Australia and New Zealand Source Registry
Edwards Sapien Aortic Valve
30 day Outcomes

A/ Professor Darren Walters
On behalf of the ANZ Source Investigators

Director of Cardiology
The Prince Charles Hospital
Brisbane, Australia
ANZ Source Registry

- Established to serve as a repository of adjudicated, independently monitored information
- Clinical use and safety and efficacy in ANZ
- Edwards-SAPIEN CE- Marked system for PAVR
- Australian and New Zealand clinical environment.
- Modeled on Source EU protocol

Data Management:
Flinders Cardiovascular Outcomes Research
Prof Derek Chew

Monitoring:
PCRG
Independent Adjudication of death and stroke
ANZ Source Registry

Three protocol revisions:

- Revision A  SAE/AE monitoring only
- Revision C  Included 100% monitoring
- Revision D  Clarified enrolment to include Heart-team agreement where Euroscore or STS criteria not met but high risk by consensus
Study Devices

Edwards SAPIEN THV
- 23 and 26 mm valves

RetroFlex
- 22 and 24 F sheaths

AscendRA
- 33 F sheath
TAVR

Transfemoral and Transapical

Transfemoral

Transapical
Criteria

INDICATIONS

1. Symptomatic Degenerative Aortic Stenosis
2. AVA \( \leq 0.8 \text{cm}^2 \)
3. Logistic Euroscore > 20% or STS > 10% or
4. Agreement between Surgeon and Cardiologist: patient not suitable for open surgery due to high risk (Revision D Amendment 5/2010)

www.euroscore.org/calc.html

ANNULUS BY TEE

- 18 to 22mm = 23mm SAPIEN
- 21+ to 25mm = 26mm SAPIEN

http://209.220.160.181/STSWebRiskCalc261
Factors might make heart team agree on high risk included but not limited to:

- Cachexia/Frailty
- Pulmonary Insufficiency: VMS <1L
- Home oxygen therapy
- Previous cardiac surgery
- Porcelain Aorta
- Pulmonary hypertension >60 mm Hg
- Recurrent Pulmonary Embolus
- RV Insufficiency
- Thoracic Burning Sequelae Contradicting Open Chest Surgery
- History of Mediastinum Radiotherapy
- Severe Connective Tissue Disease
- Cachexia/Frailty
- Liver Cirrhosis (Child A or B)
- Age over 80 yr
- Age over 90 yr

Consensus risk benefit ratio of open surgery favors TAVR
The bioprosthesis is contraindicated in patients with:

- Non-valvular aortic stenosis; congenital aortic stenosis, unicuspid, or bicuspid aortic valve; non-calcific acquired aortic stenosis;
- Evidence of intracardiac mass, thrombus, or vegetation;
- Untreated clinically significant coronary artery disease requiring revascularization;
- Severe deformation of the chest;
- Severe coagulation problems;
- Active bacterial endocarditis or other active infections;
- Previous systemic embolization from the left side of the heart;
- Myocardial infarction (MI) within 1 month;
- Unstable angina during index hospitalization;
- Recent pulmonary emboli;
- Cerebrovascular accident (CVA) within 6 months.
CONTRA - INDICATIONS

- Annulus Ø, (mm) <18 or >25
- Inability to tolerate anticoagulation therapy
- Significant atheroma of the femoral and iliac vessels
- Severe tortuositites of the femoro-iliac vessels
- Femoro-iliac vessels < 7 mm*
- Bilateral iliofemoral bypass
- Hypertrophic cardiomyopathy with or without obstruction (HOCM)
- Severe ventricular dysfunction with ejection fraction < 20%
- The bioprosthesis is not to be used in positions other than the aortic valve

*Smallest diameter > 7mm for 23mm Sapien / > 8 mm for 26 mm Sapien
Source ANZ Sites

Cases
Initiated on December-2008

Hospital Name (City, Country)

- Flinders Medical Center (Sinhal-Bennetts, Adelaide SA)
- St. Vincent’s Hospital (Baron-Spratt, Sydney, NSW)
- Waikato Hospital (Pasupati-El Gamel, Hamilton, New Zealand)
- Prince Charles Hospital (Walters-Tesar, Brisbane)
- John Hunter (Thambar-James, Newcastle, NSW)
- Royal Perth Hospital (Yong-Larbabelstier, Perth, WA)
- Prince Of Wales (Jepson-Wolfenden, Sydney, NSW)
- Royal North Shore (Bhindi-Brady, Sydney, NSW)
# Patients enrolment

## Cases Initiated on December-2008

<table>
<thead>
<tr>
<th>Hospital Name (City, Country)</th>
<th>CTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flinders Medical Center</td>
<td>38</td>
</tr>
<tr>
<td>St. Vincent’s Hospital</td>
<td>22</td>
</tr>
<tr>
<td>Waikato Hospital</td>
<td>17</td>
</tr>
<tr>
<td>Prince Charles Hospital</td>
<td>20</td>
</tr>
<tr>
<td>John Hunter</td>
<td>11</td>
</tr>
<tr>
<td>Royal Perth Hospital</td>
<td>11</td>
</tr>
<tr>
<td>Prince Of Wales</td>
<td>8</td>
</tr>
<tr>
<td>Royal North Shore</td>
<td>5</td>
</tr>
</tbody>
</table>

**Total** 132
Source - Edwards TAVI in ANZ

Total 304

- Source Registry
- NZ approved
- SAS
- AP
Enrolment

132 pts consented

2 pts protocol deviation on femoral size and were withdrawn prior to the procedure

1 pts crossed from TF to TA
Failed femoral access
1 pts TF to SAVR

130 pts Included in analysis
Enrolment

- Revision A 64 pts
- Revision C 63 pts
- Revision D 3 pts
- Monitoring 100% 66 pts
- Monitoring all AE SAE 64 pts
Enrolment by TAVR Route

22&24 Fr Femoral sheath

51.5%

Transfemoral
Trans Apical

24F 22F 18F
## Baseline Demographics and Risk Factors

<table>
<thead>
<tr>
<th></th>
<th>TF (n=67)</th>
<th>TA (n=63)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>83.67</td>
<td>81.94</td>
<td>0.252</td>
</tr>
<tr>
<td>Female</td>
<td>34.3%</td>
<td>61.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine (mmol/l)</td>
<td>116.4</td>
<td>115.2</td>
<td>0.904</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>27.1%</td>
<td>29.1%</td>
<td>0.532</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>25.8%</td>
<td>52.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Carotid Artery Stenosis (&gt;50%)</td>
<td>5.97%</td>
<td>19.1%</td>
<td>0.024</td>
</tr>
<tr>
<td>Incidence of CAD</td>
<td>80.6%</td>
<td>73.0%</td>
<td>0.307</td>
</tr>
<tr>
<td>Porcelain Aorta</td>
<td>3.0%</td>
<td>17.5%</td>
<td>0.006</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>40.3%</td>
<td>39.7%</td>
<td>0.943</td>
</tr>
<tr>
<td>Mitral valve disease</td>
<td>23.8%</td>
<td>28.6%</td>
<td>0.545</td>
</tr>
</tbody>
</table>
## Baseline Demographics and Risk Factors

<table>
<thead>
<tr>
<th></th>
<th>TF (n=67)</th>
<th>TA (n=63)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA (median)</td>
<td>2.83 (n=67)</td>
<td>2.82 (n=60)</td>
<td>0.888</td>
</tr>
<tr>
<td>Aortic Valve Area (cm²)</td>
<td>0.61 (n=56)</td>
<td>0.63 (n=55)</td>
<td>0.552</td>
</tr>
<tr>
<td>Peak gradient (mmHg)</td>
<td>49.1 (n=61)</td>
<td>55.1 (n=55)</td>
<td>0.408</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>46.7 (n=61)</td>
<td>45.3 (n=59)</td>
<td>0.727</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>58.6 (n=43)</td>
<td>55.2 (n=40)</td>
<td>0.610</td>
</tr>
</tbody>
</table>
30-Day* Paired Echo Data

**TA Peak Gradient (mm Hg)**
Mean ± SD (n = 41)

Baseline: 55.1 ± 49.1
30-Day: 17.7 ± 17.7

**TA Mean Gradient (mm Hg)**
Mean ± SD (n = 41)

Baseline: 45.3 ± 45.3
30-Day: 11.5 ± 11.5

**TF Peak Gradient (mm Hg)**
Mean ± SD (n = 51)

Baseline: 49.1 ± 49.1
30-Day: 12.8 ± 12.8

**TF Mean Gradient (mm Hg)**
Mean ± SD (n = 46)

Baseline: 46.7 ± 46.7
30-Day: 10.6 ± 10.6

All p<0.001

*Include cases with follow-up data between 1-month & 5-month
30-Day* Paired Echo Data

TA Ejection Fraction (%)
Mean ± SD (n = 51)

- Baseline: 55.2 ± 10.1
- 30-Day: 62.3 ± 10.1

All p=0.053

TF Ejection Fraction (%)
Mean ± SD (N = 20)

- Baseline: 58.6 ± 10.2
- 30-Day: 57.4 ± 10.2

All p=0.345

*Include cases with follow-up data between 1-month & 5-month
Aortic regurgitation at baseline and 30 days

P = 0.077
<table>
<thead>
<tr>
<th>Major Complications (30 Days)</th>
<th>TF % (n=67)</th>
<th>TA % (n=63)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5.97</td>
<td>9.52</td>
<td>0.449</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.99</td>
<td>4.76</td>
<td>0.600</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.49</td>
<td>4.76</td>
<td>0.283</td>
</tr>
<tr>
<td>MACCE</td>
<td>8.96</td>
<td>15.87</td>
<td>0.232</td>
</tr>
<tr>
<td>Minor Vascular</td>
<td>10.45</td>
<td>1.59</td>
<td>0.036</td>
</tr>
<tr>
<td>Major Vascular</td>
<td>4.48</td>
<td>6.35</td>
<td>0.638</td>
</tr>
<tr>
<td>Renal function deterioration</td>
<td>11.94</td>
<td>17.46</td>
<td>0.375</td>
</tr>
<tr>
<td>Permanent Pacemaker</td>
<td>1.49</td>
<td>7.94</td>
<td>0.081</td>
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</tbody>
</table>
## Major Complications (30 Days)

<table>
<thead>
<tr>
<th></th>
<th>TF % (n=67)</th>
<th>TA % (n=63)</th>
<th>Total % (n=129)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleed (All)</td>
<td>14.93</td>
<td>19.05</td>
<td>16.92</td>
</tr>
<tr>
<td>Minor Vascular</td>
<td>10.45</td>
<td>1.59</td>
<td>6.15</td>
</tr>
<tr>
<td>Major Vascular</td>
<td>4.48</td>
<td>6.35</td>
<td>5.38</td>
</tr>
</tbody>
</table>

*Defined according to VARC Criteria*

*Eurointervention:2010:5;673-679.*
Major Complications Death
(< 30 days)

TF x 4

1 annular dissection
1 post sAVR following ventricular perforation during TAVR
1 hemodynamic collapse post op
1 awaiting adjudication; left main occlusion

TA x 6

1 left main occlusion
2 following surgical intervention post valve embolisation into ventricle
1 haemorrhage from TA access site
1 day of discharge in hospital arrest post mortem inconclusive
1 awaiting adjudication
Complications
Surgical conversion

- 1 TF LV perforation
  - Open AVR
    - Died 30 days
  - Died intra-procedural

- 2 TA Valve embolisations
  - Died intra-procedural
Complications
Coronary Obstruction

- 2
  - 1 TA
    - Died
  - 1 TF
    - Died
Valve Malposition

1 TF Late
Surgical AVR
<table>
<thead>
<tr>
<th></th>
<th>ANZ TF (n=67)</th>
<th>Source TF (n=463)</th>
<th>ANZ TA (n=63)</th>
<th>Source TA (n=575)</th>
<th>Partner A TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>83.67</td>
<td>81.7</td>
<td>81.94</td>
<td>80.7</td>
<td>83.6</td>
</tr>
<tr>
<td>Female</td>
<td>34.3%</td>
<td>55.2%</td>
<td>61.9%</td>
<td>56%</td>
<td>42.2</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>27.1%</td>
<td>25.7</td>
<td>29.1%</td>
<td>29.2</td>
<td>29.3</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>25.4%</td>
<td>10.9%</td>
<td>52.4%</td>
<td>27.5%</td>
<td>43%</td>
</tr>
<tr>
<td>Carotid Artery Stenosis (&gt;50%)</td>
<td>5.97%</td>
<td>7.6%</td>
<td>19.1%</td>
<td>17.1%</td>
<td>29.3%</td>
</tr>
<tr>
<td>Incidence of CAD</td>
<td>80.6%</td>
<td>47.4%</td>
<td>73.0%</td>
<td>55.0%</td>
<td>74.9%</td>
</tr>
<tr>
<td>Porcelain Aorta</td>
<td>2.99%</td>
<td>4.6%</td>
<td>17.5%</td>
<td>11.5%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>40.3%</td>
<td>17.6%</td>
<td>39.7%</td>
<td>26.9%</td>
<td>42.6%</td>
</tr>
</tbody>
</table>
# Implantation Success

<table>
<thead>
<tr>
<th></th>
<th>ANZ TF (n=67)</th>
<th>Source TF (n=463)</th>
<th>ANZ TA (n=63)</th>
<th>Source TA (575)</th>
<th>Partner A TAVR (348)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute procedure success</td>
<td>92.5%</td>
<td>95.6%</td>
<td>87.3%</td>
<td>92.9%</td>
<td>94.5%</td>
</tr>
<tr>
<td>Conversion to sAVR</td>
<td>1.49% (1)</td>
<td>1.7 (2)%</td>
<td>3.17 % (2)</td>
<td>3.5%</td>
<td>2.6%</td>
</tr>
<tr>
<td>AR &gt;+2**</td>
<td>1.49% (1)</td>
<td>3.2%</td>
<td>1.59% (1)</td>
<td>5.9%</td>
<td></td>
</tr>
<tr>
<td>Valve migration</td>
<td>1.49% (1)</td>
<td>0.0%</td>
<td>3.17% (2)</td>
<td>0.5%#</td>
<td>2.6%</td>
</tr>
<tr>
<td>Coronary obstruction</td>
<td>1.49% (1)</td>
<td>0.7%</td>
<td>1.59% (1)</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>

TAVR implanted pt alive at the end of procedure
## Major Complications
(= 30 days)

<table>
<thead>
<tr>
<th></th>
<th>TF % (n=67)</th>
<th>TA % (n=63)</th>
<th>ANZ Total % (n=130)</th>
<th>EU Total % (n=1038)</th>
<th>Partner A TAVR % (n=348)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>5.97</td>
<td>9.52</td>
<td>7.69</td>
<td>8.5</td>
<td>12</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.99</td>
<td>4.76</td>
<td>3.85</td>
<td>2.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>1.49</td>
<td>7.94</td>
<td>4.62</td>
<td>7.0</td>
<td>3.8</td>
</tr>
<tr>
<td>Vascular Major</td>
<td>4.48</td>
<td>6.35</td>
<td>5.38</td>
<td>7.0</td>
<td>11.1</td>
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</table>
Edwards Transcatheter AVR

Survival at 1, 6 and 12 months

Transfemoral Experience

<table>
<thead>
<tr>
<th>Study</th>
<th>1 month</th>
<th>6 months</th>
<th>12 months</th>
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</thead>
<tbody>
<tr>
<td>iREVIVE</td>
<td>72.2</td>
<td>71.9</td>
<td>86.8</td>
</tr>
<tr>
<td>RECAST</td>
<td>46.2</td>
<td>71.4</td>
<td>75.8</td>
</tr>
<tr>
<td>REVIVE</td>
<td>33.6</td>
<td>92.7</td>
<td>93.4</td>
</tr>
<tr>
<td>REVIVAL</td>
<td>28.0</td>
<td>75.8</td>
<td>92.7</td>
</tr>
<tr>
<td>PARTNER EU</td>
<td>0%</td>
<td>100%</td>
<td>94.0</td>
</tr>
<tr>
<td>SOURCE</td>
<td>93.6</td>
<td>93.6</td>
<td></td>
</tr>
</tbody>
</table>

The Prince Charles Hospital

DLW2011
T-AVR Key Issues

- Patient selection beyond the Euroscore/STS
- Procedural performance
  - Hybrid OR
  - TOE/GA/LA
- Procedural Complications
  - Vascular complications - device profile
    - Acceptable with 18 Fr: ?unacceptable with 24 Fr
  - Heart Block – 7.0%-37.5%
    - Acceptable with Sapien Platform: ?unacceptable Core Valve
  - Aortic Regurgitation
    - Not yet linked to adverse outcomes
T-AVR Key Issues

- Surgically eligible patient: when not if?
  - Which surgically eligible group: where do we draw the line
    - Critical importance of longevity of device
    - Older patients remain target in medium term
  - Quality of life versus survival
  - Cost effectiveness compared to standard surgery
  - Longevity of device: long term patient follow up essential
Conclusion

• Early learning curve experience in our region appears to demonstrate results similar to the published European Experience.

• Procedural Success acceptable for early experience

• Lower than predicted 30-day mortality

• Prospective registry surveillance of procedural success and late outcomes within ANZ essential

• Increased efforts to ensure data quality and trial integrity