Value Package

INSPIRIS RESILIA aortic valve

Edwards

The INSPIRIS RESILIA aortic valve:

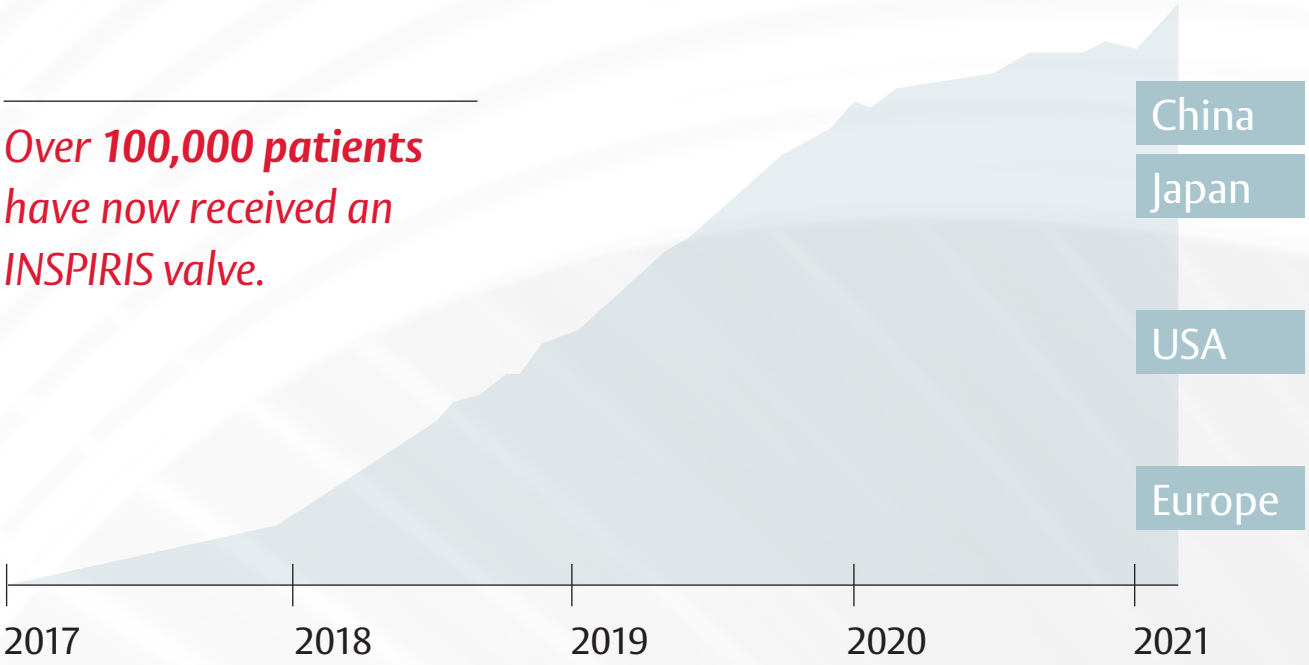
- **Is now the world's leading and most used aortic surgical valve in US and Japan**
- **Has been implanted in more than 100,000 patients in 45 countries worldwide**
- Shows Improved anti-calcification properties*
- Improved sustained hemodynamic performance*
- Built on the proven performance of the Carpentier-Edwards PERIMOUNT valve design
- Has a unique preservation allowing dry storage
- Shows no SVD through 5 years, stable gradients, and freedom from regurgitation all support durability over the observational period[2]
- Can reduce the length of stay compared to both mechanical and tissue valves, and generate savings for the hospital[1]
- Has VFit technology that incorporates two features designed for potential future valve-in-valve (VIV) procedures†

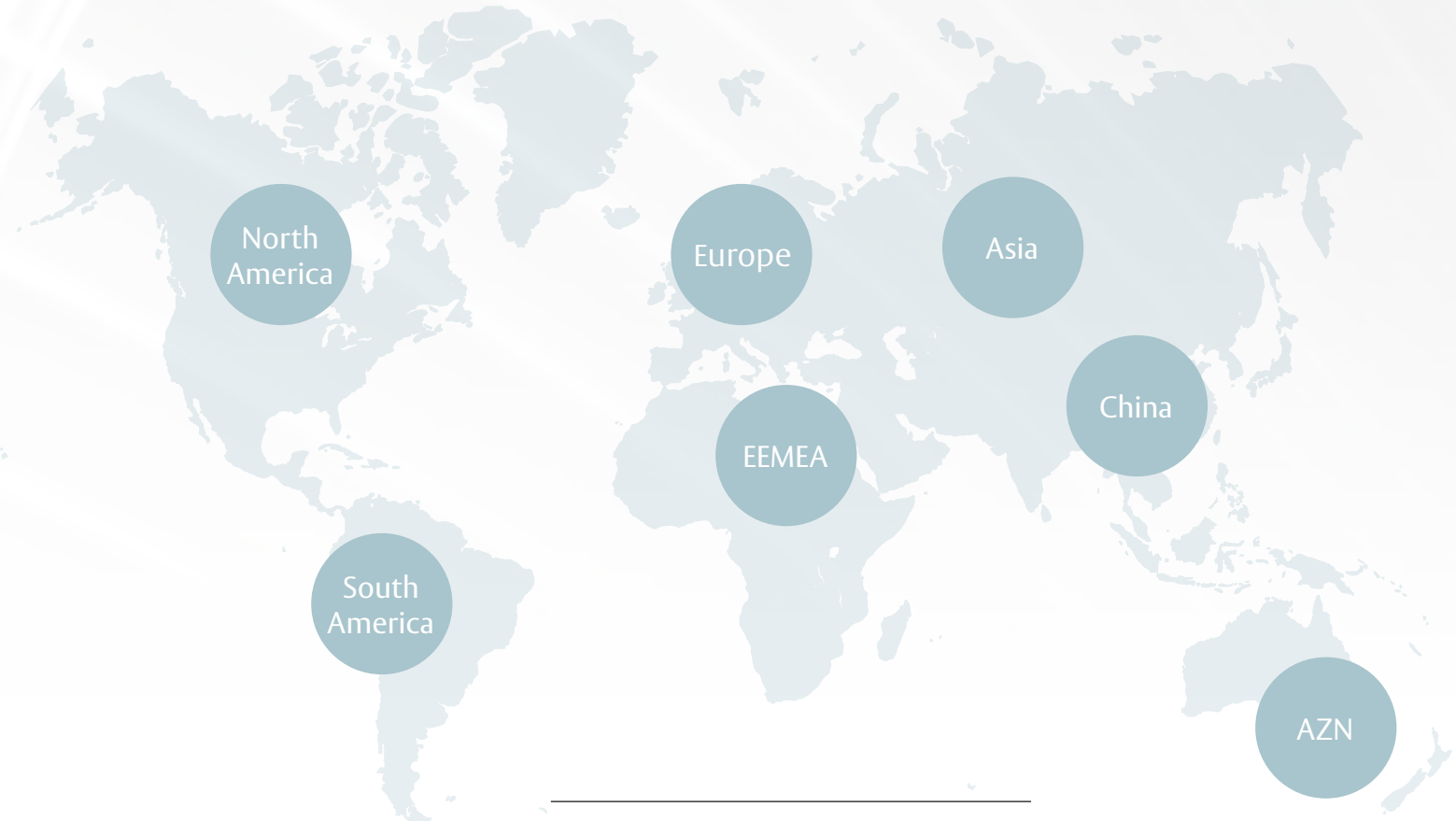
The first product offering within the latest class of resilient bovine pericardial tissue valves

* RESILIA tissue tested against commercially available bovine pericardial tissue from Edwards in a juvenile sheep model. No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients

† Refer to device Instructions for Use for important warnings related to VFit technology. These features have not been observed in clinical studies to establish the safety and effectiveness of the model 11500A for use in valve-in-valve procedures. VFit technology is available on sizes 19-25 mm.

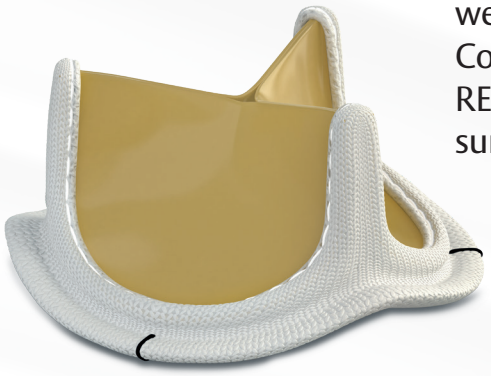
*Over **100,000 patients** have now received an INSPIRIS valve.*





*The INSPIRIS RESILIA valve is in over **45 countries** in more than **1,700 hospitals***

The INSPIRIS RESILIA Aortic Valve



Edwards Lifesciences, the leader in heart valve therapy, welcomes this opportunity to provide the Value Analysis Committee with pertinent information on the INSPIRIS RESILIA aortic valve and the value it offers to patients, surgeons, and hospitals.

The INSPIRIS RESILIA aortic valve is in the latest class of resilient tissue valves.

Key Value Considerations

Patients

People are living longer, desire to maintain an active lifestyle, and may prefer tissue valves that do not require a lifetime of anti-coagulant medication.

Surgeons

The INSPIRIS RESILIA aortic valve incorporates a more resilient tissue with superior anti-calcification properties.*

Hospitals

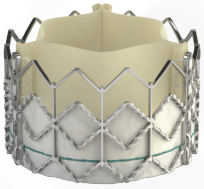
A leader in technology provides more treatment options to patients and establishes your program to address future needs.

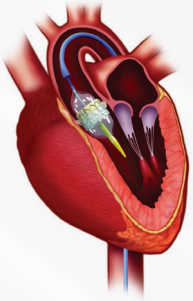
* RESILIA tissue tested against commercially available bovine pericardial tissue from Edwards in a juvenile sheep model. No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.

Edwards Lifesciences, the Leader in Heart Valve Therapy

Edwards Lifesciences has a history of building upon its proven valve platforms to develop new products and operative procedures.

Edwards SAPIEN Transcatheter Heart Valve

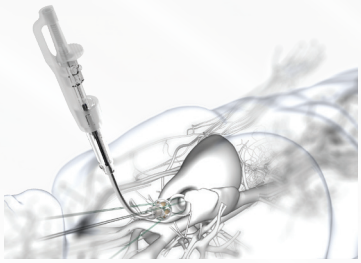




EDWARDS INTUITY Elite Valve System

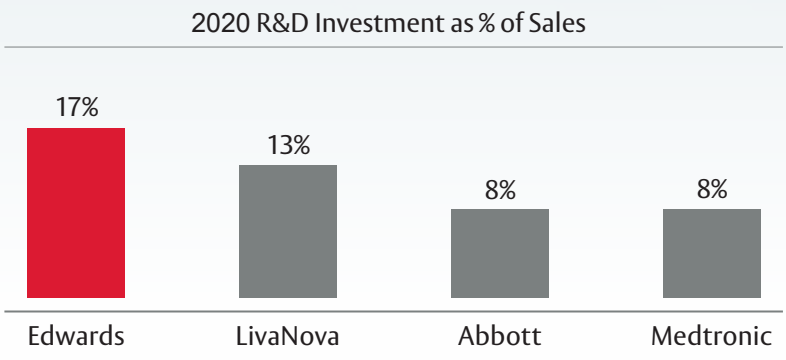
Provides rapid deployment for streamlined procedures and facilitates small incision surgery.

2016



The INSPIRIS RESILIA aortic valve is the result of extensive research and development.

Edwards Lifesciences invests 17% of its revenue into the research and development of patient-focused products and novel operative approaches to address unmet needs.

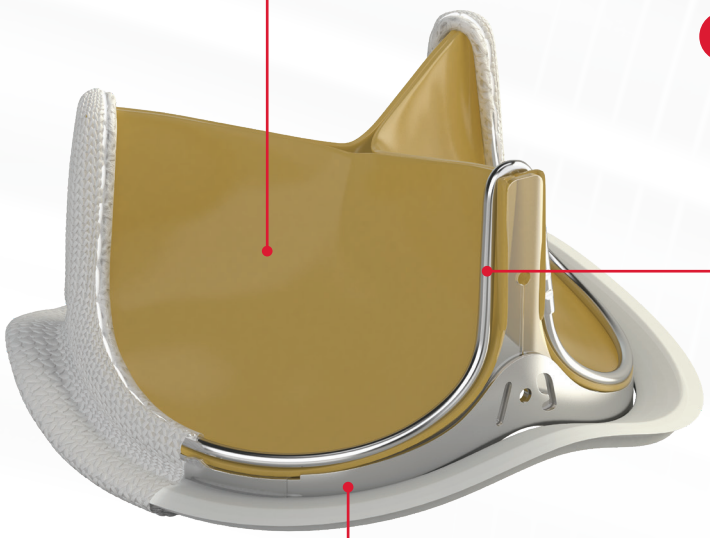


The INSPIRIS RESILIA Aortic Valve—The First Product Offering within the Latest Class of Resilient Tissue Valves

1 RESILIA Tissue

Integrity preservation technology transforms bovine pericardial tissue into RESILIA tissue, effectively eliminating free aldehydes, protecting and preserving the tissue, resulting in:[3,4]

- Improved anti-calcification properties*
- Sustained hemodynamic performance*
- Unique preservation for dry storage



2 Trusted Design and Features

Built on the proven performance of the PERIMOUNT valve design:[5–14]

- Mathematically modeled, bioengineered design
- Three independent leaflets matched for thickness and elasticity
- Flexible, radiopaque cobalt chromium alloy wireform

3 VFit Technology†

Incorporates two novel features designed for potential future valve-in-valve (VIV) procedures.

- Fluoroscopically visible size markers
- Expansion zone†

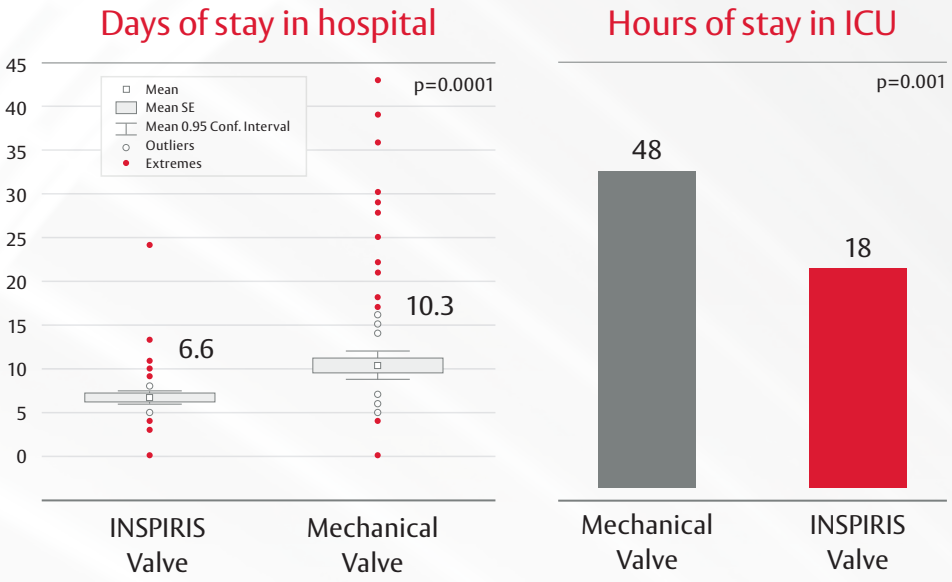
The INSPIRIS RESILIA aortic valve is an ideal foundation for your patient's future.

* RESILIA tissue tested against commercially available bovine pericardial tissue from Edwards in a juvenile sheep model. No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.

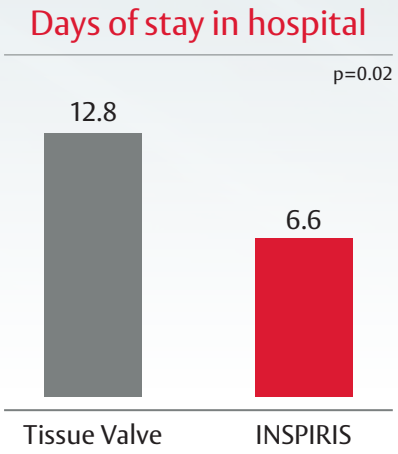
† Refer to device Instructions for Use for important warnings related to VFit technology. These features have not been observed in clinical studies to establish the safety and effectiveness of the model 11500A for use in valve-in-valve procedures. VFit technology is available on sizes 19-25 mm.

The INSPIRIS RESILIA Aortic Valve – can reduce the length of stay and ICU stay compared to mechanical valve*

Differences in length of stay can be directly translated into a cost reduction of € 1,980 in ICU stay and € 2,824 in further hospital stay



The INSPIRIS RESILIA aortic valve – can reduce the total length of stay compared to generic tissue valve*



INSPIRIS RESILIA, an innovative tissue aortic valve, can reduce the length of stay compared to both mechanical and tissue valves, and generate savings for the hospital

* Meuris B. Et al. 2021. Innovation In Anticalcification Technology In Heart Valves Leads To Lower Hospital Stay In Adults Undergoing Aortic Valve Replacement. Oral Presentation at HTAi 2021 virtual congress

Patients in the Future May Need a More Resilient Tissue Solution

Patients are living longer and would like to maintain active lifestyles.

+3 years*
of life expectancy for today's patients[15]

3.5%
AVR procedural growth rate (2017)[16,27]

* Today's surgical WHO EU patients (median age 78, born in 2020) compared to those born a decade ealier (in 2010).

Tissue valves are standard of care for older patients, but due to durability concerns, younger patients are often implanted with a mechanical valve.

A greater percentage of tissue valve patients would repeat their decision to have surgery, than mechanical valve patients.[19]

When choosing a heart valve, a provider should consider the mortality risk of future complications.[18]

* % who responded yes in a tissue valve group versus mechanical valve group when asked "If I had to do it over again, would I make the same decision to have surgery?" (P<0.005)

Mechanical Valves Come with a Lifetime of Anti-Coagulant Usage and an Increased Risk of Major Bleeding

Chronic lifetime anti-coagulant therapy is often poorly managed, time consuming, and inconvenient.

Challenges for anticoagulant therapy:

- More frequent physician visits
- Monitoring of routine blood tests
- Dietary restrictions
- Lifestyle and activity limitations

33%
of anticoagulant blood tests for patients were out of INR target range.[19, 29*]

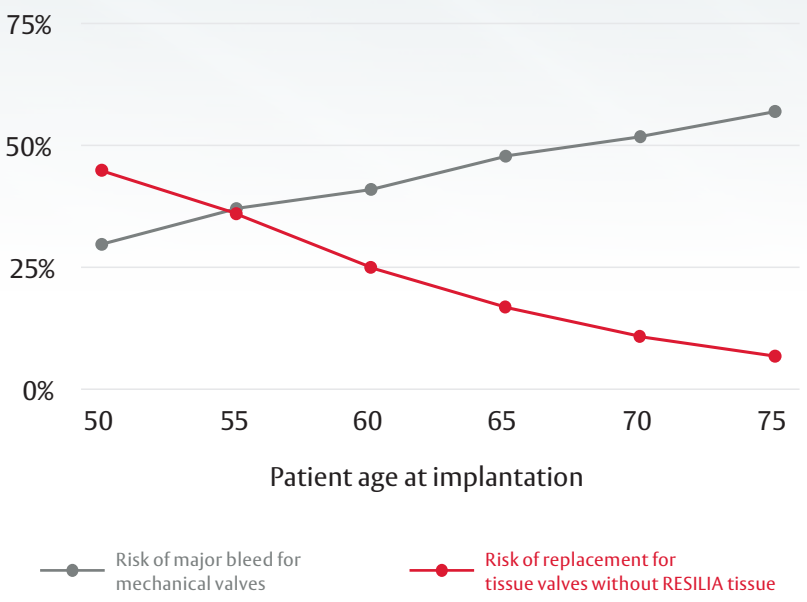
Implications of poorly managed anticoagulant therapy:[19]

- Major bleed risk when dosages are too high
- Stroke risk when dosages are too low

Factors that increase the risk of bleeding include hypertension, diabetes, anemia, congestive heart failure, history of stroke, and increasing age.

Major bleed risk increases with mechanical valves as the patient gets older.

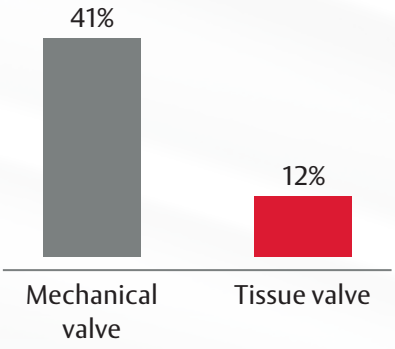
Mechanical valves have an increased risk of major bleeds as patients get older, while tissue valves have a decreased risk of replacement surgery as patients get older.[18]



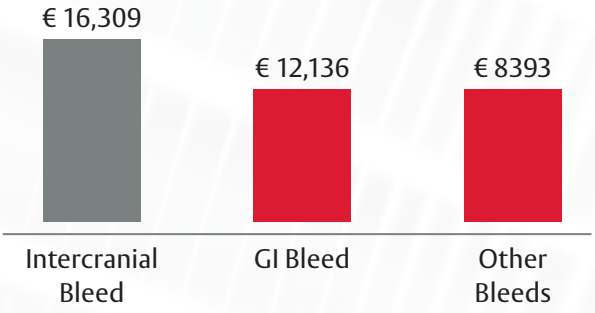
Major bleeds can be difficult to manage and costly

When hospitalization occurs for major bleeds, the 30-day re-admission cost is higher than the cost associated with the initial bleed hospitalization.

Lifetime bleed risk for patients implanted at 60 years of age[18]



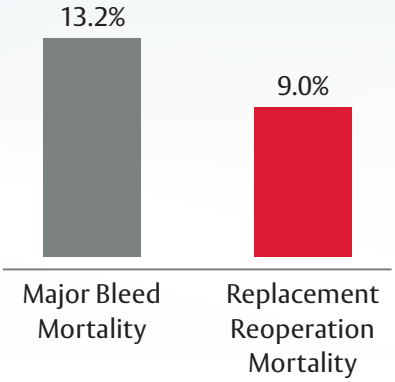
Healthcare costs for major bleed events*[24]



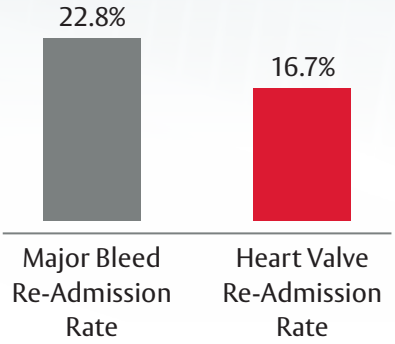
* Cost study performed in patients with primary diagnosis of AFib

Major bleeds lead to higher 30-day mortality rates and 30-day hospital readmission rates than a future valve reoperation does.[20,21]

30-day mortality rates*[20]



30-day hospital readmission rates[21]



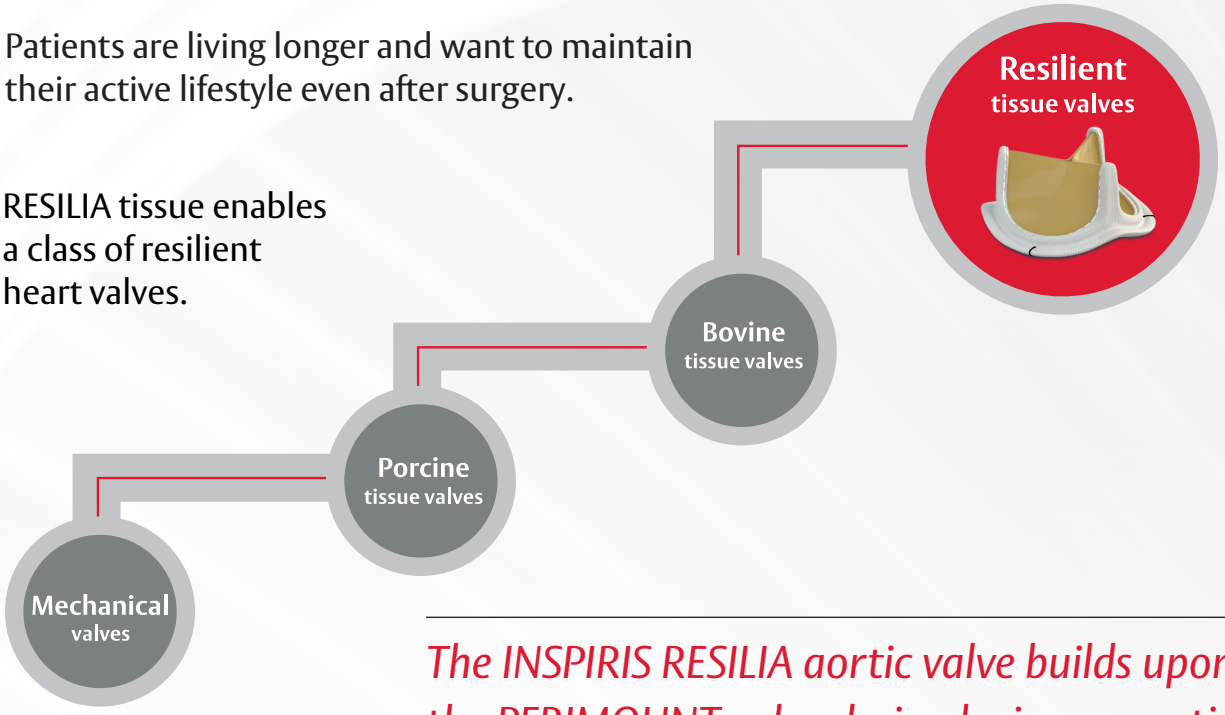
* For patients aged 50-69

Mechanical valves may not be the best option for today's patients.

While Current Tissue Valves Have Excellent Durability, Patients are at Risk of Outliving Them Due to a Longer Life Expectancy

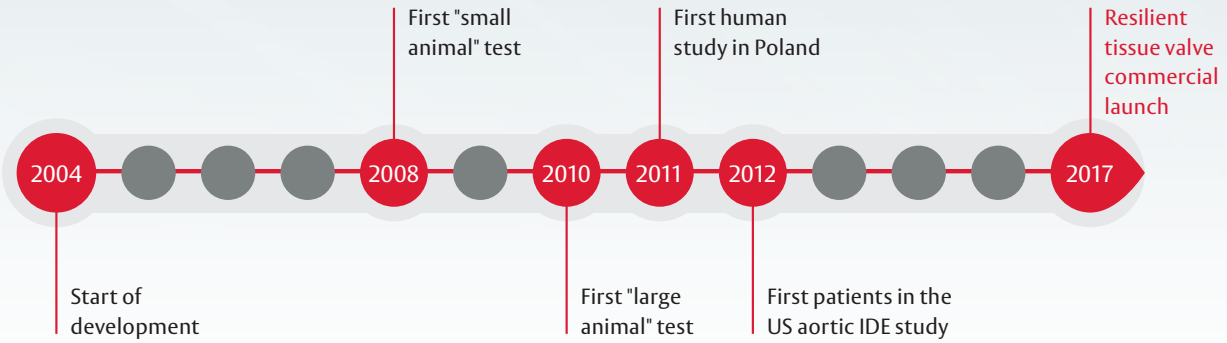
Patients are living longer and want to maintain their active lifestyle even after surgery.

RESILIA tissue enables a class of resilient heart valves.



The INSPIRIS RESILIA aortic valve builds upon the PERIMOUNT valve design by incorporating RESILIA tissue and VFit technology.

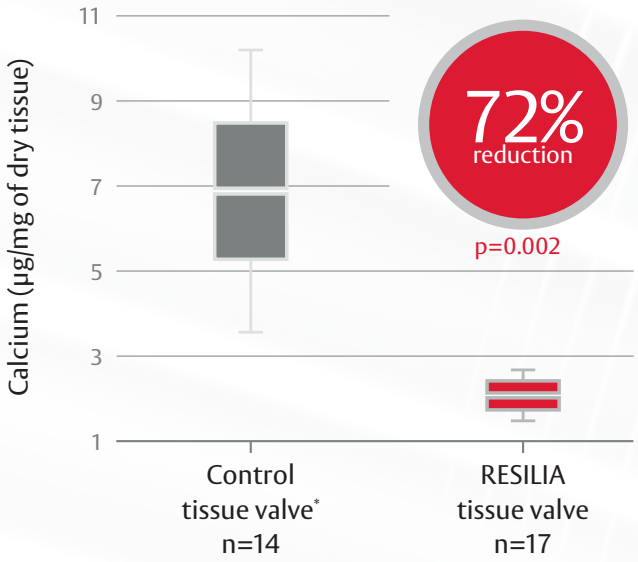
RESILIA tissue is the result of a rigorous development program of more than 12 years involving 100+ evaluations of safety and efficacy.



* No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients

Preclinical Evaluation: Valves With RESILIA Tissue

Why calcium matters: the primary mode of failure for bovine pericardial valves is calcification.

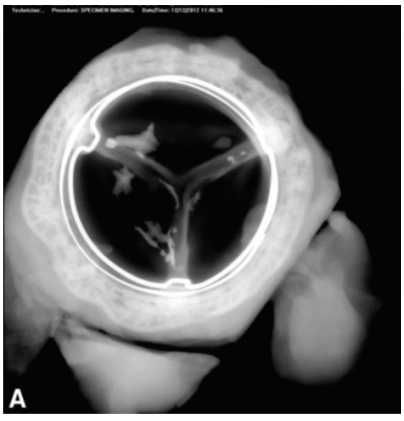


A 72% reduction in calcium content has been shown with RESILIA tissue valves when studied in a juvenile sheep model.[3]

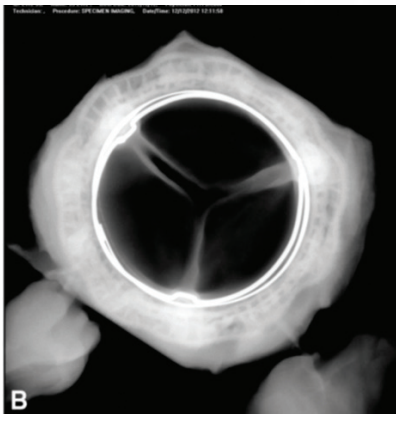
The sheep model mirrors accelerated calcification that is often seen in younger humans.

Representative radiographic examples of explanted valves from the juvenile sheep study reveal visible calcification on the leaflets in the control group (A) and visibly less calcification in the RESILIA tissue valve group (B).[3]

Control valve*



RESILIA tissue valve



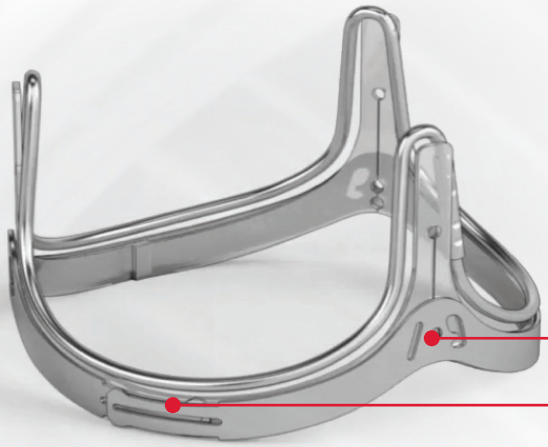
By reducing calcification, the integrity preservation technology allows the INSPIRIS RESILIA aortic valve to be resilient.

* Carpentier-Edwards PERIMOUNT Plus pericardial mitral bioprosthesis, model 6900P.

No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients.

The INSPIRIS RESILIA Aortic Valve has VFit Technology and Dry Storage Capability

VFit Technology†



VFit technology incorporates two novel features designed for potential future valve-in-valve (VIV) procedures.†

- A fluoroscopically visible labeled valve size marking at each commissure provides information after implant
- Expansion zone

† Refer to device Instructions for Use for important warnings related to band expansion and VFit technology. These features have not been observed in clinical studies to establish the safety and effectiveness of the model 11500A for use in valve-in-valve procedures. VFit technology is available on sizes 19-25 mm.

Dry Storage

RESILIA tissue valves are ready to use; no rinsing required

Current tissue valves are stored in aldehyde-based solutions, requiring rinsing and safe handling

An ideal foundation for your patient's future: RESILIA tissue, trusted design and features, and VFit technology.

Your cardiac valve program is important to the health of your community and the growth of your hospital

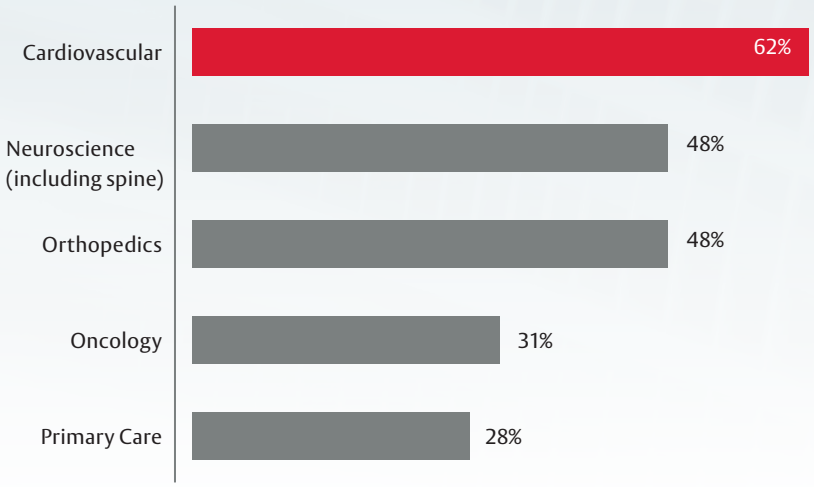
Aortic stenosis by the numbers

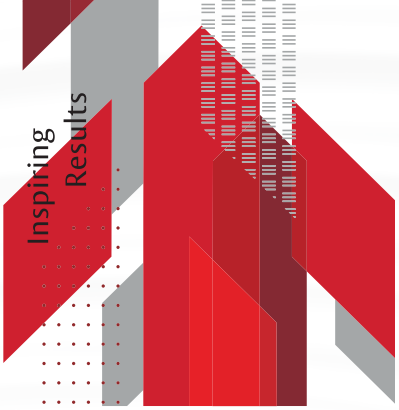
3.4%
of the elderly population will have severe aortic stenosis[22]

3.5%
survival among medically managed severe symptomatic aortic stenosis patients at 5 years.[23]

70% of cardiac surgeons would choose an Edwards tissue valve for themselves or a close family member.[26]

Hospital administrators rate Cardiovascular as the most important department to their growth strategy.[25]





Clinical Summary: Five-year outcomes of the COMMENCE trial investigating aortic valve replacement with a novel tissue bioprosthesis

Bavaria J, Griffith B, Heimansohn DA, et al. Presented at the Society of Thoracic Surgeons Annual Meeting, January 2021.

Objective

The COMMENCE trial is an FDA pivotal trial designed to evaluate the safety and effectiveness of a bioprosthetic valve with the novel RESILIA tissue. In particular, as the follow up time in this study advances beyond the early period, direct and indirect measures of RESILIA durability will be highlighted.

Methods

- Prospective, non-randomized, multicenter, single-arm Investigational Device Exemption (IDE) Trial
  - Study subjects were enrolled at 27 clinical sites in U.S. and Europe
  - All patients undergo annual follow up through 5 years; a subset will be followed through 10 years
- Safety endpoints
  - All potential safety endpoints adjudicated by an independent Clinical Events Committee
  - Structural valve deterioration (SVD) and other safety outcomes defined per "Guidelines for reporting morbidity and mortality after cardiac valve interventions" (Akins et al. 2008)
- Effectiveness endpoints
  - Hemodynamic performance evaluated by an Independent Echocardiographic Core Laboratory
  - NYHA Functional Class

Patient Demographics

- 689 patients underwent surgical AVR with the Edwards Pericardial Aortic Bioprosthesis with RESILIA tissue (model 11000A)
  - Mean age 66.9 ± 11.6 years, with 140 patients (21%) under 60 years
  - 71.8% male
  - 26% NYHA Class III/IV
  - Mean STS PROM 2.0 ± 1.8%
  - 59% isolated AVR
- 2989 aggregate patient-years of follow up
  - Follow up: 4.3 ± 1.4 yrs

Key Points

- Through a median follow up of 5 years, results of the COMMENCE aortic trial indicate a favorable safety profile and stable hemodynamic performance of a bioprosthetic valve with RESILIA tissue
- No SVD through 5 years, stable gradients, and freedom from regurgitation all support durability over the observational period*

Fig 1. Safety endpoints

Endpoint	Early (≤ 30 POD) events (%)	Kaplan-Meier probability event-free at 5 yrs (%) (95% CI)
All-cause mortality	8 (1.2%)	89.2 (86.7 – 91.6)
Stroke	11 (1.6%)	94.5 (92.7 – 96.3)
Valve thrombosis	0 (0%)	100.0 (100.0 – 100.0)
Major bleeding	5 (0.7%)	94.3 (92.4 – 96.1)
Endocarditis	0 (0%)	97.8 (96.6 – 99.0)
Major PVL†	1 (0.1%)	99.5 (99.0 – 100.0)
NSVD (other than PVL)	0 (0%)	100.0 (100.0 – 100.0)
SVD*	0 (0%)	100.0 (100.0 – 100.0)
Reoperation	1 (0.1%)	98.7 (97.8 – 99.6)

†Major PVL is PVL of any grade requiring surgical intervention or considered an SAE.
* 1 SVD diagnosed at POD 1848.

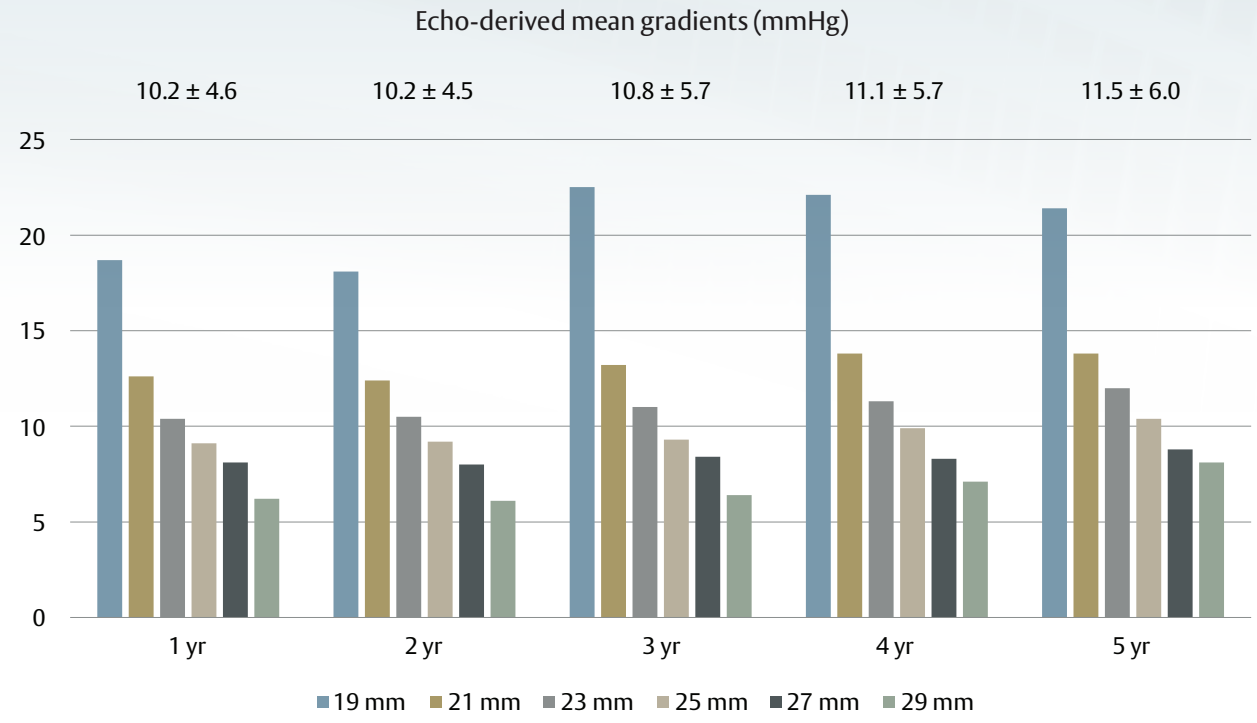
Results

- Safety endpoints, probability event-free at 5 years (shown in Fig. 1):
  - All-cause mortality, 89.2%
  - Major paravalvular leak, 99.5%
  - Endocarditis, 97.8%
- Improved hemodynamic performance compared to baseline was observed through 5 years
  - Mean gradient was 10.2 ± 4.6 at 1 year, 10.2 ± 4.5 at 2 years, and 10.8 ± 5.7 at 3 years, 11.1 ± 5.7 mmHg at 4 years, and 11.5 ± 6.0 at 5 years (shown in Fig. 2)

Conclusions

- Favorable safety profile and stable hemodynamic performance of a bioprosthetic valve with RESILIA tissue
- No SVD through 5 years*, stable gradients, and freedom from regurgitation all support durability over the observational period
- Ongoing follow-up continues to evaluate the long-term safety and effectiveness of this new tissue
  - Data from 10-year follow up in extended follow-up cohort and RESILIENCE trial with 11-year follow-up forthcoming

Fig 2. Hemodynamic performance



Conclusion

- Patients are living longer, desire to maintain an active lifestyle, and may prefer tissue valves that do not require a lifetime of anti-coagulant medication.
- While current tissue valves have excellent durability, patients are at risk of outliving tissue valves due to a longer life expectancy.
- While tissue valves are standard of care for older patients younger patients are often implanted with a mechanical valve.
- A durable tissue valve can postpone or eliminate the need for a future reoperation due to structural valve deterioration.

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