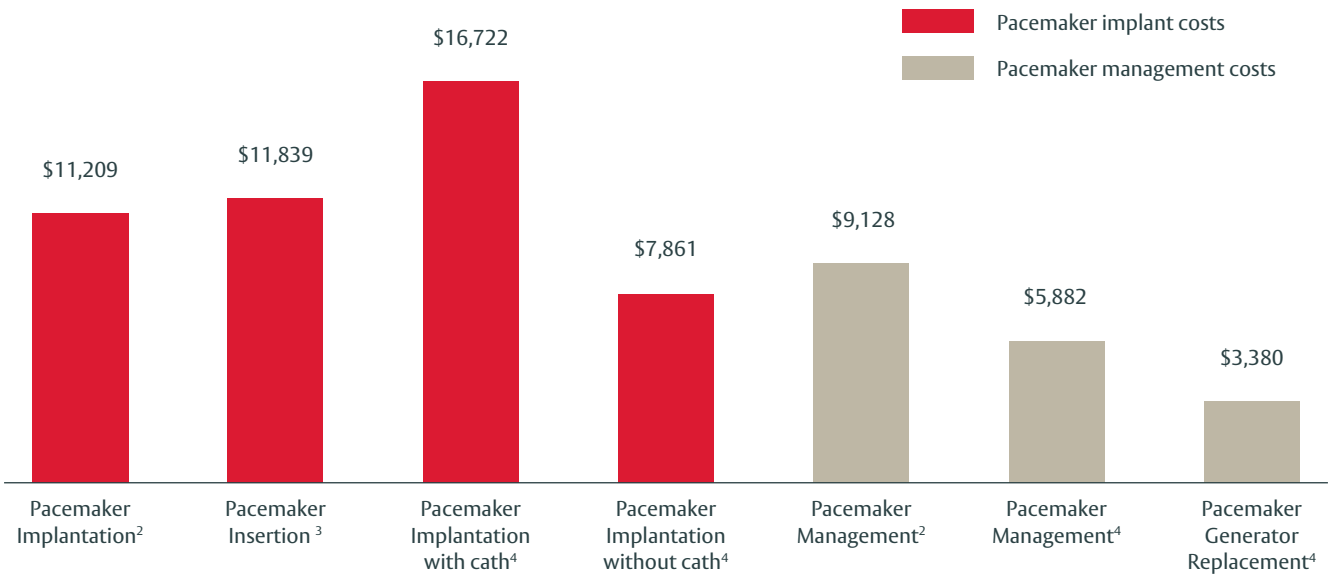
Analysis From the U.S. Society of Thoracic Surgeons/American College of Cardiology TVT Registry

Patient cohort	PPI rate
Overall	6.7%
Balloon-expanding valve	4.3%
Self-expanding valve	25.1%
Odds ratio (95% CI) of PPI. Self-expanding valve vs. balloon expanding valve	**7.56 (5.98-9.56)**

Consistent with previously reported studies, we found absence of prior aortic valve procedure, prior conduction abnormalities, transapical or transaortic access, and use of a self-expanding [valve] to be associated with increased odds of permanent pacemaker placement in multivariate analysis.[1]

PPI rate following TAVI is associated with incremental hospital cost

Cost of pacemaker implantation and management in Canada[2,3,4]



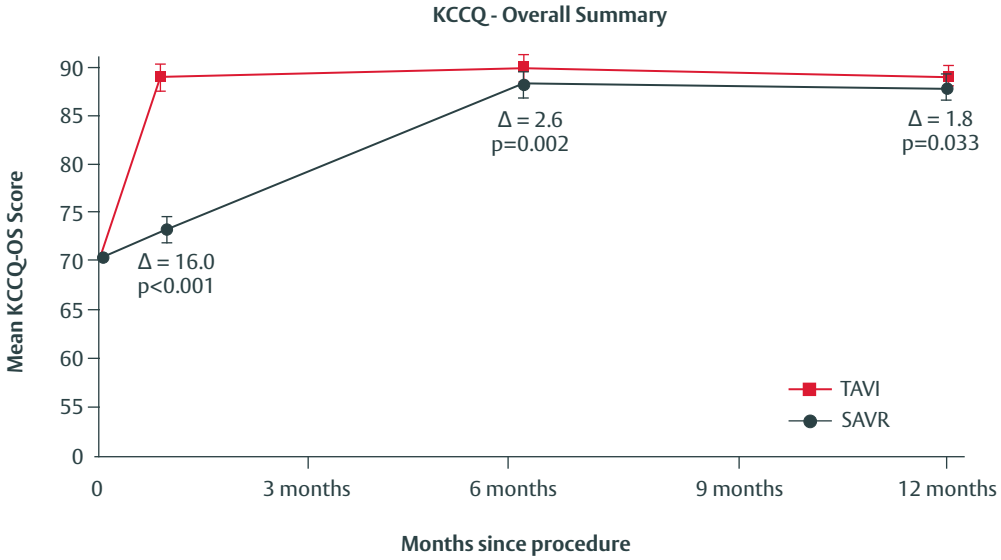
1. Fadahunsi, Opeyemi O., et al. Incidence, predictors, and outcomes of permanent pacemaker implantation following transcatheter aortic valve replacement: analysis from the US Society of Thoracic Surgeons/American College of Cardiology TVT Registry. JACC: Cardiovascular Interventions 9.21 (2016): 2189-2199.
2. CIHI Patient Cost Estimator. 2020.
3. Tam et al. The cost-effectiveness of transcatheter aortic valve replacement in low surgical risk patients with severe aortic stenosis. 2021.
4. Ontario Cardiac Volume Tool. 2023.

The SAPIEN 3 valve has demonstrated substantial early quality of life benefits compared to surgery

As part of the PARTNER 3 Trial, health-related quality of life (QOL) was captured as a secondary endpoint for all patients enrolled in the study. Health-related QOL was measured using the Kansas City Cardiomyopathy Questionnaire (KCCQ), a survey instrument developed to evaluate health status in heart failure patients that has been validated for AS patients. KCCQ scores are measured on a scale of 0 – 100 with higher scores equating to better health status.

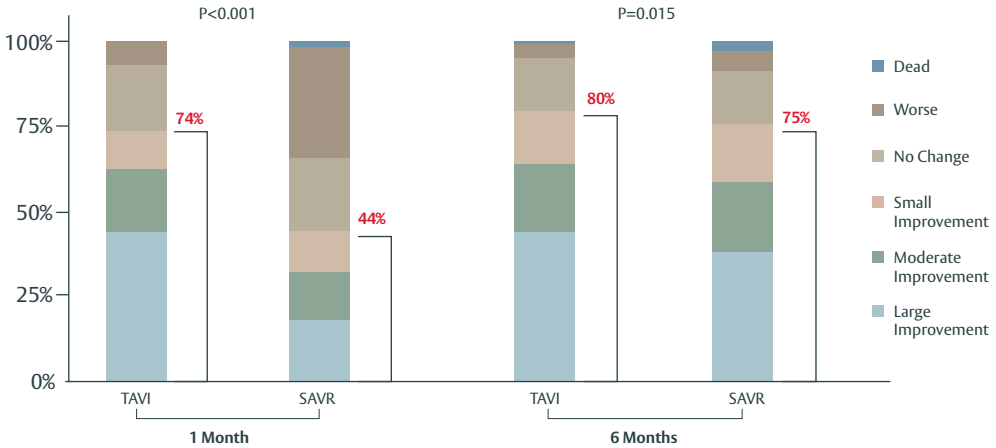
A sub-study analysis was conducted to compare the health status of TAVI with the SAPIEN 3 valve vs. SAVR in severe AS patients with low surgical risk. Health status was assessed using KCCQ at baseline and at 1, 6, and 12 months. TAVI demonstrated substantial early QOL benefits compared with SAVR.[1]

PARTNER 3 Trial KCCQ: TAVI compared to SAVR at 1 year



When compared with patients receiving SAVR, TAVI with the SAPIEN 3 valve was associated with significantly better early health status at 1 month. At 6 and 12 months, this benefit difference (albeit modest) persisted.

Proportion of patients achieving specific levels of change in the KCCQ-OS after TAVI or SAVR



When death and QOL were combined, TAVI demonstrated significant benefits at 1 and 6 months.

1. Baron, SJ, et al. Health Status After Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients With Aortic Stenosis. J Am Coll Cardiol. 2019;74(23): 2833-2842.

Edwards is the worldwide leader in heart valve innovation

Over 60 years of experience in heart valve therapy
Edwards Lifesciences has over 60 years of continuous refinement in structural heart valve technology and successful collaboration in device development with clinicians.

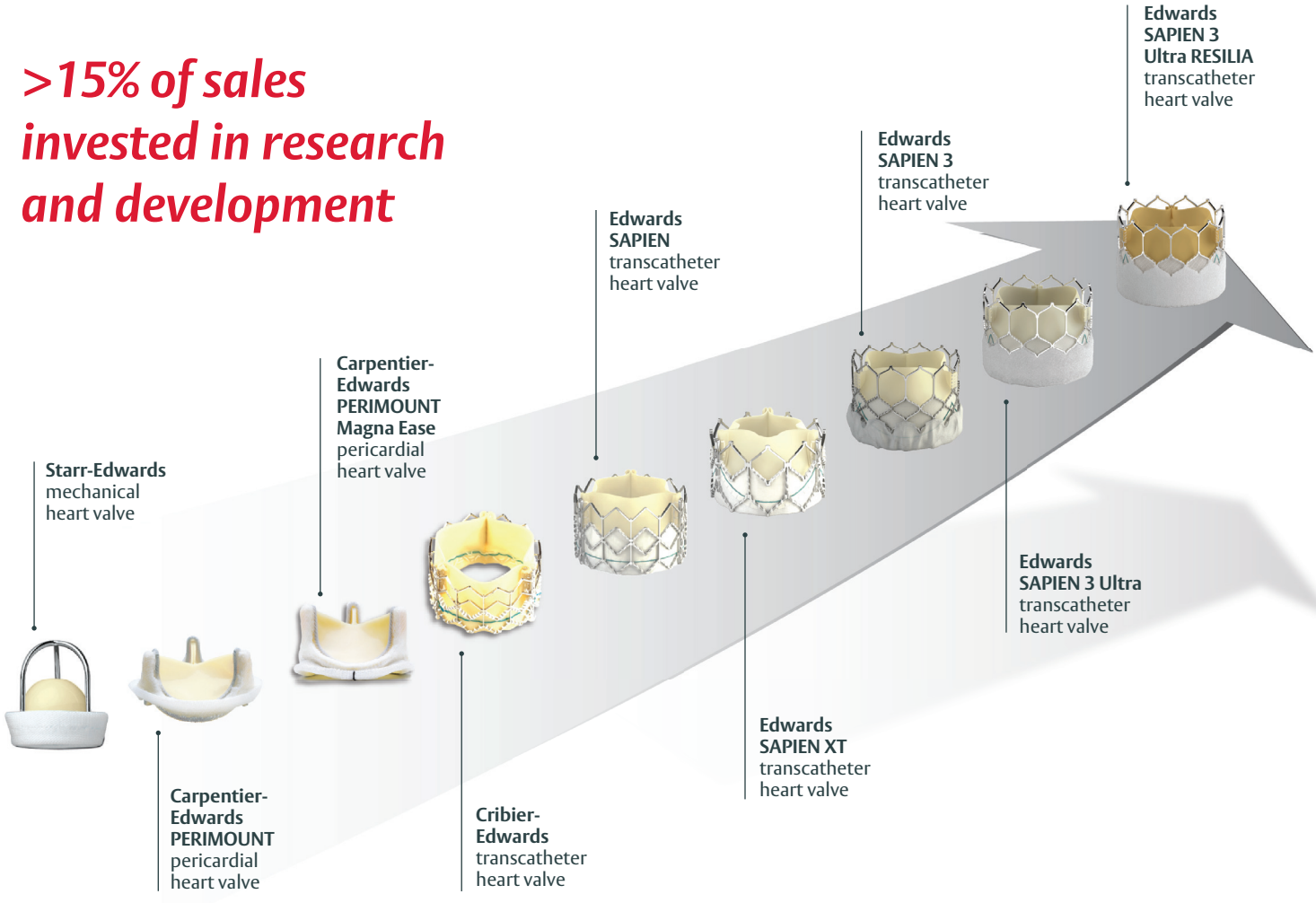
A leader in transcatheter aortic valve replacement
Edwards' first transcatheter heart valve was approved commercially in Europe in 2007 and in the United States in 2011. To date, Edwards' transcatheter heart valves have treated more than 760,000 patients in more than 70 countries across the world.

Legacy of experience
TAVI is an approved treatment option in severe, symptomatic AS patients who are deemed to be appropriate for transcatheter heart valve replacement therapy.

In low-risk patients, TAVI with the SAPIEN 3 valve is superior to surgery, demonstrating 8.5% composite all-cause mortality, stroke, or rehospitalization* at one year for TAVI compared to 15.1% for SAVR.[1]

Since the first TAVI, performed in 2002, the procedure and technology continues to be refined, resulting in improved clinical, economic, and humanistic outcomes.

>15% of sales invested in research and development

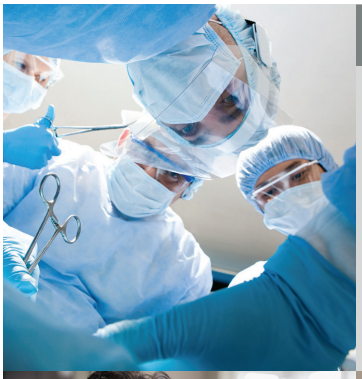


*Rehospitalization defined as valve-related or procedure-related and including heart failure.
1. The PARTNER 3 Trial showed TAVI with the SAPIEN 3 valve was superior to SAVR for the composite endpoint of death, stroke, or rehospitalization at one year.

Edwards is committed to supporting patients, hospitals, and healthcare providers

Edwards Lifesciences is the global leader of patient-focused innovations for structural heart disease and critical care monitoring. We are driven by a passion for patients, dedicated to improving and enhancing lives through partnerships with clinicians and stakeholders across the global healthcare landscape.

Edwards provides essential training on the safe and effective use of its technology, and educational resources that benefit TAVI patients.



Advancing the TAVI Heart Team

- Fundamentals training
- Advanced imaging programs
- Procedure optimization
- Valve clinic coordinator / training and resources
- Fellows programs
- Online training
- Best in Class Educational Programs: TAVI Development Program, TAVI Today, CT Sizing Program, Benchmark Program

Increasing therapy & patient awareness

- Therapy awareness education programs
- NewHeartValve.com
- Educational materials for patients, caregivers, and referrers
- Hospital education and outreach materials

Optimizing procedural outcomes

- Edwards Benchmark Program
- Patient screening support
- Clinical best practices
- Procedure proctoring
- Clinical case support
- Imaging education and proctoring

Edwards is committed to transforming patient care through innovative technology

Edwards is driven by a passion to help patients, partnering with clinicians to develop innovative technologies in the areas of structural heart disease and critical care monitoring. Edwards puts patients first and develops medical devices that transform the patient experience and improve outcomes.

Edwards has leveraged its knowledge and experience from its heart valve portfolio to develop and optimize transcatheter heart valves resulting in the SAPIEN 3 heart valve. Delivered with a minimally invasive approach, the SAPIEN 3 valve has been shown to improve quality of life as soon as 30 days post-procedure. Patients had improvements with anxiety, experienced less pain, and were able to better care for themselves.

Dawn is a 78-year-old who was diagnosed with aortic stenosis but was not told she needed a procedure until years later when she needed to have surgery on her foot. A heart murmur was detected by the anesthesiologist during a pre-op appointment and she needed to have this treated before they could proceed with her foot surgery. She thought her shortness of breath was related to her getting older. Dawn did some research on the internet to understand both open-heart surgery and a TAVI procedure. During a visit to the hospital, she met with the Heart Team and heard from the interventional cardiologist and the surgeon about the treatment options. Dawn chose TAVI! Dawn was release the next day after her TAVI procedure and eventually went on to have her foot surgery. She recently went for a check up with her cardiologist and was happy to be told “now you have a quiet heart”.

Marie is an elderly aortic stenosis patient who is the primary caregiver of her husband that has been diagnosed with early stages of dementia. Open-heart surgery would require Marie to spend up to 3 months away from her husband so she was keen to explore minimally invasive options that would permit her to return to her husband's care as soon as possible. After having a discussion with her Heart Team, Marie decided to undergo a TAVI procedure. She was discharged from the hospital 1 day after her procedure and back to her normal activities by the third post-operative day. Since Marie was 15 years old, she had a dream to skydive, so on her 80th birthday which was 1 year after her TAVI procedure she decided to jump out of a plane inspiring her friends and family to live life to the fullest no matter what your age.

To learn more about these TAVI patient stories below and others, visit NewHeartValve.com/patient-stories.

Important safety information

For professional use. For a listing of indications, contraindications, precautions, warnings, and potential adverse events, please refer to the Instructions for Use (consult eifu.edwards.com where applicable).

Regulatory

Edwards' first transcatheter heart valve was approved commercially in Europe in 2007 and in the United States in 2011. To date, Edwards' transcatheter heart valves have treated more than 760,000 patients in over 70 countries around the world.

November 2011
SAPIEN valve approved for inoperable patients via the transfemoral approach

October 2012
SAPIEN valve approved for high-risk patients via transfemoral and transapical/transaortic approaches

July 2013
Ascendra 3 delivery system approved

September 2013
SAPIEN valve approved for all access approaches

June 2014
SAPIEN XT valve approved for high-risk patients for all access approaches

June 2015
SAPIEN 3 valve with Edwards Commander delivery system approved for high or greater risk patients

October 2015
SAPIEN XT valve approved for aortic valve-in-valve procedures

February 2016
SAPIEN XT valve approved for transcatheter pulmonic valve replacement procedures

August 2016
SAPIEN 3 valve approved for intermediate-risk patients for all access approaches

June 2017
SAPIEN 3 valve approved for aortic and mitral valve-in-valve procedures in high or greater risk patients

December 2018
SAPIEN 3 Ultra valve approved for intermediate-risk or greater patients for all access approaches

August 2019
SAPIEN 3 valve and SAPIEN Ultra valve with Edwards Commander delivery system approved for low-risk patients

July 2022
SAPIEN 3 Ultra RESILIA valve approved for severe symptomatic aortic stenosis patients

Use this space to take notes, capture thoughts, or write down new contact information.

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