Inspire

Your latest news on RESILIA tissue

Newsletter #4 – March 2023

Life^{R}

Life to the power of RESILIA

A promise of freedom. That's the power of RESILIA tissue.

Edwards

In this issue

We hope you enjoy this issue of *Inspire*. Want to hear more from EACTS 2022, including our congress podcast series on our latest data? Visit **edwardseducation.com/edwardsmasters or scan the QR code.**

Introduction

For patients referred for surgical aortic valve replacement (SAVR), there are now three options: mechanical valves, conventional tissue valves or RESILIA tissue valves. When it comes to quality of life, a higher proportion of patients with mechanical valves than with tissue valves report dissatisfaction or uncertainty about their valve choice.[1]

RESILIA tissue gives surgeons the freedom to offer a resilient tissue option that brings the quality-of-life benefits of tissue valves to more patients. That's why Edwards Lifesciences is advancing the future of cardiac surgery with a growing portfolio of valves designed with RESILIA tissue.

RESILIA tissue offers the possibility of reducing the risk of costly surgical reintervention later in life when risks may be higher, providing surgeons the freedom to focus on what matters most: patient wellbeing.

RESILIA tissue is the result of several generations of tissue valve innovation that started with the Carpentier-Edwards PERIMOUNT valve in 1981. Our continued advancement of tissue technology has led to a unique understanding of associated challenges and the best ways to address them.

Edwards maintains its commitment to leadership in surgical heart valve development; that is why RESILIA tissue is the backbone of our future surgical heart valve development.

None of this would be possible without the support and partnership of the dedicated surgeons with whom we collaborate. This community and a commitment to patient-focused innovation help guide our research and development to address the most critical aspects of patient care.

RESILIA tissue offers freedom

The power of Edwards Lifesciences' heart valves with RESILIA tissue is freedom.

Excellent clinical and haemodynamic outcomes up to 5 years with the INSPIRIS RESILIA valve

D'Onofrio A. Presented at the PCR London Valves meeting in London, November 2022.

As bioprosthetic valves are increasingly being used in younger patients, the life expectancy of the patient can exceed that of the bioprosthesis; therefore, appropriate bioprosthesis selection and implantation technique are important to achieve good durability and haemodynamic performance of the valve, and for potential future valve-in-valve interventions. At PCR London Valves 2022, Prof. D'Onofrio presented 5-year safety and efficacy outcomes of the INSPIRIS RESILIA valve[2]

The INSPIRIS RESILIA aortic valve combines RESILIA tissue with the design of the PERIMOUNT valve and includes VFit technology comprising fluoroscopically visible size markers and an expandable cobalt–chromium alloy band designed for future valve-in-valve procedures.

RESILIA tissue integrity preservation technology stable-caps free aldehydes – a key factor in calcification – and glycerolisation allows dry storage of RESILIA tissue, preventing further exposure to free aldehydes, which occurs with traditional storage in solutions such as glutaraldehyde.

89%
Freedom from all-cause mortality

99%
Freedom from all-cause reoperation

99%
Freedom from study valve explant

100%
Freedom from SVD

"The INSPIRIS RESILIA valve has demonstrated excellent clinical and haemodynamic outcomes up to 5 years"

Prof. D'Onofrio

The COMMENCE clinical trial recently reported 5-year safety and efficacy outcomes for the INSPIRIS RESILIA valve in a cohort of younger patients with a mean (± SD) age of 67.0 ± 11.6 years:[2] The INDURE registry, which aims to assess clinical outcomes of the INSPIRIS RESILIA valve in patients less than 60 years old, recently reported 1-year outcomes, with a mean (± SD) gradient of 12.6 ± 5.3 mmHg and an effective orifice area of 1.9 ± 0.6 cm^2. No valve-related deaths or structural valve deterioration (SVD) were reported; there was one case of late infective endocarditis requiring reintervention. Four cases of valve thrombosis were reported, but all were treated with anticoagulation therapy and did not require intervention.

Real-world data comparing early clinical and haemodynamic outcomes of the PERIMOUNT Magna Ease valve, INSPIRIS RESILIA valve and the EDWARDS INTUITY Elite valve showed similar transaortic gradients for the INSPIRIS RESILIA and EDWARDS INTUITY Elite valves. The EDWARDS INTUITY Elite valve showed better haemodynamic performance compared with the Magna Ease valve.

In conclusion, the INSPIRIS RESILIA valve has demonstrated excellent clinical and haemodynamic outcomes up to 5 years, with studies ongoing to assess long-term performance and to evaluate the efficacy of VFit technology for valve-in-valve procedures.

ISTOCK.COM/CMONKEYBUSINESSIMAGES

Positive 3-year results for INSPIRIS RESILIA valve in young patients

El-Sayed Ahmad A *et al. J Card Surg*. 2022; **37**: 4833–40.

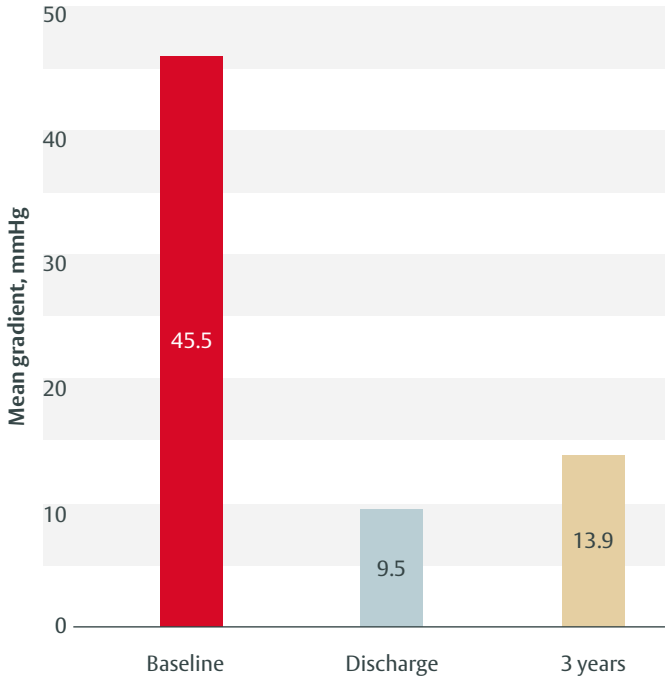
The INSPIRIS RESILIA valve demonstrates encouraging haemodynamics and mid-term durability in a study from a German high-volume centre.[3]

El-Sayed Ahmad and colleagues from Witten-Herdecke University collected data from 154 patients (mean age 56.8 years) who underwent AVR with the INSPIRIS RESILIA valve. Early postoperative outcomes were positive, with no cases of SVD, valve-related thrombosis or valve-related mortality reported during this time. Rates of paravalvular leak (2.0%) and reoperation due to endocarditis (0.6%) were within the normal range.

More than half (58.4%) of the patients in this cohort were younger than 60 years old. Haemodynamic outcomes in these young patients did not differ from those of the overall cohort. While the authors believe that younger patients will benefit most from the potential durability of the INSPIRIS RESILIA valve, they acknowledge that this needs to be assessed further in longer-term studies.

Valve choice was made on the basis of many criteria including lifestyle choice, desire for future pregnancy and contraindications for anticoagulant therapy. Where young patients opted for a bioprosthetic valve, the INSPIRIS RESILIA valve was implanted more often than other contemporary bioprostheses.

Mean gradient



"Because of the reduction in calcium deposits on the valve tissue, minimising prosthetic degeneration, we believe that patients under 60 years will benefit most from the advantages of the new generation INSPIRIS RESILIA valve"

Dr El-Sayed Ahmad

Improved haemodynamics for Japanese patients with the INSPIRIS RESILIA valve

Fukunaga N *et al*. *J Artif Organs*. 2022; **25:** 323–8.

Researchers have reported favourable postoperative haemodynamics after SAVR with the INSPIRIS RESILIA valve in Japanese patients with severe aortic stenosis.[4]

While data from the COMMENCE trial showed stable haemodynamic performance of the RESILIA tissue valve over 5 years,[5] results from Japanese patients have not previously been published.

Naoto Fukunaga and colleagues from Hyogo Prefectural Amagasaki General Medical Center in Japan performed AVR with the INSPIRIS RESILIA valve in 29 patients (mean age 75.1 years) with severe aortic stenosis. They assessed the haemodynamic performance of the valve by transthoracic echocardiography at 3–6 months, 1 year and 2 years after surgery.

Early (30-day) operative outcomes were good, with a mortality rate of 0 and no valve explant, thromboembolism, valve thrombosis or significant paravalvular leak, and no patients required early pacemaker implantation.

Freedom from all-cause mortality at 2 years was 96.6% and freedom from valve-related events was 91.2% with no major paravalvular leakage or SVD at 2 years.

ISTOCK.COM/PETESPHOTOGRAPHY

Haemodynamic performance following surgery

↓ **–41.7 mmHg**
Mean gradient

↑ **–35 g/m²**
Left ventricular mass index

↑ **+0.95 cm²**
Effective orifice area

Mean gradient remained consistent for every valve size during the 2-year follow-up.

Long-term cost savings associated with RESILIA tissue valves

Keuffel EL *et al*. *J Med Econ*. 2023; **26:** 120–7.

An economic evaluation by Keuffel *et al*. used published data from the COMMENCE study to evaluate the potential long-term savings associated with using a RESILIA tissue valve compared with a mechanical or contemporary non-RESILIA tissue valve.[6]

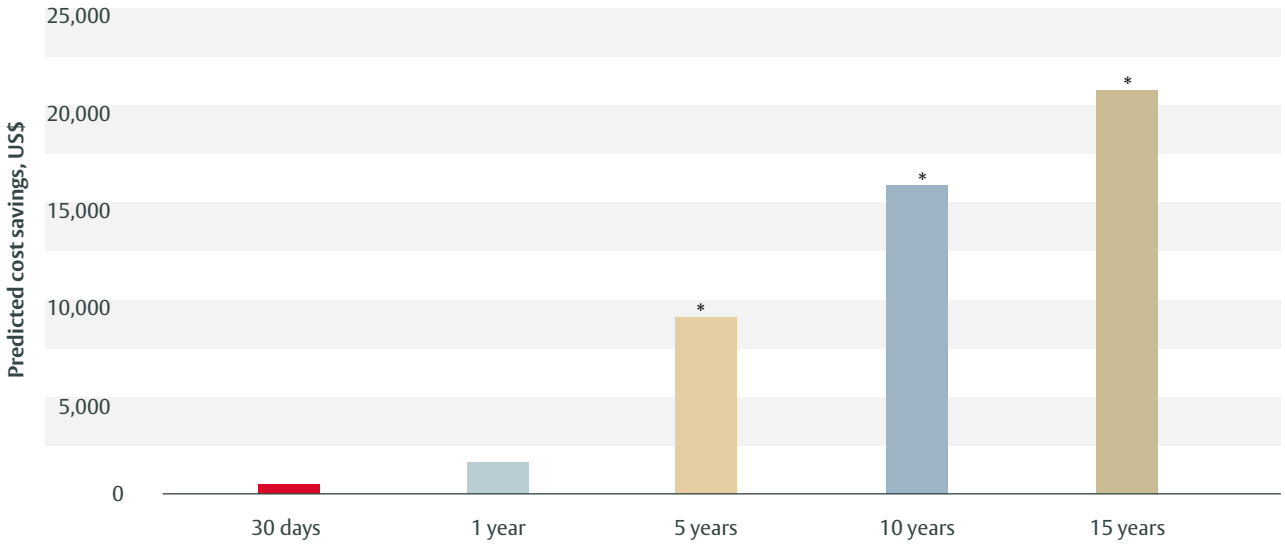
Following CHEERS (Consolidated Health Economic Evaluation Reporting Standards) methodology, the study used simulation models to estimate disease progression of two hypothetical cohorts (mechanical *vs* bioprosthetic valves) of 10,000 patients in the USA over 15 years. The model estimated SAVR-related expenditure associated with mortality, endocarditis, bleeding or haemorrhagic event, thrombosis, reoperation and anticoagulant monitoring.

Expected savings for RESILIA tissue *versus* mechanical valves reach significance after 5 years, cumulative net discounted savings per patient at 15 years $20,755 (95% CI $15,780–$26,636).

"In the long-term, RESILIA valves will be associated with lower health expenditure than mechanical valves"

Dr Keuffel

Cumulative net discounted savings per patient for RESILIA tissue *versus* mechanical valves



*Statistically significant at 99% level (99% estimates exceed $0)

Additionally, net savings for RESILIA tissue valves were 30–50% larger than the savings predicted for legacy non-RESILIA bioprostheses versus mechanical valves, indicating that, over the long term, RESILIA valves will be associated with lower health expenditure than mechanical valves.

Calcification-resistant bioprosthetic valves – are we close to achieving the holy grail?

Ricci A *et al*. *Surg Technol Int*. 2022; **40:** 235–40.

A comprehensive review of bioprosthesis evolution by Ricci *et al*. discusses the novel anticalcification technology used in RESILIA tissue along with early data for RESILIA tissue valves.[7]

The revolutionary INSPIRIS RESILIA valve builds on the Carpentier-Edwards PERIMOUNT valve design with breakthrough anticalcification technology, delivering a valve with improved durability and the potential to exceed the life expectancy of the patient. The European Hospital in Rome performed the first implant in Italy of the INSPIRIS RESILIA valve and consistently offers this valve as an option to younger patients who prefer not to have a mechanical valve.

The European Hospital have performed a total of 248 implants of the INSPIRIS RESILIA valve as of November 2021 and report an early mortality rate of 1.13% and pacemaker implantation rate of 2.26% – comparable to standard rates for this centre.

When discussing the impact of a new valve, raw data are important, but these should be considered within a wider context, including patient expectations and future quality of life; the authors highlight the three main points which should be considered.

When discussing the impact of a new valve, three main points should be considered:

1

Technical data

Early data from the INSPIRIS RESILIA valve are promising and there is potential for longer durability of these valves. Although no bioprosthesis can match mechanical valves in terms of longevity, the increased durability will offer a wider range of patients a longer period free from SVD and anticoagulation-related events.

2

Cultural considerations

Patients are willing to accept the compromise of future reoperations associated with bioprostheses for an improved quality of life free from lifelong anticoagulation.

3

Future interventions

Advances in transcatheter techniques mean that surgery is no longer always required for aortic valve replacement, and future valve-in-valve implantation is now accepted as a good alternative to conventional mechanical prostheses.

ISTOCK.COM/SOLSTOCK

Experience with INSPIRIS RESILIA valve

Vlad Gariboldi is a professor of adult cardiac surgery at Hôpital de la Timone, Marseille. He has extensive experience using Edwards valves in SAVR; Hôpital de la Timone was one of the first centres in Europe to use the INSPIRIS RESILIA valve and is one of the participating centres in the Benchmark Registry. We caught up with him to discuss his experience with the INSPIRIS RESILIA valve.

Q. What factors do you consider when choosing which surgical valve to use in your patients?

A. When I was a young surgeon, the main criteria was patient age at implantation. However, with fewer mechanical valves implanted worldwide, the key consideration now, particularly when the patient is younger than 50–55 years old, is the ability of the patients to take lifelong anticoagulants. You must explain the positives and negatives of each valve type to the patient. However, if the patient doesn't want anticoagulant treatment, or if they are between 50–70 years old, we recommend the use of the INSPIRIS RESILIA valve.

Q. When and why did you start using the INSPIRIS RESILIA valve?

A. We began to use the INSPIRIS RESILIA prosthesis right from the start: from May 2017. We were one of the first centres in France, and in Europe perhaps, to use this valve, and we have now implanted it in about 800 patients.

Q. What gave you the confidence to start using the valve?

A. We have been using Edwards Lifesciences prostheses for a long time and were very confident with the Magna Ease and PERIMOUNT valves. We found it amazing that Edwards, who is the leader in the field of bioprostheses and have a large research and development department, were bringing a new prosthesis to the market, giving lots of theoretical advantages. We thought it would be exciting and interesting to study.

Q. Which features of the valve particularly appealed to you?

A. For younger patients the key point is valve durability; therefore, the new RESILIA tissue, which showed lower calcification in animal studies, was a key feature. We hope that RESILIA tissue, being more resistant to calcification, will allow the valve to last longer, so the patient will have less need for reintervention. Also, the VFit technology that may give patients a potentially easier treatment if there is structural valve deterioration in the long term.

Q. How does the INSPIRIS RESILIA valve affect your patients' lifetime management plans?

A. Before this valve, we could tell patients that as long as they have good management of their treatment that they will not need a reoperation if they receive a mechanical valve. If they opted for a bioprosthetic valve we could tell them that their quality of life would be better (than for a mechanical valve), but if they are younger than 70 they will probably need reoperation.

We are now seeing younger and younger patients opting for a bioprosthetic valve and so we must do a lifetime plan with them. If the patient is 50–55 years old, we tell them that they will probably need one or two reoperations. We tell them that the first reoperation will likely be a standard surgical replacement (which carries no more risk than the first surgery); however, if they are really young and require a second reintervention, it would likely be TAVI [transcatheter aortic valve implantation].

"We appreciate that Edwards keeps developing valves for classic cardiac surgery"

Prof. Gariboldi

Q. Hôpital de la Timone is one of the centres involved in the INDURE registry (which will assess the outcomes of surgical aortic valve replacement with INSPIRIS RESILIA valve in patients younger than 60 years old). Why is this registry important? Can you share your experience so far?

A. When you have a new valve, you must have a registry to collect clinical and echocardiography data at both short- and long-term follow-up. This registry already has shown excellent 1-year results, which were presented at EACTS 2021. This was an important first step and we now need to go further and see the 5-year results and beyond.

Q. Would you recommend the INSPIRIS RESILIA valve to other surgeons?

A. Of course, we now use it routinely in our institution. The sizing is easy, and the dry packaging avoids the need to rinse the valve.

Q. What experience do you have with other Edwards valves and technologies?

A. We currently use all of the different Edwards prostheses in our institution, in both aortic and mitral surgery. We are also hoping for the new RESILIA tissue valve in the mitral position in the future and that the KONECT RESILIA aortic valve conduit will become available in France.

Q. What inspires your trust in Edwards' valves and technologies?

A. Our long-term partnership gives us confidence. Also, despite the increase in TAVI procedures, we appreciate that Edwards keeps developing valves for classic cardiac surgery, such as the EDWARDS INTUITY valve system and now the INSPIRIS RESILIA valve. It allows us to give patients the best options, whether that's conventional surgery or TAVI.

References:

1. Ruel M, Kulik A, Lam BK *et al*. Long-term outcomes of valve replacement with modern prostheses in young adults. *Eur J Cardiothorac Surg*. 2005; **27:** 425–33; discussion 33.
2. D'Onofrio A. INSPIRIS RESILIA aortic valve: A new-age bioprosthesis from development to clinical data. PCR London Valves 27–29 November 2022, London, UK.
3. El-Sayed Ahmad A, Giammarino S, Salamate S *et al*. Clinical performance of a novel bioprosthetic surgical aortic valve in a German high-volume center. *J Card Surg. 2022*; **37:** 4833–40.
4. Fukunaga N, Yoshida S, Shimoji A *et al*. Hemodynamic performance of INSPIRIS RESILIA aortic bioprosthesis for severe aortic stenosis: 2-year follow-up in Japanese cohort. *J Artif Organs*. 2022; **25:** 323–8.
5. Bavaria JE, Griffith B, Heimansohn DA *et al*. Five-year outcomes of the COMMENCE trial investigating aortic valve replacement with RESILIA tissue. *Ann Thorac Surg*. 2022; doi:10.1016/j.athoracsur.2021.12.058.
6. Keuffel EL, Reifenberger M, Marfo G *et al*. Long-run savings associated with surgical aortic valve replacement using a RESILIA tissue bioprosthetic valve versus a mechanical valve. *J Med Econ*. 2023; **26:** 120–7.
7. Ricci A, Weltert LP, Lucertini G *et al*. Biological valves impervious to calcification: Is this holy grail a cup ready to drink? *Surg Technol Int*. 2022; **40:** 235-40.

Important safety information:

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

Based on bench data. Refer to device Instructions for Use for important warnings related to VFit technology. These features have not been evaluated 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

Use of the EDWARDS INTUITY Elite valve system may be associated with new or worsened conduction disturbances, which may require a permanent cardiac pacemaker implant (PPI). The rate of PPI for the EDWARDS INTUITY Elite valve is within the range reported in the literature for various rapid deployment valves, but higher than that reported for surgical aortic valves. Physicians should assess the benefits and risks of the EDWARDS INTUITY Elite valve prior to implantation. See instructions for use for additional information.

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

Edwards Lifesciences • Route de l'Etraz 70, 1260 Nyon, Switzerland • edwards.com

Edwards