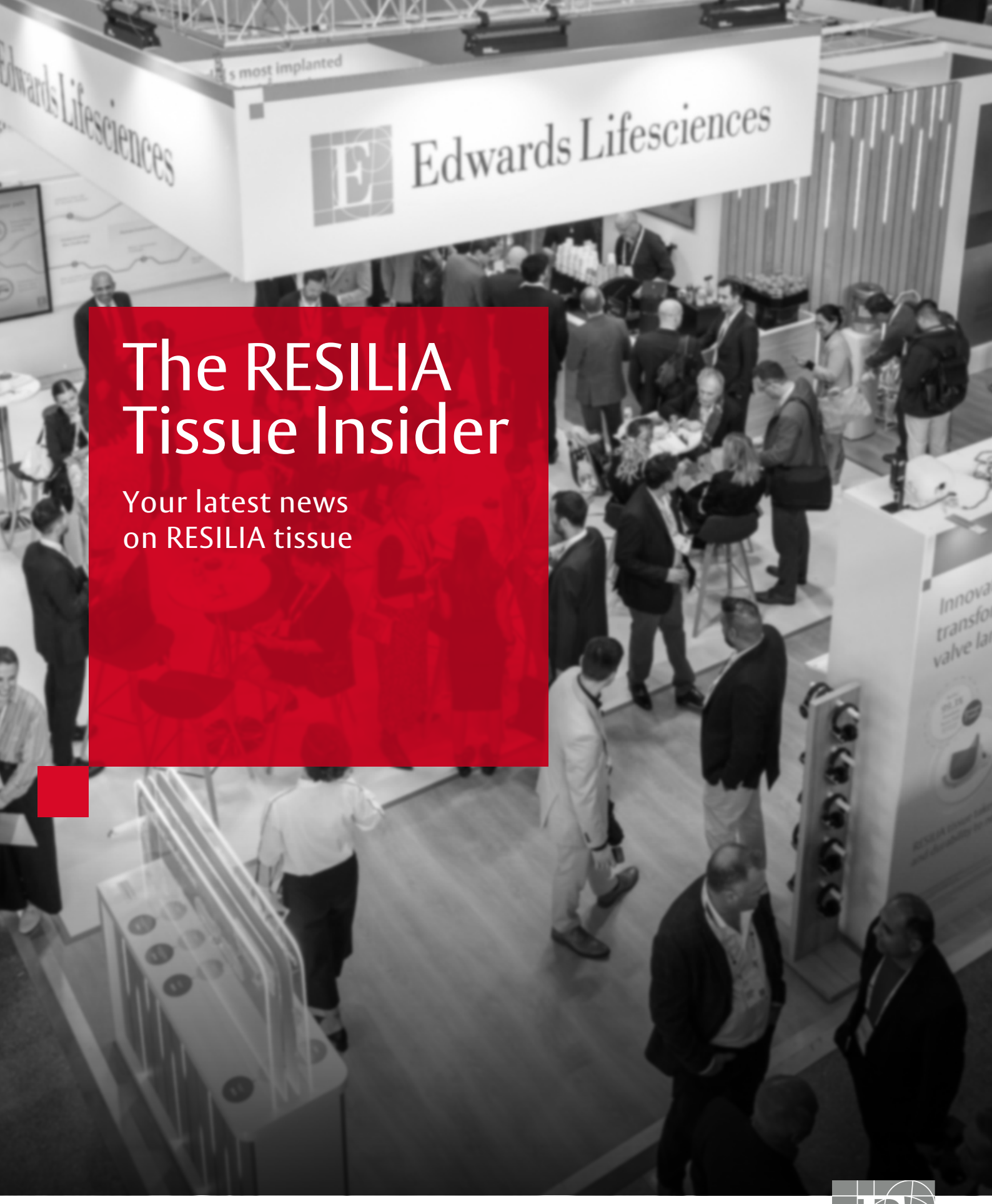

The RESILIA Tissue Insider

Your latest news on RESILIA tissue

Newsletter #10 – November 2024

Edwards

In this issue

We hope you enjoy this issue of *The RESILIA Tissue Insider*.

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Introduction

In the previous edition of *The RESILIA Tissue Insider*, we announced that **300,000 patients** worldwide had now received an INSPIRIS RESILIA aortic valve, making it the most implanted surgical aortic tissue valve worldwide. This exciting milestone has provided 300,000 patients with the possibility of an innovative valve with increased durability, built on the trusted, proven Carpentier-Edwards PERIMOUNT valve design. We are delighted that surgeons rely on Edwards valves more than any other surgical heart valve brand!

In this issue, we summarise the latest data and research on RESILIA tissue from **the European Association for Cardio-Thoracic Surgery (EACTS) 2024 Annual Meeting,** which took place in Lisbon, Portugal on 9–12 October.

On page 3, Professor Francesco Onorati describes the 6-year results from the longest and largest real-world registry with the INSPIRIS RESILIA valve to date.[3] At EACTS 2024, Professor Onorati presented late-breaking data on this registry in patients with and without chronic kidney dysfunction.[4] Valvular heart disease, particularly aortic and mitral valve disease, is highly prevalent in those patients with renal insufficiency, with its progression accelerating in those with end-stage renal disease.[5] Turn to page 4 to learn how the INSPIRIS RESILIA aortic valve performs in these patients. Furthermore, we caught up with Professor Onorati to discuss both studies; read our interview with him on page 10. Also at EACTS 2024, Professor Ruggero de Paulis used the combined power of the IMPACT and INDURE registries to investigate if a patient's sex impacts on clinical outcomes following INSPIRIS RESILIA aortic valve implantation – check out the findings on page 5.[6]

The INSPIRIS RESILIA aortic valve also maintains its positive track record in the literature, with a publication by Professor Augusto D'Onofrio comparing clinical outcomes and haemodynamics with the EDWARDS INTUITY and Carpentier-Edwards PERIMOUNT Magna Ease valves – read a summary on page 6.[7] On page 7, we present the latest cost-saving analysis of RESILIA tissue, incorporating the 7-year COMMENCE trial results.[8] Finally, the evidence behind the MITRIS RESILIA valve continues to grow; turn to page 8 to hear about Dr Giulia Ciccarelli's early experiences with the valve[9] and page 9 to read about the first microinvasive fully endoscopic case series.[10]

Enjoy reading!

Six years of the INSPIRIS RESILIA aortic valve in the real world

Onorati F *et al*. Poster accepted at the 38th EACTS Annual Meeting, 9–12 October 2024, Lisbon, Portugal.[3]

While clinical trials, such as the COMMENCE trial, have shown promising results for RESILIA tissue valves through to 7 years,[1] registry data are essential to evaluate the success of the INSPIRIS RESILIA valve in the real world. In a poster presented at EACTS 2024, Professor Francesco Onorati reported a 6-year follow-up of the INSPIRIS RESILIA valve from a European real world multicentre registry, highlighting the valve's performance in patients above and below 65 years of age.

Patients aged 65 years or younger (n=1,257) had a mean (± standard deviation [SD]) age of 55.6 ± 8.4 years; 56.1% had a bicuspid aortic valve, and mean EuroSCORE II was 3.6 ± 6.2%. Patients over 65 years old (n=614) had a mean age of 71.5 ± 4.4 years, 24.2% had a bicuspid aortic valve, and mean EuroSCORE II was 4.8 ± 6.8%.

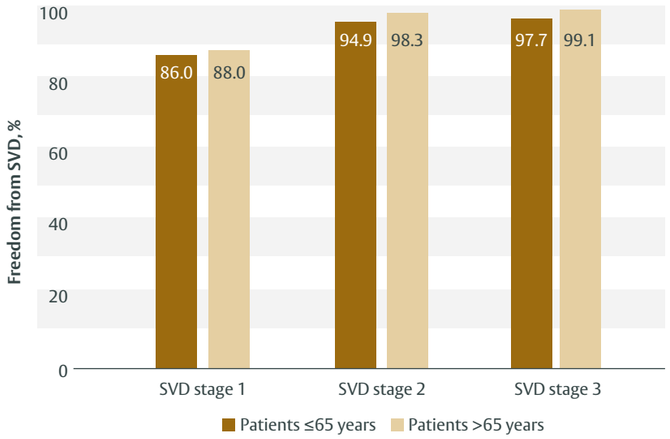
Explants (1.5%) were mostly due to endocarditis (1.2%). Only four valves were explanted due to structural valve deterioration (SVD) (0.2%), with the remaining due to patient–prosthesis mismatch (0.1%). Valve haemodynamics were stable over time up to 6 years, and SVD rates (staged according to Valve Academic Research Consortium 3 [VARC-3] criteria) were low and comparable across both age groups.

At 6-year follow-up:

	Freedom from explant due to SVD	Freedom from explant due to non-SVD	Freedom from endocarditis
Patients ≤65 years	97.0%	99.5%	95.0%
Patients >65 years	99.0%	100%	98.0%

SVD: structural valve deterioration.

Freedom from each stage of SVD (VARC-3) was comparable between patients younger and older than 65 years at 6 years



SVD: structural valve deterioration.

Conclusions

Mid-term follow-up results from a multicentre registry show the INSPIRIS RESILIA valve has good durability with stable haemodynamic gradients in both age groups at 6 years. These data represent the largest and longest real-world follow-up of the INSPIRIS RESILIA valve to date.

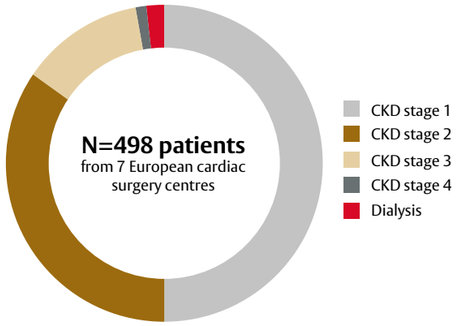
The INSPIRIS RESILIA valve in patients with chronic kidney dysfunction

Onorati F. Presented at the 38th EACTS Annual Meeting, 9–12 October 2024, Lisbon, Portugal.[4]

Stage 3 chronic kidney disease (CKD) is associated with secondary hyperparathyroidism with dystrophic calcification; this has been linked to early degeneration of bioprosthetic heart valves.

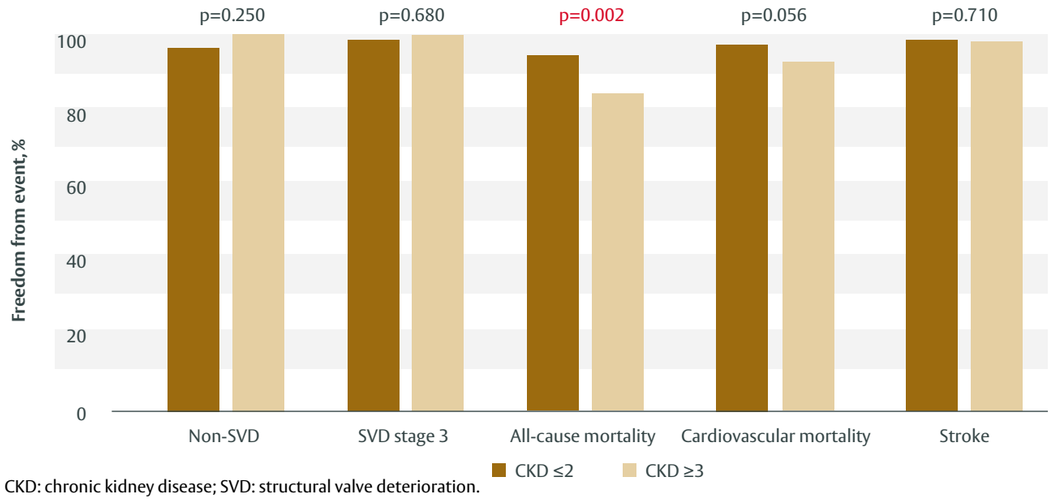
At EACTS 2024, Professor Onorati gave the first report on the 5-year performance of the INSPIRIS RESILIA valve in young patients with CKD from the multicentre real-world registry described on page 3.

After 5 years, haemodynamic gradients were stable and consistent in all patients, regardless of stage of CKD.



CKD: chronic kidney disease.

SVD (staged according to VARC-3), non-SVD and stroke rates were similar between patients with CKD ≤2 and ≥3; however, patients with advanced CKD had significantly increased all-cause mortality



CKD: chronic kidney disease; SVD: structural valve deterioration.

Conclusions

Mid-term outcomes of the INSPIRIS RESILIA valve in young patients with CKD were satisfactory, with no difference in SVD rates or haemodynamics compared with patients with advanced CKD; however, the 5-year all-cause mortality rate was higher in in patients with CKD ≥3.

INDURE and IMPACT registries: Similar clinical and quality-of-life outcomes in male and female patients at 3 years

De Paulis R *et al*. Presented at the 38th EACTS Annual Meeting, 9–12 October 2024, Lisbon, Portugal.[6]

The INDURE and IMPACT registries are designed to investigate INSPIRIS RESILIA valve performance in younger patients (≤60 years old) and patients with comorbidities, respectively. Combined, these real-world observational registries include data from 993 patients who underwent surgical aortic valve replacement (SAVR) with the INSPIRIS RESILIA valve across Europe and Canada between 2019 and 2021: 442 males with a mean age of 60.1 ± 8.6 years, and 247 females with a mean age of 59.9 ± 9.6 years.

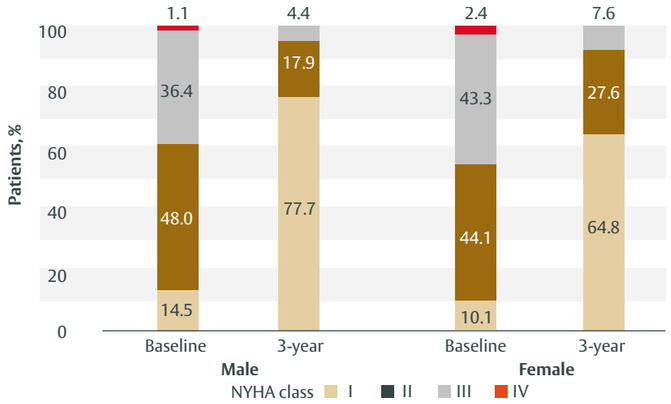
At EACTS 2024, Professor De Paulis presented a propensity score-matched analysis to answer the question: **does SAVR represent a greater risk to female patients than male patients?**

Before propensity score-matching, **female patients in this analysis were at greater preoperative risk compared with male patients** (EuroSCORE II [mean ± SD]: 2.4 ± 3.1% *vs* 1.6 ± 1.7%, p<0.001). They were also in a worse functional state, with 45.7% of females in New York Heart Association (NYHA) class III or IV, compared with 37.6% of males (p=0.036). However, at 3-year follow-up, after propensity matching, clinical outcomes were satisfactory in both sexes.

Late events (30 days–3 years, linearised rate/valve-years)			
	Male	**Female**	**p value**
All-cause mortality	1.6	1.6	0.456
Valve-related mortality	0.6	0.4	0.169
Endocarditis	0.8	0.4	0.301
Thromboembolic events	0.4	0.7	0.459
Valve-related dysfunction	0.3	1.1	0.102

Left ventricular (LV) mass index was significantly decreased in females at all time points compared with males (p=0.002) but was within normal levels for both sexes by 1-year follow-up. Three years following SAVR, **both sexes had good-to-excellent quality of life and improved NYHA class**.

NYHA class was improved at 1 year and maintained to 3 years in male and female patients



NYHA: New York Heart Association.

Conclusions

In patients who received an INSPIRIS RESILIA valve within the INDURE and IMPACT registries, there was no significant difference in clinical outcomes, quality-of-life measures or valve performance between male and female patients at 3-year follow-up. LV mass index reached a normal range but was lower in females compared with males across follow-up.

Excellent early outcomes with the INSPIRIS RESILIA, EDWARDS INTUITY and Magna Ease valves

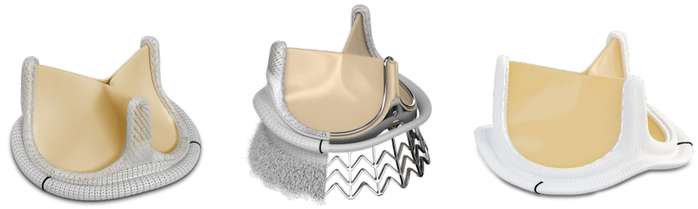
D'Onofrio A *et al*. *Int J Cardiol Heart Vasc*. 2024; **54:** 101487.[7]

Early outcomes from a multicentre, propensity-weighted comparison of stented, rapid deployment and new-generation aortic valves were recently published in the *International Journal of Cardiology Heart & Vasculature.*

Results from 2,589 patients who were implanted with Magna Ease (11.4%), EDWARDS INTUITY/INTUITY Elite (65.2%) or INSPIRIS RESILIA (23.4%) valves were analysed.

Early (30-day) outcomes

Device success rate was similar across all valves (96% overall). Permanent pacemaker implantation rate was lower in patients with the INSPIRIS RESILIA valve (Magna Ease valve 6% *vs* EDWARDS INTUITY 6% valve, p=0.679; EDWARDS INTUITY valve 6% *vs* INSPIRIS RESILIA 2% valve, p<0.001). Bleeding (p<0.001), acute myocardial infarction (p=0.01) and stroke (p=0.02) were also reduced in patients with INSPIRIS RESILIA valves compared with those who received EDWARDS INTUITY valves, while these outcomes were similar between patients with Magna Ease and EDWARDS INTUITY valves.

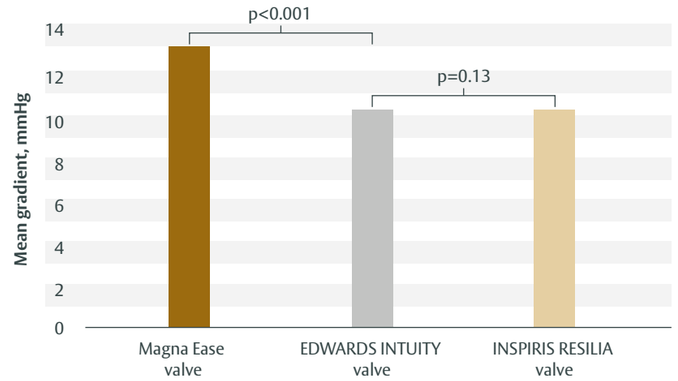


Magna Ease valve
Median age: 71.5 years

EDWARDS INTUITY valve
Median age: 75.0 years

INSPIRIS RESILIA valve
Median age: 60.0 years

The EDWARDS INTUITY valve performed better haemodynamically compared with the Magna Ease valve, while the INSPIRIS RESILIA valve showed similar results to the EDWARDS INTUITY valve.



Conclusions

Overall, all three valves showed good early clinical and haemodynamic performance. The INSPIRIS RESILIA valve showed significantly lower rates of pacemaker implantation and had similar transaortic gradients to EDWARDS INTUITY valves, which were lower than those of Magna Ease valves.

Long-term cost savings with RESILIA tissue valves

Keuffel EL *et al. J Med Econ*. 2024; **27:** 910–18.[8]

A previous economic analysis used 5-year data from the COMMENCE trial to compare anticipated cost savings, up to 15 years post implantation, between RESILIA tissue valves and mechanical valves. Now this model has been updated to account for the 7-year COMMENCE data, reducing the uncertainty of the long-term projected savings.

The authors used a mathematical model to analyse three hypothetical cohorts: a traditional tissue valve cohort, a RESILIA tissue cohort and a mechanical valve cohort (n=10,000 each). The model estimated the probabilities of various clinical events occurring following implantation of a valve, up to 15 years post operation.

$23,315

median savings at 15 years with RESILIA tissue valves *vs* mechanical valves

$5,594

reoperation cost savings at 15 years with RESILIA tissue valves *vs* traditional tissue valves

At 7 years, RESILIA tissue valves significantly reduced healthcare system expenditure compared with mechanical valves by $13,415 (median; 95% CI $10,472–$17,321). Projected 15-year savings were $23,315 (median; 95% CI $17,802–$30,421), slightly larger than anticipated from the prior analyses.

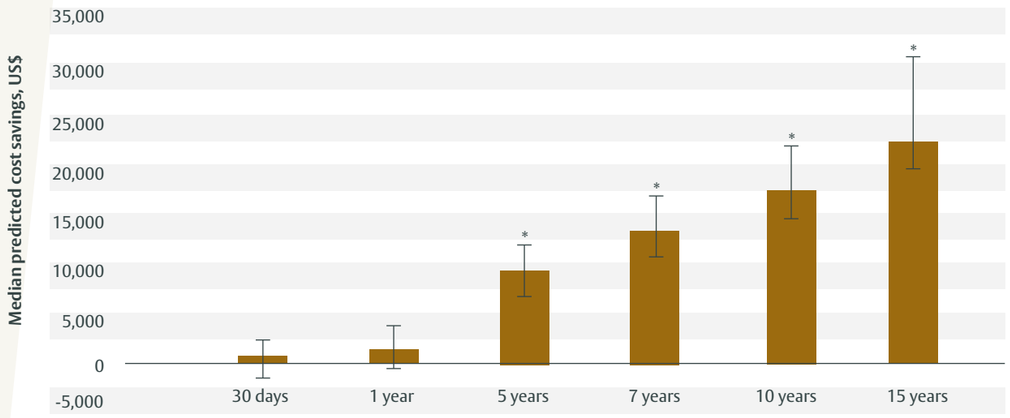
These savings are primarily due to lower anticoagulation monitoring costs, but also due to lower bleeding and thromboembolism-related expenditure.

Traditional tissue valves also showed cost savings over mechanical valves ($14,528 at 15 years), but not to the same extent as RESILIA tissue valves because of the larger reoperation costs.

Conclusions

Current projections based on the 7-year COMMENCE data show that RESILIA tissue valves are associated with lower healthcare expenditure compared with mechanical and traditional tissue valves.

Cumulative net cost savings per initial SAVR surgery with RESILIA tissue valves *versus* mechanical valves



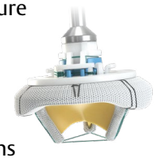
*Statistically significant at 99% level (99% of estimates exceed $0). SAVR: surgical aortic valve replacement.

MITRIS RESILIA valve: Two case studies demonstrating enhanced implantability

Ciccarelli M *et al. Surg Technol Int*. 2024; **44:** doi: 197–201.[9]

The MITRIS RESILIA mitral valve incorporates features from the trusted Carpentier-Edwards PERIMOUNT Magna Mitral Ease valve with RESILIA tissue. Dr Guilia Ciccarelli *et al*. describe the technology and present two patient case reports demonstrating the valve's improved implantability profile.

The mitral valve has complex architecture and is supported by chordae tendineae of inconsistent lengths and angles. The authors consider features of the MITRIS RESILA valve to be advantageous over previous generations of mitral valves in this complex space:



Feature	Benefits
External markers along posteromedial/anterolateral commissures and anterior valve segment	Fast and easy orientation
Stents can be temporarily adjusted inward at a 55° angle	Facilitates valve implantation
Low stent height	Minimises the risk of LV outflow tract (LVOT) obstruction
Saddle-shaped annular ring	Good fit within the mitral annulus and throughout the cardiac cycle
RESILIA tissue	Potential increased durability with no rinsing required

Case studies

Both patients received a MITRIS RESILIA valve with no periprocedural complications and no LVOT obstructions. At discharge, neither patient had paravalvular leaks, and gradients remained stable to 1-month follow-up.

Patient 1

- Male, 71 years old
- Diagnosed with heart failure, severe mitral regurgitation, moderate tricuspid and aortic regurgitation and severe reduced LV ejection fraction
- Received a 29 mm MITRIS RESILIA valve
- Cardiopulmonary bypass time: 146 min
- Post-implantation mean gradient: 3 mmHg
- Hospital stay: 12 days

Patient 2

- Female, 66 years old
- Diagnosed with rheumatic mitral valve disease, severe mitral stenosis, moderate-severe functional tricuspid regurgitation and significant mitral regurgitation
- Received a 27 mm MITRIS RESILIA valve
- Cardiopulmonary bypass time: 82 min
- Post-implantation mean gradient: 5 mmHg
- Hospital stay: 13 days

Conclusions

The authors conclude that their early experience with the MITRIS RESILIA valve demonstrated an overall enhanced implantability profile, and reduced leaflet stress, along with the potential durability advantages that RESILIA tissue offers.

The first microinvasive fully endoscopic case series of the MITRIS RESILIA valve

Kruse J *et al. J Clin Med*. 2024; **13:** 4358.[10]

Minimally invasive mitral valve surgery involves making a small incision in a right mini-thoracotomy, reducing surgical trauma and the risk of postoperative complications. In this case series published in the *J Clin Med*, the authors report on the use of this technique to implant 11 patients with the MITRIS RESILIA valve through fully endoscopic access, using three-dimensional visualisation.

The MITRIS RESILIA valve has a low profile height of less than 7 mm, to potentially reduce LVOT obstruction, which can occur when a new prosthesis displaces the anterior mitral leaflet towards the LVOT. In this case series, the average reduction in LVOT area was 65.35 ± 34.99 mm^2, numerically less pronounced than that of the Epic valve (Abbott Cardiovascular Inc. 68.69 ± 32.71 mm^2).

Parameter	Mean ± SD
Age, years	56.50 ± 18.70
Cardiopulmonary bypass time, min	66.83 ± 14.27
Cross-clamp time, min	40.17 ± 13.72
Length of hospital stay, days	10.42 ± 6.10
Intensive care unit stay, days	2.92 ± 1.74

SD: standard deviation.

Postoperative haemodynamics:

0.0% **Paravalvular leak**

4.5 mmHg **Mean gradient**

415 mm^2 **LVOT area**

Mean data are shown. LVOT: left ventricular outflow tract.

At 90-day follow-up:

100% **Freedom from mortality**

100% **Freedom from rehospitalisation for cardiac reasons**

100% **NYHA class I–II**

Conclusion

In this first-of-its-kind case series, the MITRIS RESILA valve was implanted with a microinvasive fully endoscopic technique, resulting in good early clinical outcomes with short operative times.

INSPIRIS RESILIA valve: Real-world insights from Professor Francesco Onorati*

Professor Francesco Onorati is lead surgeon in the Heart Transplant and Mechanical Assisted Devices programmes at Verona University Hospital, Italy. We caught up with him to discuss the latest results from the longest real-world follow-up of the INSPIRIS RESILIA valve (see page 3) as well as his EACTS late-breaking session on the performance of the INSPIRIS RESILIA valve in patients with CKD (page 4).

Q. How long have you been using RESILIA tissue valves in your practice?

A. Previously, our practice used the Magna Ease valve for aortic valve replacements; however, in 2017, we shifted to using the INSPIRIS RESILIA valve due to the VFit technology and the potential for decreased calcification with RESILIA tissue.

Q. Can you describe the importance of real-world data for the INSPIRIS RESILIA aortic valve?

A. Controlled trials provide an excellent level of scientific and statistical evidence, but their applicability is limited by strict inclusion and exclusion criteria. Real-world registry data may have a lower evidence quality, but they more accurately mirror actual daily practice so can be generalised to all patients. We have built a European multicentre registry, retrospectively andprospectively collecting data for 1,871 patients, and the 6-year outcomes show low rates of SVD with stable haemodynamics.

Q. In this registry, you analysed data from patients older and younger than 65 years old separately. Why is it interesting to separate the cohort in this way?

A. The current European guidelines advise that patients older than 65 years old receive a bioprosthetic valve, whereas a mechanical valve is recommended for younger patients. This analysis allows us to understand how the valve performs in younger patients. Our data seem to confirm the safety, and reveal excellent clinical results, of the INSPIRIS RESILIA valve in patients aged 50–60 years old.

Q. At EACTS 2024, you presented the performance of the INSPIRIS RESILIA valve in patients with CKD. Why is analysing this subpopulation of patients important?

A. One of the main aims of RESILIA tissue is to reduce calcification; patients with CKD ≥3 have an accelerated calcification process, with early SVD observed in advanced stages. We compared results from patients with early *versus* advanced CKD and found comparable rates of SVD, with stable mean haemodynamic gradients. However, the mortality rate was higher in patients with advanced CKD, potentially due to an increased risk profile and comorbidity prevalence.

Q. How does the handling, preparation and implantation of the INSPIRIS RESILIA valve compare with other prosthetic valves?

A. Since the first use, I loved the handling and quick implantability of the INSPIRIS RESILIA valve. The pliability of the sewing cuff and the posts during the knotting process is excellent.

Q. What do your patients think about the option of receiving a valve with RESILIA tissue?

A. In my experience, there are a growing number of younger patients asking to avoid lifelong anticoagulation. Therefore, discussing the possibility of a biological valve with potential increased durability and valve-in-valve technology is embraced with enthusiasm. I had a patient with obesity who was 42 years old with congenital unicuspid severe aortic stenosis and other aortic complications. This patient first received a mechanical valve but, unfortunately, contracted early endocarditis at 10 months post surgery. I discussed with him the potential benefits of an INSPIRIS RESILIA valve, and the patient was fascinated. He consented to a redo operation and received a 21 mm INSPIRIS RESILIA valve within a Bio-Bentall procedure. The patient returned to his normal daily life with no limitations.

*Expert opinions, advice and all other information expressed represent contributors' views and not necessarily those of Edwards Lifesciences.

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10. Kruse J, Silaschi M, Russu K *et al*. Case series of first microinvasive fully endoscopic use of a new mitral prosthesis. *J Clin Med*. 2024; **13:** 4358.

No clinical data are available that evaluate the long-term impact of RESILIA tissue in patients. Additional clinical data for up to 10 years of follow-up are being collected to monitor the long-term safety and performance of RESILIA tissue.

Important safety information:
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).

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