Transcatheter Aortic Valve Replacement with the Edwards SAPIEN Transcatheter Heart Valve

What You and Your Loved Ones Should Know Before Your Procedure
Please remember, this information is not meant to tell you everything you need to know about your treatment options for aortic stenosis, or about the TAVR procedure. Regular check-ups with your doctor are essential. Call or see your doctor whenever you have questions or concerns about your health, especially if you experience unusual symptoms or changes in your overall health.

This booklet was created for patients who feel sick from severe aortic stenosis (a narrowing of the aortic valve opening that does not allow normal blood flow) and who are at high risk or cannot have open-heart surgery, in order to inform them of their options. This information will help you and your loved ones learn more about your heart, how it works, and aortic stenosis. In addition, you will learn about a new procedure called transcatheter aortic valve replacement (TAVR).

Be sure to ask your doctor to explain your treatment options, and their risks, to help you decide which option is best for you.

See pages 19-28 to review the risks of the TAVR procedure.

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Your heart beats between 60 and 100 times per minute. At 60 beats per minute, that’s approximately 31.5 million beats per year.

HOW DOES YOUR HEART WORK?
The heart is a muscular organ located in your chest between your lungs. The heart is designed to pump blood through your body. The right side of your heart pumps blood through the lungs, where the blood picks up oxygen. The left side of the heart receives this blood and pumps it to the rest of your body.

Chambers and Valves
The heart is divided into four main areas, or chambers—two upper chambers (called the left and right atrium) and two lower chambers (called the left and right ventricle). There are four valves that control the flow of blood through your heart. They are called the aortic, mitral, pulmonary, and tricuspid valves, and each is made of flaps of tissue called leaflets. (See figure on page 4)

Each time your heart beats, it pumps blood through these valves by contracting (squeezing) its chambers. These valves open in one direction, like one-way gates, allowing blood to flow forward. In between beats, the heart’s chambers quickly relax, and its valves close, preventing blood from flowing backward.

There are two common problems that can develop in heart valves:

- **When your valve is narrowed and does not completely open because of things like a build-up of calcium (mineral deposits), high cholesterol (a waxy fat), age, or genetics (such as a birth defect), this is called stenosis.**
- **When your valve does not fully close and allows blood to leak backwards through the valve, this is called regurgitation.**

With either problem, your heart needs to work harder and may not pump enough oxygen-rich blood to your body.

NOTE: The left and the right side of the heart is pictured as the heart sits in your body.

The 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.

The aortic valve has three leaflets. It controls blood flow from the left ventricle to the aorta, sending blood to the rest of the body.

The mitral valve has two leaflets. It controls blood flow between the left atrium and left ventricle.

The tricuspid valve has three leaflets. It controls blood flow from the right atrium to the right ventricle.
WHAT IS SEVERE AORTIC STENOSIS?
Severe aortic stenosis is a narrowing of your aortic valve opening that does not allow normal blood flow. It can be caused by a birth defect, rheumatic fever, radiation therapy, or can be related to age.
In elderly patients, severe aortic stenosis is sometimes caused by the build-up of calcium (mineral deposits) on the aortic valve’s leaflets. Over time the leaflets become stiff, reducing their ability to fully open and close. When the leaflets don’t fully open, your heart must work harder to push blood through the aortic valve to your body.
Eventually, your heart gets weaker, increasing the risk of heart failure (your heart cannot supply enough blood to your body). Severe aortic stenosis is a very serious problem. Without treatment, half of the people who feel sick from this problem die within an average of 2 years.
WHAT ARE YOUR TREATMENT OPTIONS?

Treatment for aortic stenosis depends on how far the disease has progressed. If your stenosis is mild, medication may be prescribed to help regulate your heartbeat and prevent blood clots. However, as the severity of your stenosis progresses, your doctor may recommend replacing the diseased valve.

Aortic valve replacement (AVR) through open-heart surgery is the most common treatment for patients with aortic stenosis. In this operation your diseased heart valve is removed and a new heart valve is inserted. However, some patients may be at high risk or too sick to undergo open-heart surgery. A minimally invasive procedure, referred to as minimal incision valve surgery, can also be performed to replace a malfunctioning valve. In minimal incision valve surgery the surgeon can replace the diseased valve through a smaller incision while looking directly at the heart or through a small, tube-shaped camera. The incisions are made either between the ribs or in the chest and may use a small incision in the groin for the heart-lung machine. Minimal incision valve surgery may be an option for some patients. However, some patients may be at high risk or too sick to undergo minimally invasive open-heart surgery. Please consult your doctor for more information on minimally invasive procedures.

Another treatment option is transcatheter aortic valve replacement (TAVR). TAVR is a procedure that inserts a new valve inside your diseased aortic valve, and does not require your chest to be opened. This procedure is intended only for patients with age-related aortic stenosis. There are two different approaches for TAVR – transfemoral and transapical. The transfemoral approach, an incision is made in the leg (or slightly higher up). In the transapical approach, an incision is made between the ribs to access the apex (lowest point) of the heart. Your doctor will recommend the best treatment option for you based on your overall health. If you are too sick to undergo chest surgery, the transapical approach may not be an option for you.

What is Surgical Aortic Valve Replacement?

Surgical AVR is an open-heart procedure. After the chest is opened, you are put on cardiopulmonary bypass – which temporarily takes over providing blood flow and oxygen to your body during surgery. During surgical AVR, the surgeon removes the diseased aortic valve and replaces it with either a mechanical valve (made from man-made materials) or a biological valve (made from animal tissue). Surgical AVR has been performed for many years and has consistently produced excellent results in lengthening patients’ lives and improving their quality of life.

What is Transcatheter Aortic Valve Replacement?

If a cardiac surgeon determines that you are at high risk or too sick for open-heart surgery, and if medicine is not helping you feel better, TAVR may be an alternative. This less invasive procedure allows a new valve to be inserted within your diseased aortic valve while your heart is still beating. Cardiopulmonary bypass is usually not required. However, during parts of the procedure your heart rate needs to be temporarily increased to a very fast rate resulting in lower than normal blood flow to vital organs for short periods of time. The TAVR procedure can be performed through two different approaches – transfemoral or transapical. Your doctor will decide which approach is best for you based on your medical condition and other factors.

The TAVR procedure is not right for everyone. In certain cases, the risks of the procedure may outweigh the benefits. See pages 19-28 to review the risks of the TAVR procedure.

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* The time required to perform the procedures necessary for the entire procedure
**Which Products Will Be Used During the Procedure?**
The Edwards SAPIEN transcatheter heart valve and other accessories are used to perform the TAVR procedure. The Edwards SAPIEN transcatheter heart valve is a biological (made from animal tissue) valve that replaces your aortic valve. It is provided in two sizes, 23 mm and 26 mm in diameter. Your doctor will determine the right size for you.

**What Will Happen During the Procedure?**

The procedure will be performed in the hospital. General anesthesia will be given to put you into a deep sleep. After you are asleep, a tube will be placed down your throat and connected to a mechanical ventilator (a machine that will help you breathe during the procedure). Your heart’s pumping function will be briefly suspended at least twice during the procedure. To do this, your doctor will place a temporary pacing wire in your heart which causes the heart to race. This prevents your heart from pumping blood through your body well, which may result in low blood flow to your brain, kidneys, and other organs for a few seconds. After the procedure is done, the temporary pacing wire is removed.

Your doctor will use fluoroscopy (a type of X-ray that delivers radiation to you) during the procedure. Your doctor will explain the risks of radiation to you. Your doctor will also use contrast medium (fluid used to see your internal structures) during the procedure in order to see your aortic valve. Some patients may have kidney problems or an allergic reaction as a result of the contrast medium. Your doctor will also use echocardiography (a type of ultrasound) to see your aortic valve.

**Who Should Not Have the Procedure?**
The Edwards SAPIEN transcatheter heart valve should not be used in the following:

- Patients who already have a prosthetic (man-made) valve or repair device implanted in any of their four heart valves
- Patients who have aortic stenosis along with aortic regurgitation (when your valve does not fully close and allows blood to leak backwards through the valve)
- Patients who have severe disease with their mitral valve
- Patients whose aortic valve is either too small or too big
- Patients who have severe disease in their vessels leading to the heart, small vessels, or vessels that have a lot of bends that would not allow passage of the products necessary to perform the procedure
- Patients who have thick aortic leaflets which are very close to the arteries that supply the heart with blood
- Patients who have aortic valve disease
- Patients who have aortic valve disease to the right
- Patients who have aortic valve disease to the left
- Patients who are taking aspirin, heparin, ticlopidine (Ticlid), clopidogrel (Plavix), or have sensitivity to contrast medium (fluid used to see your internal structures during the procedure)

If the Edwards SAPIEN transcatheter heart valve is used in the patients mentioned above, it may not work properly. This could make you feel very sick, or even cause death.

**What Do You Need to Do Before the Procedure?**
Be sure to tell your doctor what medicine you are taking and whether you have any allergies. Your doctor may ask you to change the medicine you are on before the procedure. Your doctor will also explain the procedure and answer any questions you may have.

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**TRANSCATHETER AORTIC VALVE REPLACEMENT PROCEDURE**

**Who Should Not Have the Procedure?**
The Edwards SAPIEN transcatheter heart valve should not be used in the following:

- Patients who have other serious illnesses that they would not benefit from isolated correction of their aortic stenosis
- Patients whose aortic valve is not calcified
- Patients whose aortic valve only has one or two leaflets (usually due to a birth defect)
- Patients who have coronary artery disease that needs to be treated
- Patients who have a blood clot or an abnormal growth
- Patients who have an infection in the heart or infections elsewhere

**What Will Happen During the Procedure?**
The procedure will be performed in the hospital. General anesthesia will be given to put you into a deep sleep. After you are asleep, a tube will be placed down your throat and connected to a mechanical ventilator (a machine that will help you breathe during the procedure). Your heart’s pumping function will be briefly suspended at least twice during the procedure. To do this, your doctor will place a temporary pacing wire in your heart which causes the heart to race. This prevents your heart from pumping blood through your body well, which may result in low blood flow to your brain, kidneys, and other organs for a few seconds. After the procedure is done, the temporary pacing wire is removed.

Your doctor will use fluoroscopy (a type of X-ray that delivers radiation to you) during the procedure. Your doctor will explain the risks of radiation to you. Your doctor will also use contrast medium (fluid used to see your internal structures) during the procedure in order to see your aortic valve. Some patients may have kidney problems or an allergic reaction as a result of the contrast medium. Your doctor will also use echocardiography (a type of ultrasound) to see your aortic valve.

**Which Products Will Be Used During the Procedure?**
The Edwards SAPIEN transcatheter heart valve and other accessories are used to perform the TAVR procedure. The Edwards SAPIEN transcatheter heart valve is a biological (made from animal tissue) valve that replaces your aortic valve. It is provided in two sizes, 23 mm and 26 mm in diameter. Your doctor will determine the right size for you.

**What Do You Need to Do Before the Procedure?**
Be sure to tell your doctor what medicine you are taking and whether you have any allergies. Your doctor may ask you to change the medicine you are on before the procedure. Your doctor will also explain the procedure and answer any questions you may have.
1. You will be placed under general anesthesia (you will be in a deep sleep).

2. An incision will be made in your leg (or slightly higher up), where your doctor will put in a sheath (a short hollow tube) that is slightly larger than the width of a pencil.

3. Your doctor will take a balloon and put it through the sheath into your blood vessel to reach your aortic valve. The balloon will be inflated with fluid to break open your narrowed valve, deflated, and then removed.

4. The Edwards SAPIEN transcatheter heart valve will be placed on the delivery system (long tube with a balloon on the end), and compressed on the balloon (using a crimper) to make it small enough to fit through the sheath. It will be about the width of a pencil.

5. The delivery system carrying the valve will be placed through the sheath and pushed up to your aortic valve, guided by a type of X-ray.

6. The balloon of the delivery system carrying the valve will be inflated with fluid, expanding this new valve within your diseased valve. During valve expansion, the heart is stabilized by temporarily speeding up the heartbeat. The new valve will push the leaflets of your diseased valve aside. The frame of the new valve is very strong and it will use the leaflets of your diseased valve to secure in place. Next, the balloon will be deflated.

7. Your doctor will make sure that your new valve is working properly before removing the delivery system and closing the incision in your leg (or slightly higher up). If your new valve is not working properly, your doctor may need to do something else which may include open-heart surgery or other additional surgery.

Transfemoral Procedure  The average time required to perform the transfemoral TAVR procedure is between 4 and 5 hours.
1. You will be placed under general anesthesia (you will be in a deep sleep).

2. An incision will be made in your chest between your ribs to access the apex (the lowest part) of your heart. Your doctor will place a sheath (a short hollow tube) that is slightly larger than the width of a pencil through the apex and into the left ventricle.

3. Your doctor will take a balloon and put it through the sheath to reach your aortic valve. The balloon will be inflated with fluid to break open your narrowed valve, deflated, and then removed.

4. The Edwards SAPIEN transcatheter heart valve will be placed on the delivery system (long tube with a balloon on the end), and compressed on the balloon (using a crimper) to make it small enough to fit through the sheath. It will be about the width of a pencil.

5. The delivery system carrying the valve will be placed through the sheath and pushed up to your aortic valve, guided by a type of X-ray.

6. The balloon of the delivery system carrying the valve will be inflated with fluid, expanding this new valve within your diseased valve. During valve expansion, the heart is stabilized by temporarily speeding up the heartbeat. The new valve will push the leaflets of your diseased valve aside. The frame of the new valve is very strong and it will use the leaflets of your diseased valve to secure in place. Next, the balloon will be deflated.

7. Your doctor will make sure that your new valve is working properly before removing the delivery system and closing the chest incision between your ribs. If your new valve is not working properly, your doctor may need to do something else which may include open-heart surgery or other additional surgery.
What Happens After the Procedure?

After the procedure, you will be moved to the intensive care unit (ICU) for careful monitoring. You may be given blood-thinning medications. Patients who receive a transcatheter heart valve may be given blood-thinning medicine for 6 months after the procedure and aspirin for the rest of their lives, unless otherwise specified by their doctor. Patients who do not take blood-thinning medicine may be at increased risk of developing a dangerous blood clot after the procedure which may result in a stroke. Blood-thinning medicine may increase the risk of bleeding in the brain (stroke).

While in the hospital after the TAVR procedure, the following examinations will be completed:

- Physical exam that includes an exam for stroke
- Chest X-ray
- Blood tests
- Electrocardiography (ECG or EKG) (a test that records your heart’s electrical activity)
- Ultrasound of your heart

You will remain in the ICU until your doctor feels you can be transferred to a regular hospital room, where you will continue to be monitored until you leave the hospital.

You should feel better soon after your procedure. Your doctor will give you specific instructions to help you with your recovery, which may include a special diet, exercise, and medicine. It is important to carefully follow your doctor’s directions, especially if blood-thinning drugs are prescribed. Your doctor will monitor your medicine and advise you when or if you can stop taking it.

Regular check-ups by your doctor are very important. It is easier for patients with an artificial heart valve to get infections, which could lead to future heart damage. Call or see your doctor whenever you have questions or concerns about your health, especially if you experience any unusual problems such as bleeding, pain, other discomfort, or changes in your overall health.

Even after you have fully recovered from the procedure, your doctor may want to check your progress occasionally. You will need to take any medicine as prescribed and have your heart checked from time to time. Be sure to discuss all your medicine (including over-the-counter medicine) with your doctor, and don’t change any dosage unless instructed to, even if you feel better.

Always inform other doctors about your heart valve replacement before any medical or dental procedure. Before undergoing an MRI (magnetic resonance imaging) procedure, always notify the doctor (or medical technician) that you have an implanted heart valve. Failure to do so may result in damage to the valve that could lead to death.
Patients with Severe Native Aortic Stenosis

The PARTNER Trial

The PARTNER Trial Overview

In the United States, The PARTNER Trial studied the safety and effectiveness of the Edwards SAPIEN transcatheter heart valve in 1,057 patients whose doctors had determined them to be at high risk or too sick to undergo open-heart surgery. The PARTNER Trial was made up of two trial parts—Cohort A (high-risk patients) and Cohort B (inoperable patients). Patient enrollment for the trial was initiated in May 2007 and completed in March 2009.

Cohort A (699 patients) evaluated the safety and effectiveness of the Edwards SAPIEN transcatheter heart valve in patients who were deemed by their doctor to be at high risk of death from surgery, but could still undergo an open-chest procedure to replace their aortic valve. These patients are referred to as high-risk patients. Approximately half of the patients in Cohort A were treated with the Edwards SAPIEN transcatheter heart valve (either through the transfemoral or transapical approach) and half were treated with a surgical aortic valve through an open-heart procedure.

Cohort B (358 patients) evaluated the safety and effectiveness of the Edwards SAPIEN transcatheter heart valve in patients who were deemed by their doctor to be too sick to undergo open-heart surgery. These patients are referred to as inoperable patients. Half of the patients in Cohort B were treated with the Edwards SAPIEN transcatheter heart valve (only through the transfemoral approach) and half were treated with standard therapy. Standard therapy included medicine or other procedures that treat aortic stenosis such as balloon aortic valvuloplasty (procedure to stretch the aortic valve opening). The transapical approach was not offered to this patient population as they could not undergo surgery.

Patients in both Cohorts A and B were examined at 30 days, 6 months, and 1 year after the procedure, and will continue to be examined every year for 5 years.
What Are the Most Common Procedural Risks 30 Days After the Procedure? As with any medical intervention, there is a possibility that complications may occur during or after receiving the Edwards SAPIEN transcatheter heart valve, even after leaving the hospital.

The most serious risks of the TAVR procedure with the Edwards SAPIEN transcatheter heart valve through the transfemoral or transapical approach at 30 days in high-risk patients (Cohort A) include:

- **Death from any cause** – death occurred in 6 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, as compared to 8 out of every 100 patients who received a surgical aortic valve.

- **Stroke** – a condition when blood stops flowing to the brain, which may cause partial or severe disability. Stroke occurred in 4 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 3 times more often than seen in patients who received a surgical aortic valve.

- **Major vascular complications** – a tear or hole in blood vessels or a hematoma (a large blood clot under the skin), which will require another surgery. Vascular complications occurred in 11 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 4 times more often than seen in patients who received a surgical aortic valve.

- **Bleeding event** – a loss of blood that requires 2 or more units of a blood transfusion within the indexed procedure. A bleeding event occurred in 11 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 9 times more often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

The most serious risks of the TAVR procedure with the Edwards SAPIEN transcatheter heart valve through the transfemoral approach at 30 days in inoperable patients (Cohort B) include:

- **Death from any cause** – death occurred in 5 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-third less often than seen in patients who received a surgical aortic valve.

- **Aortic insufficiency** – a leakage of blood back through the implanted valve or between the valve and the heart that causes the heart to work harder. Mild aortic insufficiency occurred in 49 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 3 times more often than seen in patients who received a surgical aortic valve.

- **Moderate or severe aortic insufficiency** occurred in 17 out of every 100 patients within 30 days after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 8 times more often than seen in patients who received a surgical aortic valve.

What Are the Possible Benefits and Risks 1 Year After the Procedure? In the high-risk patient group (Cohort A), The PARTNER Trial study results showed that patients who received the Edwards SAPIEN transcatheter heart valve through the transfemoral or transapical approach lived just as long as those patients who received a surgical aortic valve. Approximately 3 out of 4 patients in each group were alive at 1 year after receiving either the Edwards SAPIEN transcatheter heart valve or a surgical aortic valve. Patients who received the Edwards SAPIEN transcatheter heart valve through the transfemoral approach felt better sooner than those patients who received a surgical aortic valve, but the same at 6 months and longer. Patients who received the Edwards SAPIEN transcatheter heart valve through the transapical approach felt worse early on, but the same at 1 year as those patients who received a surgical aortic valve. Patients who received the Edwards SAPIEN transcatheter heart valve had a higher stroke rate than those patients who received a surgical aortic valve.
The most serious risks of the TAVR procedure with the Edwards SAPIEN transcatheter heart valve through the transfemoral or transapical approach at 1 year in high-risk patients (Cohort A) include:

- Death from any cause - death occurred in 24 out of 100 patients after receiving an Edwards SAPIEN transcatheter heart valve. This rate was the same for patients who received a surgical aortic valve. The most serious risks of the TAVR procedure with the Edwards SAPIEN transcatheter heart valve through the transfemoral approach at 1 year in inoperable patients (Cohort B) include:

- Death from any cause - death occurred in 31 out of 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately the same for patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty). Moderate or severe aortic insufficiency occurred in 20 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 8 times more often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty). Moderate or severe aortic insufficiency occurred in 20 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one and a half times more often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

- Stroke – a condition when blood stops flowing to the brain, which may cause partial or severe disability. Stroke occurred in 6 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 2 times more often than seen in patients who received a surgical aortic valve. Bleeding event – a loss of blood that requires 2 or more units of a blood transfusion within the indexed procedure. A bleeding event occurred in 11 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-third less often than seen in patients who received a surgical aortic valve. Aortic insufficiency – a leakage of blood back through the implanted valve or between the valve and heart that causes the heart to work harder. Mild aortic insufficiency occurred in 50 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 3 times more often than seen in patients who received a surgical aortic valve. Moderate or severe aortic insufficiency occurred in 23 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 8 times more often than seen in patients who received a surgical aortic valve. In the inoperable patient group (Cohort B), the PARTNER Trial study results showed that patients who received the Edwards SAPIEN transcatheter heart valve through the transfemoral approach lived longer and felt better, but had a higher stroke rate than those patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

- Bleeding event – a loss of blood that requires 2 or more units of a blood transfusion within the indexed procedure. A bleeding event occurred in 17 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-third less often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty). Moderate or severe aortic insufficiency occurred in 20 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one and a half times more often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

- Major vascular complications – a tear or hole in blood vessels or a hematoma (a large blood clot under the skin), which will require another procedure. Major vascular complications occurred in 11 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 3 times more often than seen in patients who received a surgical aortic valve. Moderate or severe aortic insufficiency occurred in 23 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately 8 times more often than seen in patients who received a surgical aortic valve. Aortic insufficiency – a leakage of blood back through the implanted valve or between the valve and heart that causes the heart to work harder. Mild aortic insufficiency occurred in 59 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one and a half times more often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty). Moderate or severe aortic insufficiency occurred in 20 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-third less often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).

- Stroke – a condition when blood stops flowing to the brain, which may cause partial or severe disability. Stroke occurred in 11 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-third less often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty). Moderate or severe aortic insufficiency occurred in 20 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-and-a-half times more often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty). Moderate or severe aortic insufficiency occurred in 20 out of every 100 patients within 1 year after receiving an Edwards SAPIEN transcatheter heart valve, which was approximately one-third less often than seen in patients who did not receive a new valve (most of whom had balloon aortic valvuloplasty).
Clinical Risk Tables

The following table is a summary of the clinical risks observed within 1 year in high-risk patients (Cohort A) from The PARTNER Trial. The frequency is shown as the number of patients out of every 100. Risk frequencies for TAVR are broken out by the transfemoral and transapical approach.

<table>
<thead>
<tr>
<th>Risks Within 1 Year After the TAVR Procedure</th>
<th>TRANSFEMORAL ARM</th>
<th>TRANSAPICAL ARM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Transfemoral TAVR 21 out of 100 patients</td>
<td>Surgical AVR 25 out of 100 patients</td>
</tr>
<tr>
<td>From any cause</td>
<td>29 out of 100 patients</td>
<td>25 out of 100 patients</td>
</tr>
<tr>
<td>From cardiovascular (heart-related) causes</td>
<td>Transapical TAVR 11 out of 100 patients</td>
<td>Surgical AVR 11 out of 100 patients</td>
</tr>
<tr>
<td>Stroke</td>
<td>16 out of 100 patients</td>
<td>10 out of 100 patients</td>
</tr>
<tr>
<td>Repeat hospitalizations</td>
<td>Transapical TAVR 14 out of 100 patients</td>
<td>Surgical AVR 3 out of 100 patients</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>4 out of 100 patients</td>
<td>5 out of 100 patients</td>
</tr>
<tr>
<td>Bleeding event</td>
<td>Transapical TAVR 11 out of 100 patients</td>
<td>Surgical AVR 29 out of 100 patients</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>9 out of 100 patients</td>
<td>28 out of 100 patients</td>
</tr>
<tr>
<td>Mild</td>
<td>Transapical TAVR 53 out of 100 patients</td>
<td>Surgical AVR 18 out of 100 patients</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>42 out of 100 patients</td>
<td>17 out of 100 patients</td>
</tr>
<tr>
<td>New pacemaker (device that can help regulate the heart) implantation</td>
<td>Transapical TAVR 6 out of 100 patients</td>
<td>Surgical AVR 4 out of 100 patients</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>6 out of 100 patients</td>
<td>8 out of 100 patients</td>
</tr>
</tbody>
</table>

The following table is a summary of the clinical risks observed within 1 year in high-risk patients (Cohort A) from The PARTNER Trial. The frequency is shown as the number of patients out of every 100. Risk frequencies for TAVR are broken out by the transfemoral and transapical approach.

**Days Alive Out of Hospital at 1 Year**

<table>
<thead>
<tr>
<th>Days alive out of hospital at 1 year</th>
<th>TRANSFEMORAL ARM</th>
<th>TRANSAPICAL ARM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfemoral TAVR</td>
<td>306 Days</td>
<td>277 Days</td>
</tr>
<tr>
<td>Transapical TAVR</td>
<td>280 Days</td>
<td>277 Days</td>
</tr>
</tbody>
</table>

**Myocardial infarction (heart attack)**

- Transfemoral TAVR: 0 out of 100 patients
- Transapical TAVR: 0 out of 100 patients

**Endocarditis (inflammation or infection of any internal heart structures, including the valves)**

- Transfemoral TAVR: 1 out of 100 patients
- Transapical TAVR: 1 out of 100 patients

**Death from any cause**

- Transfemoral TAVR: 21 out of 100 patients
- Transapical TAVR: 25 out of 100 patients

**Death from cardiovascular (heart-related) causes**

- Transfemoral TAVR: 10 out of 100 patients
- Transapical TAVR: 7 out of 100 patients

**Repeat hospitalizations**

- Transfemoral TAVR: 14 out of 100 patients
- Transapical TAVR: 13 out of 100 patients

**Major vascular complications**

- Transfemoral TAVR: 4 out of 100 patients
- Transapical TAVR: 5 out of 100 patients

**Bleeding event**

- Transfemoral TAVR: 8 out of 100 patients
- Transapical TAVR: 28 out of 100 patients

**Aortic insufficiency**

- Transfemoral TAVR: 42 out of 100 patients
- Transapical TAVR: 17 out of 100 patients

**New pacemaker (device that can help regulate the heart) implantation**

- Transfemoral TAVR: 6 out of 100 patients
- Transapical TAVR: 8 out of 100 patients

**Kidney failure**

- Transfemoral TAVR: 6 out of 100 patients
- Transapical TAVR: 9 out of 100 patients
The following tables are a summary of the clinical risks observed within 1 year, and between 1 and 2 years in inoperable patients (Cohort B) from The PARTNER Trial. The frequency is shown as the number of patients out of every 100.

### Risks Within 1 Year After the TAVR Procedure

<table>
<thead>
<tr>
<th>Risk</th>
<th>Transfemoral TAVR</th>
<th>Standard Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death</strong></td>
<td>31 out of 100</td>
<td>50 out of 100</td>
</tr>
<tr>
<td>From any cause</td>
<td>20 out of 100</td>
<td>42 out of 100</td>
</tr>
<tr>
<td>From cardiovascular (heart-related) causes</td>
<td>11 out of 100</td>
<td>4 out of 100</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>24 out of 100</td>
<td>44 out of 100</td>
</tr>
<tr>
<td><strong>Repeat hospitalizations</strong></td>
<td>17 out of 100</td>
<td>2 out of 100</td>
</tr>
<tr>
<td><strong>Major vascular complications</strong></td>
<td>17 out of 100</td>
<td>2 out of 100</td>
</tr>
<tr>
<td><strong>Bleeding event</strong></td>
<td>17 out of 100</td>
<td>2 out of 100</td>
</tr>
<tr>
<td><strong>Aortic insufficiency</strong></td>
<td>59 out of 100</td>
<td>43 out of 100</td>
</tr>
<tr>
<td>Mild</td>
<td>20 out of 100</td>
<td>19 out of 100</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>4 out of 100</td>
<td>8 out of 100</td>
</tr>
<tr>
<td>New pacemaker (device that can help regulate the heart) implantation</td>
<td>2 out of 100</td>
<td>4 out of 100</td>
</tr>
<tr>
<td><strong>Kidney failure</strong></td>
<td>1 out of 100</td>
<td>1 out of 100</td>
</tr>
<tr>
<td><strong>Myocardial infarction (heart attack)</strong></td>
<td>1 out of 100</td>
<td>1 out of 100</td>
</tr>
<tr>
<td><strong>Endocarditis (inflammation or infection of any internal heart structures, including the valves)</strong></td>
<td>1 out of 100</td>
<td>1 out of 100</td>
</tr>
</tbody>
</table>
### Days Alive Out of Hospital at 1 Year

<table>
<thead>
<tr>
<th></th>
<th>Transfemoral TAVR</th>
<th>Standard Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days alive out of hospital at 1 year</td>
<td>275 days</td>
<td>247 days</td>
</tr>
</tbody>
</table>

### Risks Between 1 and 2 Years After the TAVR Procedure

<table>
<thead>
<tr>
<th>Risk</th>
<th>Transfemoral TAVR</th>
<th>Standard Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From any cause</td>
<td>13 out of 100 patients</td>
<td>16 out of 100 patients</td>
</tr>
<tr>
<td>From cardiovascular (heart-related) causes</td>
<td>9 out of 100 patients</td>
<td>14 out of 100 patients</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 out of 100 patients</td>
<td>0 out of 100 patients</td>
</tr>
<tr>
<td>Repeat hospitalizations</td>
<td>9 out of 100 patients</td>
<td>14 out of 100 patients</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>0 out of 100 patients</td>
<td>0 out of 100 patients</td>
</tr>
<tr>
<td>Bleeding event</td>
<td>0 out of 100 patients</td>
<td>0 out of 100 patients</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>13 out of 100 patients</td>
<td>5 out of 100 patients</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>2 out of 100 patients</td>
<td>2 out of 100 patients</td>
</tr>
<tr>
<td>New pacemaker (device that can help regulate the heart implantation)</td>
<td>2 out of 100 patients</td>
<td>0 out of 100 patients</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>1 out of 100 patients</td>
<td>2 out of 100 patients</td>
</tr>
<tr>
<td>Myocardial infarction (heart attack)</td>
<td>1 out of 100 patients</td>
<td>1 out of 100 patients</td>
</tr>
<tr>
<td>Endocarditis (inflammation or infection of any internal heart structures, including the valves)</td>
<td>1 out of 100 patients</td>
<td>0 out of 100 patients</td>
</tr>
</tbody>
</table>

Note: Inoperable patients who participated in Cohort B have now been followed out to 2 years. Therefore, these data are available for this patient population.
PRECAUTIONS

• How long your new valve will last is unknown at this time. Regular medical follow-up is essential to evaluate how your valve is performing.

• Transcatheter heart valve patients should stay on blood-thinning medicine for 6 months after the procedure and aspirin for the rest of their lives, unless otherwise specified by their doctor. Patients who do not take blood-thinning medicine may be at increased risk of developing a dangerous blood clot after the procedure which may result in a stroke. Blood-thinning medicine may increase the risk of bleeding in the brain (stroke).

• Transcatheter heart valve patients who are undergoing dental procedures should receive prophylactic antibiotic therapy to minimize the possibility of infection.

• The safety of the transcatheter heart valve has not been established in patients who have:
  - A previously implanted artificial aortic heart valve.
  - A ventricle that does not pump efficiently.
  - An enlarged heart.
  - The safety and performance of the transcatheter heart valve has not been established for patients who have:
    - An aortic heart valve that is not calcified.
    - An aortic heart valve that only has one or two leaflets.
    - A diseased aortic valve in which the main problem is valve leakage.
    - A previously implanted medical device in any heart valve.
    - A diseased mitral valve that is calcified or leaking.
    - Low white blood cell count, low red blood cell count, or other abnormalities in the blood.
    - Unusual ultrasound images of the heart that could represent abnormalities such as a blood clot.
  - Allergies to blood-thinning medications or dye that is injected during the procedure.
  - An aortic valve that is too small or too big to fit the transcatheter heart valve.
  - Diseased or normally shaped vessels leading to the heart.
  - Femoral vessels that are heavily diseased or too small for the delivery device.
  - Aortic valve leaflets with large pieces of calcium that may block the vessels that supply blood to the heart.

WARNINGS

• The safety and performance of the transcatheter heart valve when placed through the transapical approach has not been established for patients who are not candidates for open-heart surgery.

• There is an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to other treatment options for aortic stenosis.

• There is an increased risk of major blood vessel complications in transcatheter aortic valve replacement procedures, as compared to other treatment options for aortic stenosis.

• The artificial valve may not last as long in patients whose bodies process calcium abnormally.

• Talk to your doctor if you are allergic to materials such as chromium, nickel, molybdenum, manganese, copper, silicon, and/or polymeric materials.

• X-ray is used during the procedure and may cause radiation injury to the skin.

• In the trial, the transapical procedure was not offered to and not studied in patients who were appropriate for the transfemoral procedure.

HOW LONG WILL YOUR NEW VALVE LAST?

How long your new valve will last is unknown at this time. Edwards Lifesciences has tested the valve in the laboratory to replicate 5-year durability. All valves tested for 5-year durability passed the test. The first Edwards transcatheter heart valve was implanted in 2002. However, at this time there is limited long-term information to assess durability beyond 3 years.

The most common reason that a biological valve may fail is a gradual build-up of calcium (mineral deposits). In this situation, the valve may not work properly, which may cause your aortic stenosis to return, and possibly chest pain, shortness of breath, irregular heartbeat, and fatigue. If your stenosis returns or the valve leaks, you may need an additional procedure. Talk to your doctor if you experience any of these symptoms. Regular medical follow-up is essential to evaluate how your valve is performing.

CONTACT INFORMATION

For More Information on the Edwards TAVR Procedure
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Mail: Edwards Lifesciences LLC
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Irvine, CA 92614 USA
Online: www.yourheartvalve.com
(Click on “FOR PATIENTS”)
www.edwards.com
(Click on “FOR PATIENTS”)
Data on file at Edwards Lifesciences.

**CAUTION:** Federal (United States) law restricts the Edwards SAPIEN transcatheter heart valve to sale by or on the order of a physician. This device has been approved by the FDA for specific indications for use. See instructions for use for full prescribing information, including indications, contraindications, warnings, precautions and adverse events.

**CAUTION:** Federal (United States) law restricts the RetroFlex 3 delivery system, RetroFlex 3 introducer sheath set, RetroFlex dilator kit, RetroFlex balloon catheter, Edwards transfemoral balloon catheter, Ascendra balloon catheter, Ascendra introducer sheath set, Ascendra balloon aortic valvuloplasty catheter, crimper and Atrion inflation device to sale by or on the order of a physician. See instructions for use for full prescribing information, including indications, contraindications, warnings, precautions and adverse events.

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