

Transforming the Treatment of Aortic Valve Disease



Edwards

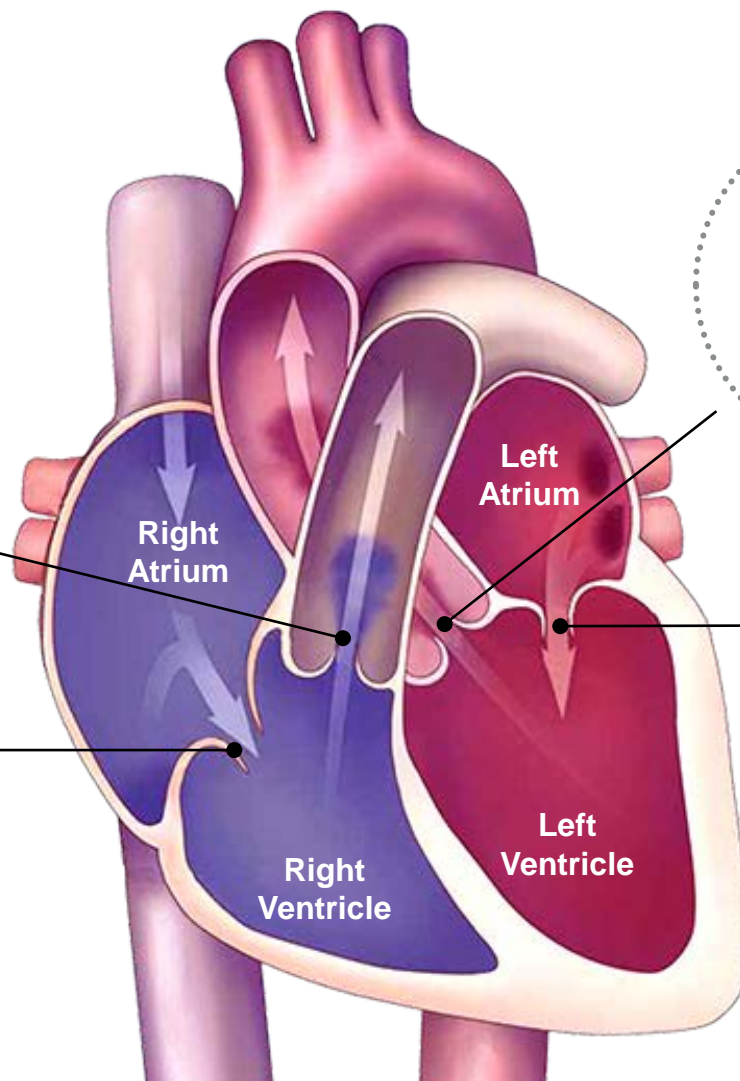
How Do Your Heart Valves Work?

Pulmonary Valve

Has three leaflets.
It controls blood flow from the right ventricle to the pulmonary artery, sending blood to the lungs to pick up oxygen.

Tricuspid Valve

Has three leaflets.
It controls blood flow from the right atrium to the right ventricle



Aortic Valve

Has three leaflets.
It controls blood flow from the left ventricle to the aorta, sending blood to the rest of the body.

Left
Atrium

Mitral Valve

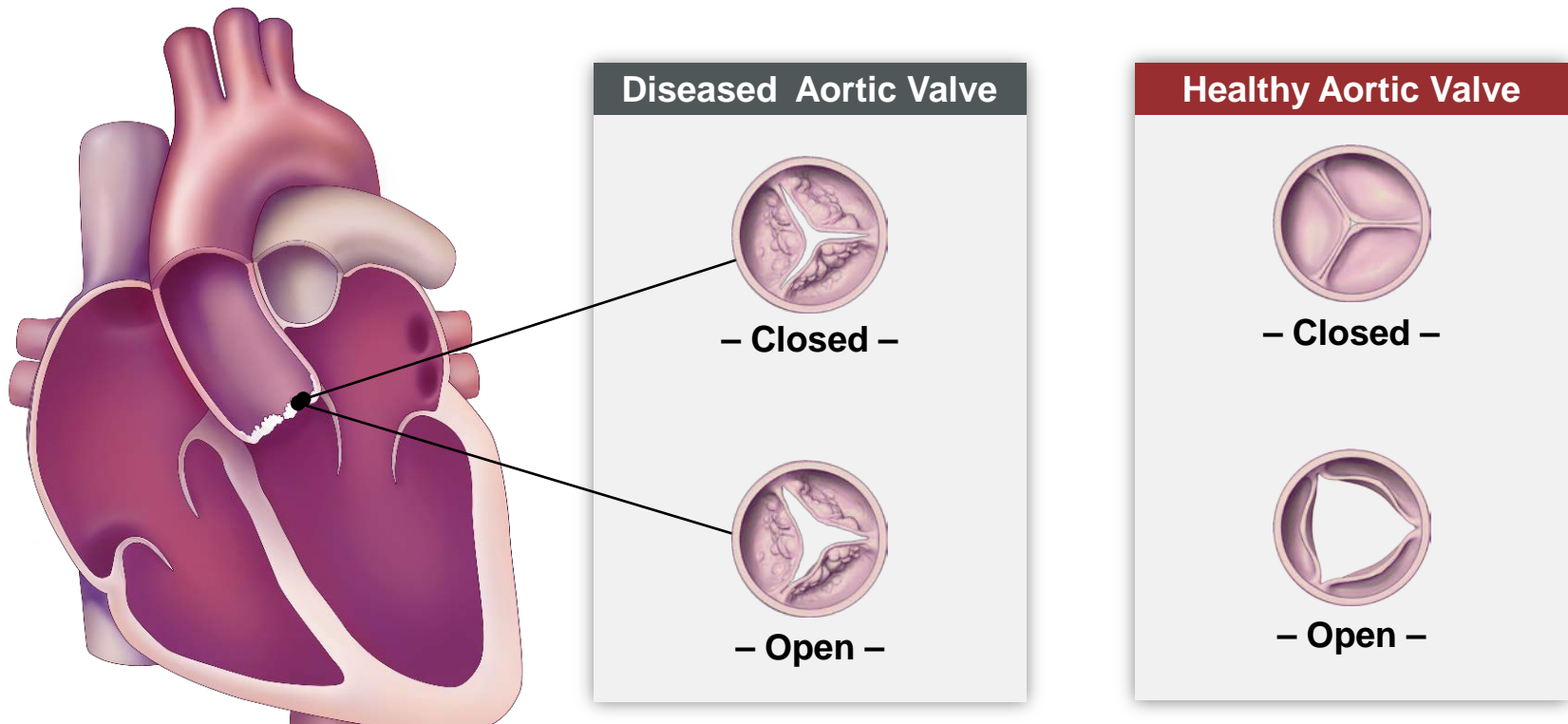
Has two leaflets.
It controls blood flow between the left atrium and left ventricle.

Right
Ventricle

Left
Ventricle

What is Aortic Stenosis?

Aortic Stenosis: is a buildup of calcium deposits on the valve, which causes it to narrow and reduce blood flow to the rest of your body.



Aortic Stenosis is Progressive



Images displayed are representative of aortic valves.

What are the Symptoms of Aortic Stenosis?



The symptoms of aortic valve disease are commonly misunderstood by patients as 'normal' signs of aging.

Symptom Checklist

- ✓ Shortness of breath
- ✓ Fatigue
- ✓ Difficulty walking short distances
- ✓ Light-headedness, dizziness and/or fainting
- ✓ Swollen ankles and feet
- ✓ Rapid fluttering heartbeat
- ✓ Chest pain
- ✓ No longer taking part in physical activities that you used to enjoy

These could also be symptoms of heart failure.

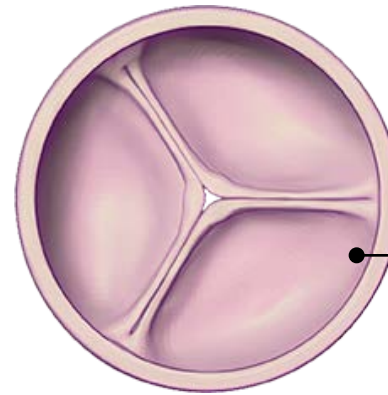
What are the Causes and Risk Factors of Severe Aortic Stenosis?

Causes

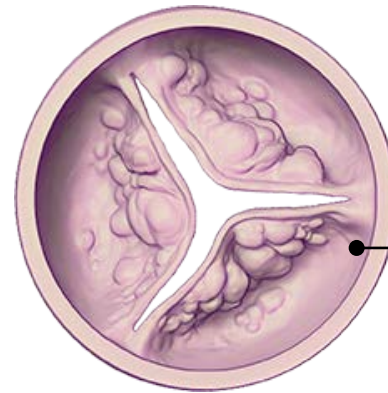
- Calcium buildup
- Congenital birth defect
- Rheumatic fever
- Radiation therapy

Risk Factors

- Increasing age
- High blood pressure
- Abnormal cholesterol levels
- Smoking
- Deformed aortic valve
- Family history



Healthy
Aortic Valve

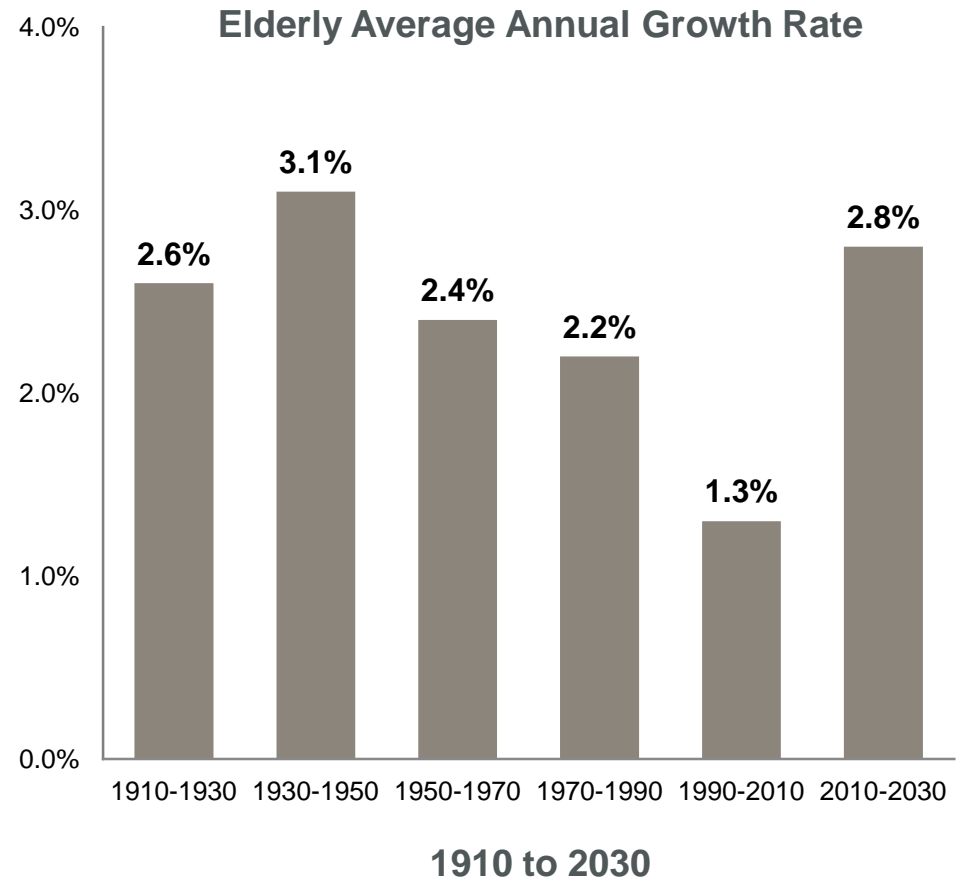


Diseased
Aortic Valve

Population at Risk for Aortic Stenosis is Increasing

Approx. **2.5 million** people in the U.S. over the age of 75 suffer from this disease¹

- Aortic stenosis is estimated to be prevalent with 12.4% of the population over the age of 75²
- The elderly population will more than double between now and the year 2050, to 80 million³

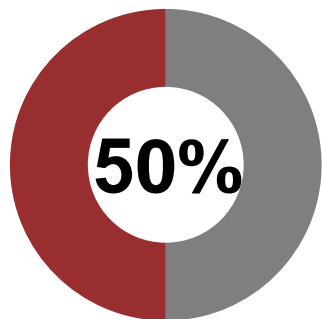


¹U.S. Census Bureau, Population Division. June 2015;

²Ruben L.J.et al. Heart. 2000;84:211-21;

³U.S. Census Bureau Statistical Brief. May 1995;

How Serious is Aortic Stenosis?



People who have developed symptoms from severe aortic stenosis have about a **50% chance of living 2 years and 20% at 5 years**, without aortic valve replacement.*



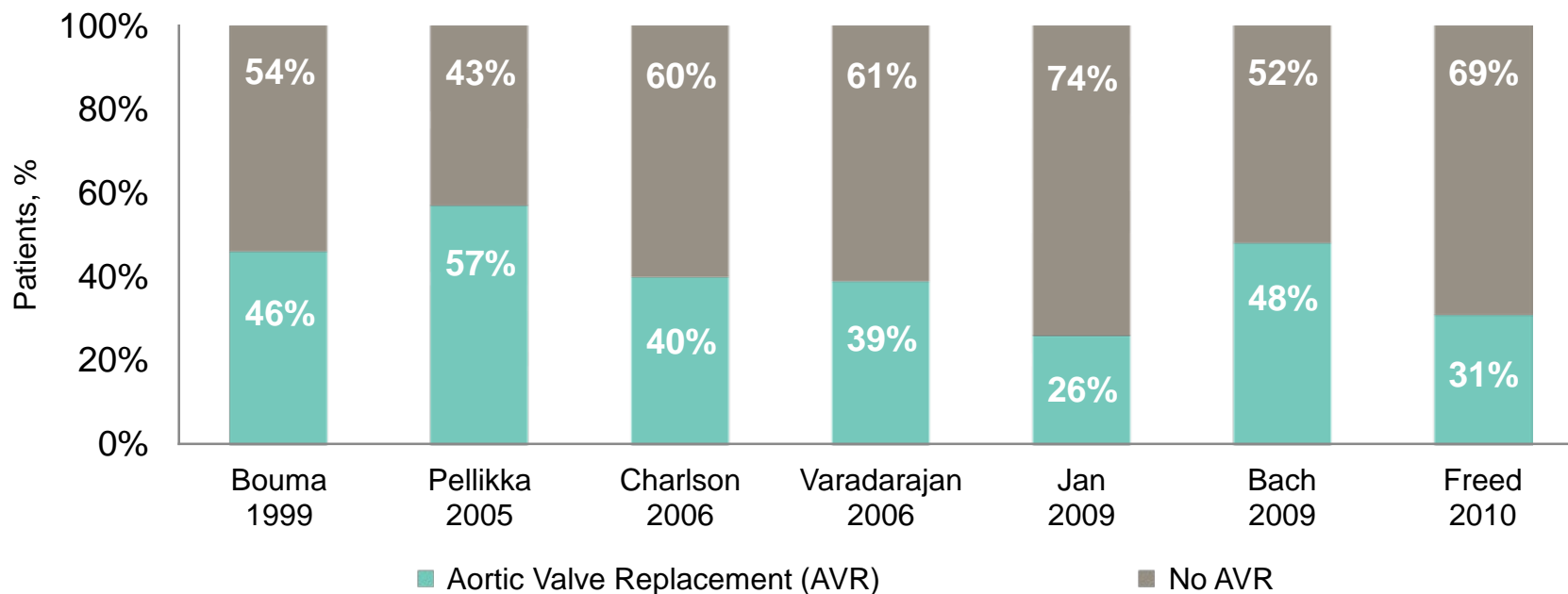
1 Year

2 Year

*Otto CM. Timing of aortic valve surgery. Heart. 2000;84:211-18.

At Least 40% of Patients Who Need Valve Replacement Do Not Get Treatment

Under Treatment of Aortic Stenosis



Studies show that patients with severe aortic stenosis are under-diagnosed and under-treated

¹Bouma BJ et al. Heart. 1999;82:143-148; ²Pellikka PA et al. Circulation. 2005;111:3290-3295; ³Charlson E et al. J Heart Valve Dis. 2006;15:312-321; ⁴Varadarajan P et al. Ann Thorac Surg. 2006;82:2111-2115; ⁵Jan F et al. Circulation. 2009;120:S753; ⁶Bach DS et al. Circ Cardiovasc Qual Outcomes. 2009;2:533-539; ⁷Freed BH et al. Am J Cardiol. 2010;105:1339-1342.

How Do You Get Diagnosed?



Echocardiography

This is also known as an ultrasound; it uses sound waves to produce an image of your heart, which helps your doctor closely examine the aortic valve.



Auscultation

Your cardiologist will use a stethoscope to listen to the sounds of your heart which may detect a murmur.



Electrocardiography (ECG)

Sensors are attached to your skin to measure the electrical impulses given off by your heart, displayed as waves on a monitor or printed on paper.



Chest X-Ray

An X-ray of your chest allows your doctor to check the size and shape of your heart. The X-ray image can also reveal calcium deposits on the aortic valve.

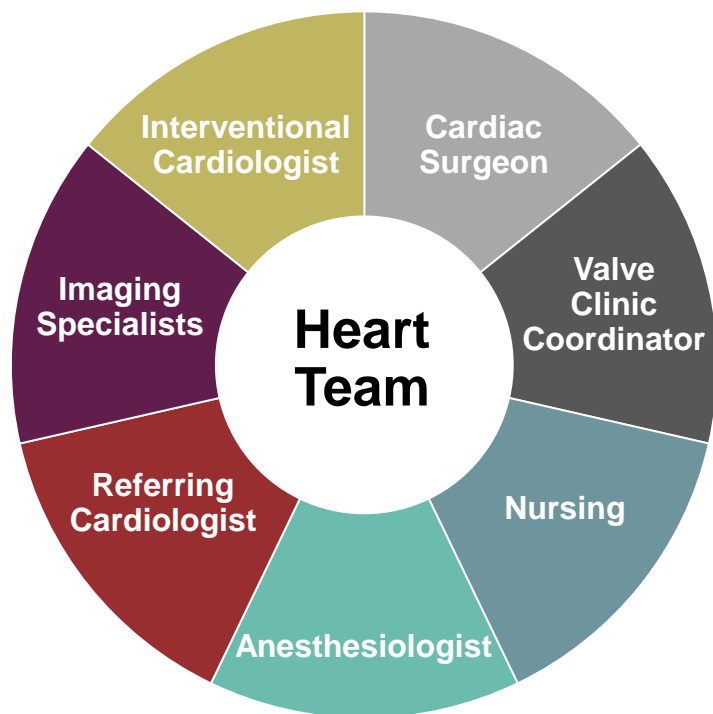


Cardiac Catheterization (Angiography)

In this test, a dye is injected into your heart through your arm or groin to make your heart more visible on an X-ray.

Call or see your doctor whenever you have questions or concerns about your health, especially if you experience any symptoms or unusual changes in your overall health.

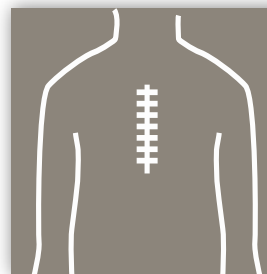
Only a Specialized Heart Team Can Decide Which Treatment Option is Right For You



What are the Treatments for Severe Aortic Stenosis?



Medicine



Surgical Aortic Valve Replacement (SAVR)



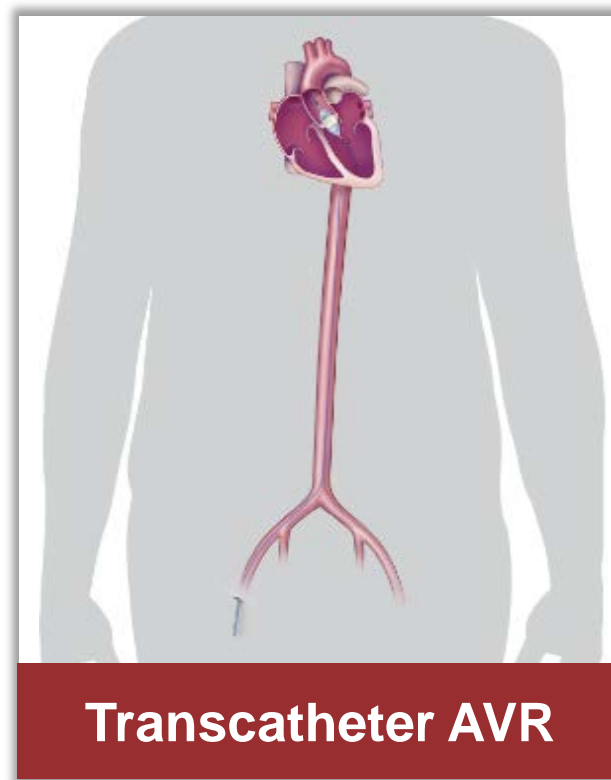
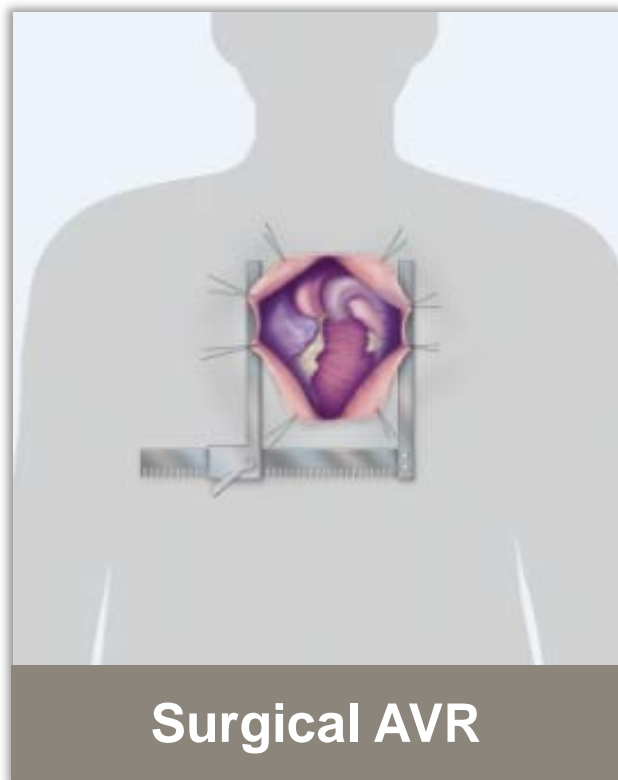
Balloon Aortic Valvuloplasty (BAV)



Transcatheter Aortic Valve Replacement (TAVR)

The only effective treatment for severe aortic stenosis is to have your aortic valve replaced

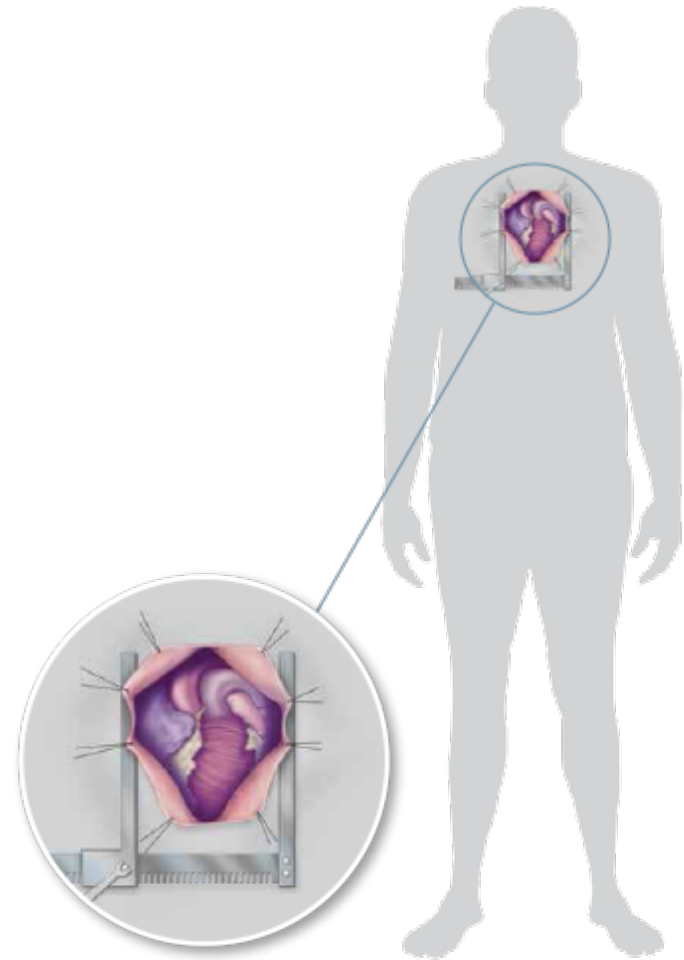
What are Your Options for Aortic Valve Replacement?



Please talk to a specialized Heart Team about which treatment options are right for you.

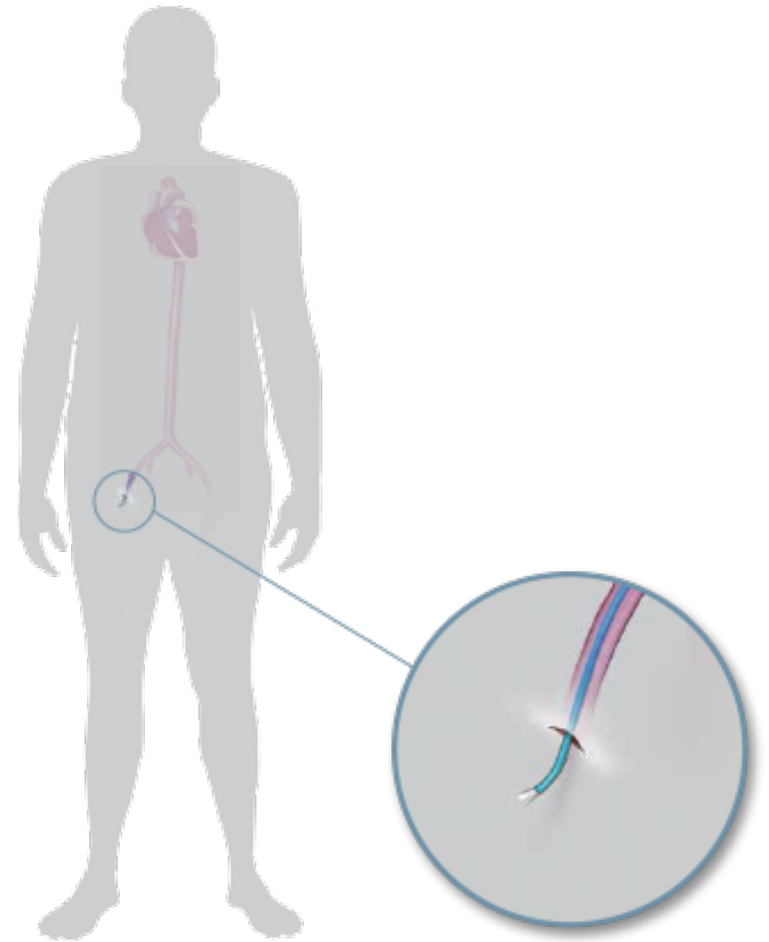
Surgical Aortic Valve Replacement (SAVR)

- Typically requires incision across the full length of the breast bone
- Requires heart / lung machine
- Diseased aortic valve is completely removed and a new valve is inserted
- Typically associated with longer hospital stay



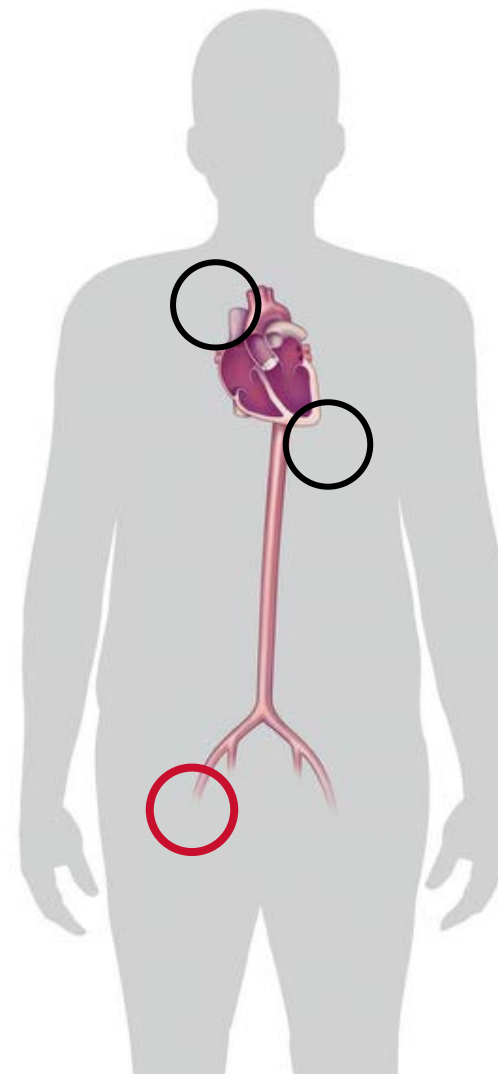
Transcatheter Aortic Valve Replacement (TAVR)

- Catheter-based technique performed while the heart is still beating
- May be a better alternative for those who are at intermediate or greater risk for open-heart surgery
- Typically associated with shorter hospital stay and recovery time



How is TAVR Performed?

- Transfemoral is the most common approach (access via upper leg, groin area)
- For patients without adequate vascular access, alternative access approaches are available



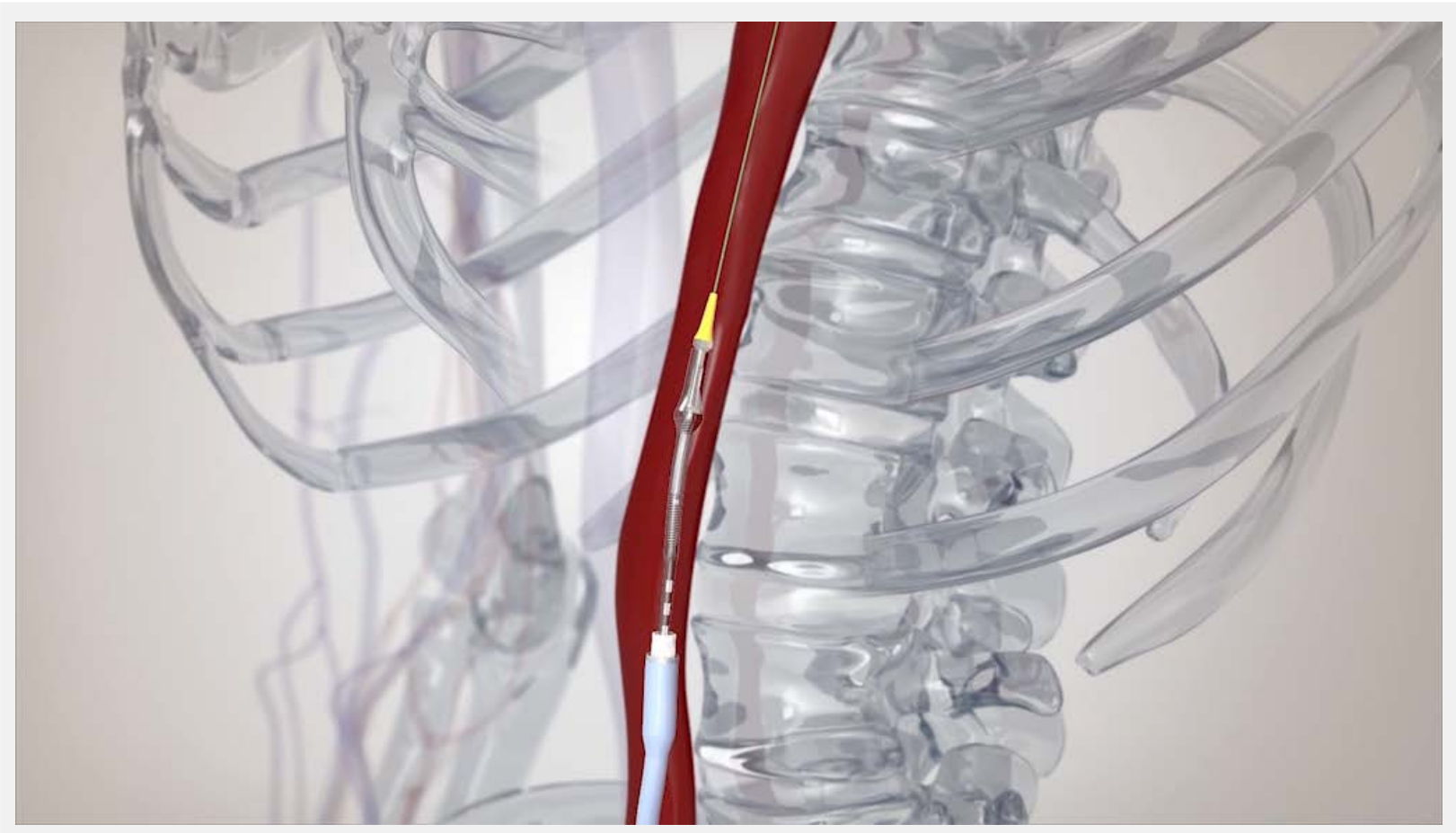
Who is Eligible for TAVR?



People with symptomatic severe aortic stenosis who are **intermediate or greater risk for open-heart surgery** as determined by a specialized Heart Team*

*As of August 18, 2016 Edwards SAPIEN valves are the only transcatheter heart valves approved for use in intermediate-risk patients in the United States

TAVR Procedure Animation



Expanding Indications to Treat More Patients



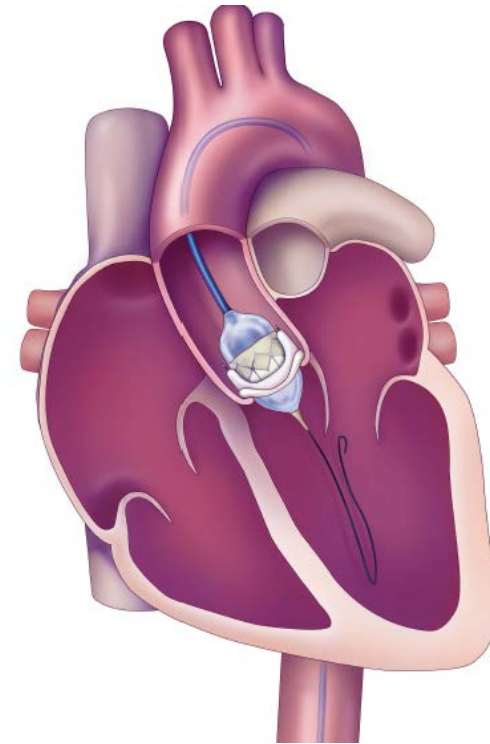
TAVR Procedure for a Failing Surgical Valve (Valve-within-Valve)

Stenosis

When your valve is narrowed and does not completely open. This can be caused by things like a build-up of calcium or high cholesterol.

Regurgitation

When your surgical valve does not fully close and allows blood to leak backwards through the valve.

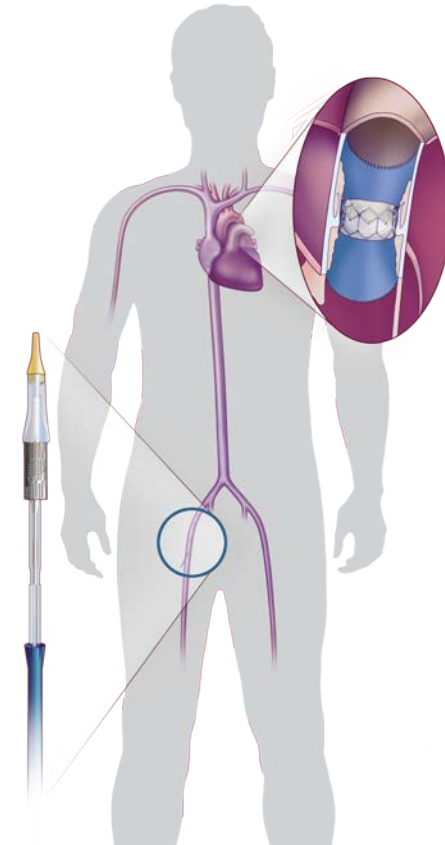


Patients who feel sick from a failing aortic surgical heart valve and who are at high or greater risk for open heart surgery can benefit from transcatheter aortic valve replacement

Transcatheter Pulmonary Valve (TPV) Therapy

Congenital Heart Disease

- Congenital Heart Disease, also known as CHD, is one of the **most common birth defects** in the United States
- Approximately **40,000** babies are born each year with CHD
- Most people with CHD have a heart that does not develop normally



Patients who have a narrowed (stenosis) and/or leaky (regurgitation) conduit in their right ventricular outflow track (RVOT) can benefit from transcatheter aortic valve replacement

TAVR: A Proven Treatment Option



More Than

150,000 Patient Worldwide*
Treated with Edwards SAPIEN
Transcatheter Heart Valves



Available to Patients

in over **65** Countries



First

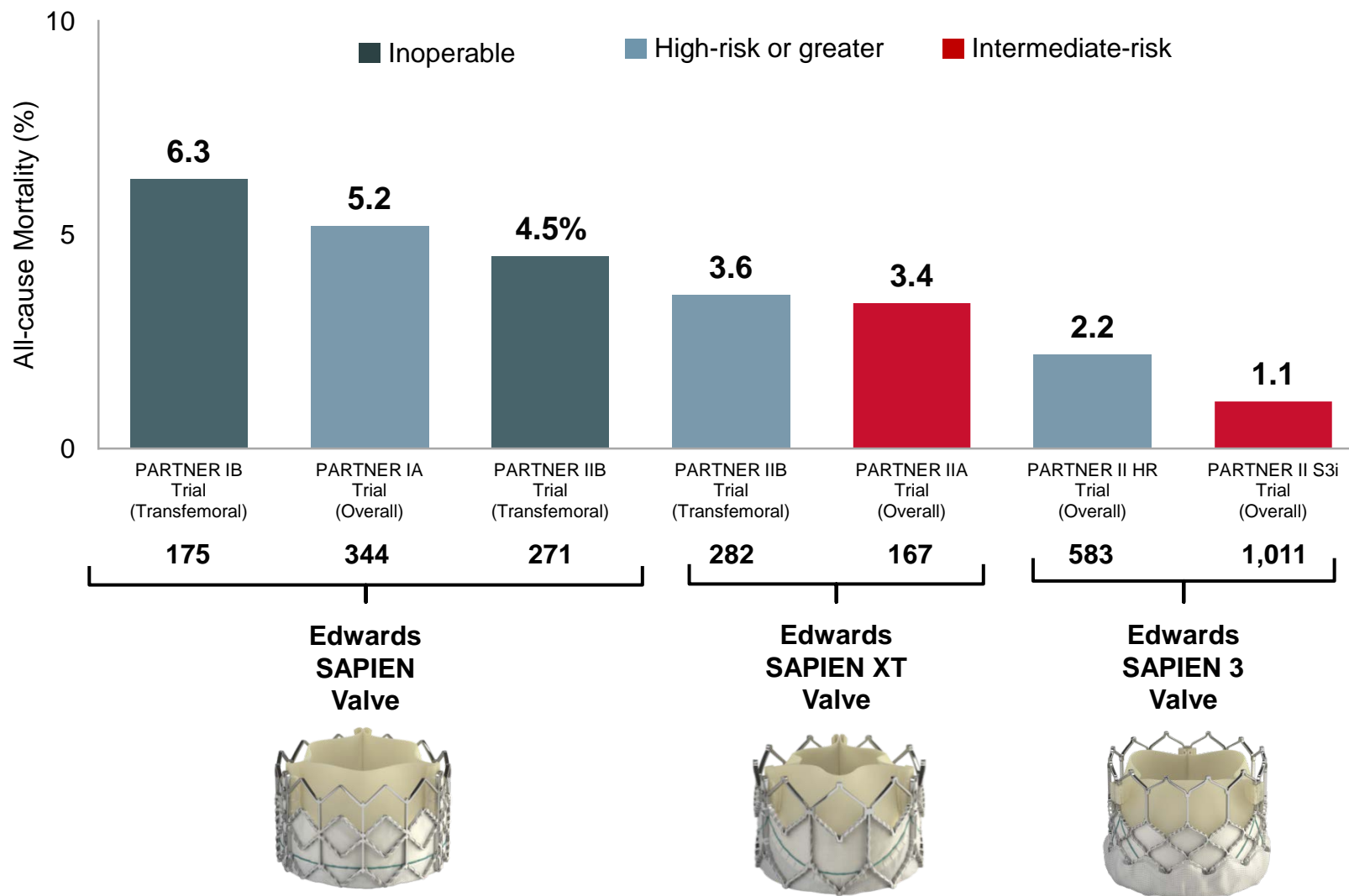
Transcatheter Aortic Valve

approved in the

U.S. in **2011**

*Includes all valves from the Edwards SAPIEN transcatheter heart valve platform.

Patient Outcomes Continue to Improve as Technology and Experience Evolve



Clinical Data for Intermediate-Risk Patients TAVR with Edwards SAPIEN 3 Valve and Surgery

Unadjusted Clinical Events as Treated (AT)		30 Days	
Events (%)	PARTNER II S3i Trial TAVR with SAPIEN 3 Valve (n=1,077)	PARTNER IIA Trial Surgery (n=944)	
All-Cause Mortality	1.1	4.0	
Cardiac Mortality	0.9	3.1	
All Stroke	2.7	6.1	
Disabling Stroke	1.0	4.4	

KM estimates

Clinical Data for Intermediate-Risk Patients TAVR with Edwards SAPIEN 3 Valve and Surgery

SAPIEN 3 valve patients had a shorter length of stay (LOS) than surgery patients from the PARTNER IIA trial

Unadjusted Procedural Factors (AT)

	PARTNER II S3i Trial TAVR with SAPIEN 3 Valve (n=1,077)	PARTNER IIA Trial Surgery (n=944)
Mean Total Hospitalization LOS (Days)	5.6	11.9
Mean ICU Stay (Days)	2.7	5.6

Where Can You Find More Info?

- American Heart Association
www.heart.org/heartvalves
- Mended Hearts
www.mendedhearts.org
- American College of Cardiology
www.heart.org/heartvalves
- Family Caregiver Alliance
www.caregiver.org
- WomenHeart
www.womenheart.org
- Industry-sponsored educational site for patients and caregivers
www.NewHeartValve.com



SAPIEN 3 Transcatheter Heart Valve

Important Risk Information

Indications:

The Edwards SAPIEN 3 transcatheter heart valve, model 9600TFX, and accessories 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 at intermediate or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality \geq 3% at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

Contraindications (Who should not use):

The Edwards SAPIEN 3 transcatheter heart valve and delivery system should not be used in patients who:

- Cannot tolerate medications that thin the blood or prevent blood clots from forming.
- Have an active infection in the heart or elsewhere.

Warnings:

- There may be an increased risk of stroke in transcatheter aortic valve replacement procedures, compared to other standard treatments for aortic stenosis in the high or greater risk population.
- If an incorrect valve size for your anatomy is used, it may lead to heart injury, valve leakage, movement, or dislodgement.
- Patients should talk to their doctor if they have significant heart disease, a mitral valve device or are allergic to chromium, nickel, molybdenum, manganese, copper, silicon, and/or polymeric materials.
- The SAPIEN 3 valve may not last as long in patients whose bodies do not process calcium normally.
- During the procedure, your doctors should monitor the dye used in the body; if used in excess it could lead to kidney damage. X-ray guidance used during the procedure may cause injury to the skin, which may be painful, damaging, and long-lasting.
- Transcatheter aortic heart valve patients should take medications that thin the blood or prevent blood clots from forming, except when likely to have an adverse reaction, as determined by their physician. The Edwards SAPIEN 3 transcatheter heart valve has not been tested for use without medications that thin the blood or prevent blood clots from forming.

Precautions:

The long-term durability of the Edwards SAPIEN 3 transcatheter heart valve is not known, at this time. Regular medical follow-up is recommended to evaluate how well a patient's heart valve is performing. For patients who have previously had aortic valve replacement, the safety, effectiveness, and durability of putting a transcatheter valve in an already implanted artificial valve are not known at this time.

SAPIEN 3 Transcatheter Heart Valve

Important Risk Information (Cont.)

Precautions:

The long-term durability of the Edwards SAPIEN 3 transcatheter heart valve is not known, at this time. Regular medical follow-up is recommended to evaluate how well a patient's heart valve is performing. For patients who have previously had aortic valve replacement, the safety, effectiveness, and durability of putting a transcatheter valve in an already implanted artificial valve are not known at this time.

The safety and effectiveness of the transcatheter heart valve is also not known for patients who have:

- An aortic heart valve that is not calcified, contains only one or two leaflets, has leaflets with large pieces of calcium that may block the vessels that supply blood to the heart or in which the main problem is that the valve leaks
- Previous heart valve replacement or repair
- A heart that does not pump well, has thickening of the heart muscle, with or without blockage, unusual ultrasound images of the heart that could represent irregularities such as a blood clot, a diseased mitral valve that is calcified or leaking, or Gorlin syndrome, a condition that affects many areas of the body and increases the risk of developing various cancers and tumors
- Low white, red or platelet blood cell counts, or history of bleeding because the blood does not clot properly
- Diseased or irregularly shaped vessels leading to the heart. Vessels in the legs which are heavily diseased or too small for associated delivery devices, or a large amount of calcification at the point of entry to the heart
- Allergies to blood-thinning medications or dye injected during the procedure

Potential risks associated with the procedure include:

- Death, stroke, paralysis (loss of muscle function), permanent disability, or severe bleeding
- Risks to the heart, including heart attack or heart failure, a heart that does not pump well, irregular heartbeat that may result in a need for a permanent pacemaker, chest pain, heart murmur, false aneurysm, recurring aortic stenosis (narrowing), too much fluid around the heart
- Risks to your lungs or breathing, including difficulty breathing, fainting, buildup of fluid in or around the lungs, weakness or inability to exercise
- Risks involving bleeding or your blood supply, including formation of a blood clot, high or low blood pressure, limited blood supply, a decrease in red blood cells, or abnormal lab values, bleeding in the abdominal cavity, collection of blood under the skin
- Additional risks, including life-threatening infection, dislodgement of calcified material, air embolism (air bubbles in the blood vessels), poor kidney function or failure, nerve injury, fever, allergic reaction to anesthesia or dye, reoperation, pain, infection or bleeding at incision sites, or swelling

Additional potential risks specifically associated with the use of the heart valve include:

- Valve movement after deployment, blockage or disruption of blood flow through the heart, need for additional heart surgery and possible removal of the SAPIEN 3 valve, a blood clot that requires treatment, damage to the valve (e.g., wear, breakage, recurring aortic stenosis), nonstructural valve dysfunction (e.g., leakage, inappropriate sizing or positioning, blockage, excess tissue in growth, blood cell damage, etc.) or mechanical failure of the delivery system and/or accessories

SAPIEN XT Transcatheter Heart Valve

Important Risk Information

Indications:

The Edwards SAPIEN XT transcatheter heart valve, model 9300TFX, and accessories 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 at intermediate or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality $\geq 3\%$ at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

The Edwards SAPIEN XT transcatheter heart valve and accessories are also indicated for 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 (i.e., STS operative risk score $\geq 8\%$ or at a $\geq 15\%$ risk of mortality at 30 days).

Contraindications (Who should not use):

The Edwards SAPIEN XT transcatheter heart valve and delivery systems should not be used in patients who:

- Cannot tolerate medications that thin the blood or prevent blood clots from forming.
- Have an active infection in the heart or elsewhere.

Warnings:

- There is a higher risk of stroke in transcatheter aortic valve replacement procedures, compared to balloon aortic valvuloplasty and other standard treatments for aortic stenosis in the high or greater risk population.
- Implanting a valve that is too small may cause blood leakage and valve movement. Implanting a valve that is too large can cause a buildup of pressure in the valve or a rupture of blood vessels in or around your heart. Your Heart Team will do tests to determine the best valve size for you.
- The SAPIEN XT valve may not last as long in patients whose bodies do not process calcium normally.
- Patients should talk to their doctor if they have significant heart disease, a mitral valve device or are allergic to chromium, nickel, molybdenum, manganese, copper, silicon, and/or polymeric materials.
- During the transfemoral procedure, your doctors should monitor the dye used in the body; if used in excess it could lead to kidney damage. X-ray guidance used during the procedure may cause injury to the skin, which may be painful, damaging, and long-lasting.
- Transcatheter aortic heart valve patients should take medications that thin the blood or prevent blood clots from forming, except when likely to have an adverse reaction, as determined by their physician. The Edwards SAPIEN XT transcatheter heart valve has not been tested for use without medications that thin the blood or prevent blood clots from forming.

SAPIEN XT Transcatheter Heart Valve

Important Risk Information (Cont.)

Precautions:

The long-term durability of the Edwards SAPIEN XT transcatheter heart valve is not known, at this time. Regular medical follow-up is recommended to evaluate how well a patient's heart valve is performing.

The safety and effectiveness of implanting:

- A transcatheter valve inside a transcatheter valve is not known
- A transcatheter valve inside a surgical tissue valve is not known in the intermediate-risk population

The safety and effectiveness of the transcatheter heart valve is also not known for patients who have:

- An aortic heart valve that is not calcified, contains only one or two leaflets, has leaflets with large pieces of calcium that may block the vessels that supply blood to the heart or in which the main problem is that the valve leaks.
- Previous heart valve replacement or repair
- A heart that does not pump well, has thickening of the heart muscle, with or without blockage, unusual ultrasound images of the heart that could represent irregularities such as a blood clot, a diseased mitral valve that is calcified or leaking, or Gorlin syndrome, a condition that affects many areas of the body and increases the risk of developing various cancers and tumors
- Low white, red or platelet blood cell counts, or history of bleeding because the blood does not clot properly
- Diseased or irregularly shaped vessels leading to the heart. Vessels in the legs which are heavily diseased or too small for associated delivery devices, or a large amount of calcification at the point of entry to the heart, depending on delivery method
- Allergies to blood-thinning medications or dye injected during the procedure

Potential risks associated with the procedure include:

- Death, stroke, paralysis (loss of muscle function), permanent disability, or severe bleeding
- Risks to the heart, including heart attack or heart failure, a heart that does not pump well, irregular heartbeat that may result in a need for a permanent pace maker, chest pain, heart murmur, false aneurysm, recurring aortic stenosis(narrowing), too much fluid around the heart
- Risks to your lungs or breathing, including difficulty breathing, fainting, buildup of fluid in or around the lungs, weakness or inability to exercise
- Risks involving bleeding or your blood supply, including formation of a blood clot, high or low blood pressure, limited blood supply, a decrease in red blood cells, or abnormal lab values, bleeding in the abdominal cavity, collection of blood under the skin
- Additional risks, including life-threatening infection, dislodgement of calcified material, air embolism (air bubbles in the blood vessels), poor kidney function or failure, nerve injury, fever, allergic reaction to anesthesia or dye, reoperation, pain, infection or bleeding at incision sites, or swelling
- For a valve in valve procedure, there is a risk of leakage if the previously implanted tissue valve is not securely in place or if it is damaged. There is also the possibility that a partially detached valve leaflet from the previously implanted valve could block a blood vessel. The safety and effectiveness of the transcatheter heart valve has not been determined when the valve is implanted:
 - Inside a stented previously implanted valve smaller than 21 mm
 - Inside an unstented previously implanted aortic tissue valve
- Your Heart Team will do tests to determine the exact size of the new valve you should receive and communicate what to expect.

Important Risk Information (Cont.)

Additional potential risks specifically associated with the use of the heart valve include:

- Valve movement after deployment, blockage or disruption of blood flow through the heart, sudden loss of heart function, heart failure, need for additional heart surgery and possible removal of the SAPIEN XT valve, a blood clot that requires treatment, damage to the valve (e.g., wear, breakage, recurring aortic stenosis), nonstructural valve dysfunction (e.g., leakage, inappropriate sizing or positioning, blockage, excess tissue ingrowth, blood cell damage, etc.) or mechanical failure of the delivery system and/or accessories

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician

Edwards, Edwards Lifesciences, the stylized E logo, Edwards SAPIEN, Edwards SAPIEN XT, Edwards SAPIEN 3, NewHeartValve.com, PARTNER, PARTNER II, S3, SAPIEN, SAPIEN XT, SAPIEN 3, and TFX are trademarks of Edwards Lifesciences Corporation. All other trademarks are the property of their respective owners.

© 2016 Edwards Lifesciences Corporation. All rights reserved. PP--US-0439 v1.0



Edwards