Background

Transcatheter Aortic Valve Implantation (TAVI) was the subject of discussion at the 10 August 2012 meeting of the Australasian Health Policy Advisory Committee on Technology (HealthPACT) in Brisbane. This highlighted two recent articles published in the British Medical Journal (BMJ)\textsuperscript{1,2} highlighting a 2011 Belgian Health Technology Assessment (HTA) on TAVI\textsuperscript{3}. These indicated that recent evidence may have the potential to change the approach that Australia and New Zealand take towards TAVI.

Aortic Stenosis

TAVI is used to treat patients with aortic stenosis, a condition where the main outflow valve from the heart thickens and does not open fully. Once they notice symptoms, around 50\textsuperscript{4,5} - 80\textsuperscript{6} of aortic stenosis patients will die within two years. Aortic stenosis is prevalent in approximately 1-2\% of people aged over 65 and 4\% of people aged over 85 years\textsuperscript{7}. It has been estimated that there may be around 10,000 aortic stenosis patients in New Zealand\textsuperscript{8}.

Treatments

Open heart surgery is the conventional treatment for aortic stenosis, however, not all patients are suitable for this. Around a third\textsuperscript{5} to a half\textsuperscript{4} of patients will have conditions that make it too dangerous to perform open heart surgery. For these inoperable patients there has previously been no treatment option available and they face disabling symptoms and frequent hospital admissions.

\textsuperscript{*} HealthPACT provides advance notice of significant new and emerging technologies, and evidence-based advice on them and their potential impact, to health departments in Australia and New Zealand. This information is used to inform financing decisions and assist in the managed introduction of new technologies.
TAVI involves the implantation of a new bio-prosthetic valve inside the old one through a catheter, and has a much shorter recovery time than open heart surgery. Alternative valve delivery approaches to the heart have developed. These include delivery through a large artery, eg, transfemoral (through the upper leg) and subclavian (beneath the collarbone), as well as surgical approaches, eg, transapical (with thoracotomy and puncture of the left ventricle) and transaortic (requiring a sternotomy). The access route used can depend on various factors.

Development of TAVI

A timeline of key events in the development of TAVI is included in Appendix 1.

In New Zealand the first TAVIs were performed in 2008, in both the private and public sector. Waikato District Health Board (DHB) then put a proposal to the National Service and Technology Review Advisory Committee (NSTR) for a publicly funded programme for high-risk surgical candidates. NSTR found TAVI to be an emerging technology with low levels of evidence and did not recommend the development of a full business case for public funding. NSTR did, however, acknowledge the need for ‘funding with evidence’ so that DHBs could implement such technologies as part of formal clinical trials that include utility analysis. The Ministry of Health then supported a TAVI pilot at Waikato DHB, from which results were provided in September 2010.

With NSTR discontinued and the National Health Committee (NHC) not yet reconfigured, the National Health Board (NHB) sought an independent evaluation of TAVI from Auckland DHB’s Clinical Practice Committee (Auckland CPC), which included input from the National Cardiac Surgery Clinical Network (NCSCN) and Auckland DHB’s cardiology service. Based on the evidence available at the time, Auckland CPC recommended interim approval for high risk surgical candidates, although it felt cost utility was heavily dependent on complication rates.

Auckland CPC did not recommend TAVI for non-surgical candidates because of unfavourable cost utility, although it did agree there was a high level of evidence of both safety and efficacy for this group. Auckland CPC also made recommendations around patient selection processes, including the use of multi-disciplinary committees, and indicated it would further review TAVI as more evidence became available. The NCSCN provided a provisional recommendation which was consistent with the Auckland CPC recommendations.

Ministerial approval of public funding for TAVI was sought in March 2011. A letter from the NHB to DHB CEOs in April 2011 informed them that TAVIs had been approved for high-risk surgical candidates, subject to nationally consistent criteria and patient prioritisation, including regional multi-disciplinary patient review committees. Coding advice was provided for identification of
TAVI in the national collections and information provided on the likely average national case-mix price ($38,800-$40,200). Parameter guidelines and the patient process were notified to DHBs in October 2011. In the 2011/12 financial year, TAVIs were performed by the Waikato, Auckland and Canterbury DHB cardiac units. The three units have evolved slightly different pathways (in terms of where surgical input enters) and work continues on a protocol for prioritisation criteria. There has been discussion about the potential for New Zealand Cardiac Network (NZCN) oversight and the development of a national registry.

**Numbers of TAVI procedures**

Currently more than 50,000 patients world-wide had received TAVI\(^1\), although most procedures to date have been performed in Europe. Up-to-date numbers of TAVIs being performed in Australia require collating, however, up until January 2010 over 180 had been conducted in their public hospitals over at least four states\(^2\).

Based on reported hospital events to the National Minimum Dataset (NMDS), there appear to have been in the order of 100 publicly funded TAVIs performed in DHBs from August 2008 until July 2012. However, this may be incomplete, subject to data quality issues, and also excludes private events. The majority of identified TAVIs (over three quarters) have been performed at Waikato DHB. TAVIs are now also being performed at the Auckland and Canterbury DHBs. The provision of TAVI across different DHB populations reflects the pilot development within the Midland region.

**TAVI Valve Devices**

Internationally, there are at least five different TAVI valve devices available (and a number of others under development):

- CoreValve\(^\circledR\) (Medtronic, Inc.; Minneapolis, Minn);
- Edwards SAPIEN\(^\circledR\) Transcatheter Heart Valve (Edwards Lifesciences LLC; Irvine, Calif);
- Edwards SAPIEN XT\(^\text{TM}\) (Edwards Lifesciences LLC; Irvine, Calif);
- JenaValve (JenaValve Technology, Munich, Germany);
- Acurate TA\(^\text{TM}\) valve (Symetis, Ecublens, Switzerland).

Other related devices include the catheter delivery systems, which can be specific or variable for different valves and for different delivery approaches.
Devices Used In New Zealand

Based on NMDS information, there appear to be at least three different devices currently used in New Zealand, CoreValve (the majority), Sapien and Sapien XT, although often the specific device used is not reported.

Regulatory Status

The CoreValve, Sapien, Sapien XT, JenaValve and Acurate TA valve devices all have the Conformité Européenne (CE - European Conformity) mark of approval, however this is more a quality certificate of manufacturing, compared with Federal Drug Administration (FDA) requirements for a randomised trial to demonstrate efficacy before approval. There is also separate CE marking for the different catheter delivery approaches. Sapien is approved in Europe for implantation via the transfemoral and transapical approaches, whereas CoreValve can also be implanted via a subclavian approach or by direct puncture of the aorta.

Neither the CoreValve nor Sapien valve devices have Therapeutic Goods Administration (TGA) approval for use in Australia, although TAVIs are being conducted under trial conditions or with special approval.

The Sapien device was given FDA approval in November 2011 for a transfemoral approach in non-surgical patients and in June 2012 an FDA panel suggested this be expanded to high-risk surgical candidates.

Safety, Efficacy and Cost Effectiveness

Registry data provide the largest source of information for assessing TAVI and several multicentre registries have reported early and late outcome data (from 2-5 years, hence limited information is available on the durability of TAVI valves). The PARTNER trial, under the auspices of the FDA, is the key completed Randomised Controlled Trial (RCT) on Sapien and other RCTs on different devices are in progress.

July-August 2012 BMJ articles have highlighted a 2011 Belgian HTA, which included Cost-Utility Analysis, on TAVI that concluded that it was inappropriate to fund TAVI for high-risk operable patients given high rates of stroke compared with standard surgery and an average Incremental Cost-Effectiveness Ratio (ICER) over €750,000 per Quality Adjusted Life-Year.

* The panel voted 12:0 that the device was effective and 10:2 that the device is safe and there were 11 votes (one abstainion) in favour of the statement that its benefits outweighed any risk. One of the panel members voting "no" on the safety question noted "at the current time, compared with standard AVR, this device has a higher stroke rate and high rate of aortic insufficiency, did not meet the criteria for noninferiority in males, and has a high incidence of vascular complications".
(QALY) (NZ$1.14M per QALY). In inoperable patients they found TAVI significantly reduces death rates compared with a non-surgical approach, with an average ICER of about €45,000 per QALY (NZ$68.5k per QALY), and noted that targeting anatomically inoperable patients was most prudent from an economic perspective. The authors also noted non-published negative results from a follow-up study to the PARTNER trial and that this study does not provide answers as to the efficacy of transapical TAVI. They concluded that many of the TAVI procedures carried out world-wide over the last decade cannot be justified on medical or cost effectiveness grounds and that Belgian health authorities should only pay for 10% of those currently considered for treatment.

The PARTNER trial, as reported in the Belgian HTA, showed that in high risk patients the overall differences in mortality between surgical aortic valve replacement and TAVI patients were not statistically significant. However, there were significantly more strokes following TAVI (5.5% vs 2.4% at 30 days and 8.3% vs 4.3% after one year). These strokes can be caused by both the debris from the native valve during insertion of the prosthesis and from embolic material forming in spaces between the aortic wall and prosthesis following implantation.

**Conclusion**

Differences have been found in the clinical outcomes and cost-effectiveness of the use of TAVI in different patient groups. There may also be differences in outcomes with different delivery approaches and from the different types of devices in use. TAVI can be associated with adverse effects which include stroke/transient ischemic attack, vascular complications and aortic regurgitation following valve implantation. Patients need to understand the risk of stroke and death and the uncertainty about the long term efficacy of the procedure.
## Appendix 1: Timeline of key TAVI events

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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<tbody>
<tr>
<td>1992</td>
<td>Investigation of bioprosthesies delivery to aortic sites in animal models.</td>
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<tr>
<td>2000</td>
<td>Seminal experience of percutaneous implantation of a heart valve in a 12 year old.</td>
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<tr>
<td>2002</td>
<td>First successful TAVI procedure for calcific aortic stenosis by Cribier in France.</td>
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<tr>
<td>2004</td>
<td>National Heart Foundation Project Grant for Overseas Training Fellowship to doctor who becomes lead researcher in a Canadian study pioneering the use of of percutaneous aortic valve insertions as an alternative for high-risk patients with severe stenosis.</td>
</tr>
<tr>
<td>2007</td>
<td>Sapien and CoreValve gain CE marks.</td>
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<tr>
<td>August 2008</td>
<td>First nine TAVIs (CoreValve) performed in the Asia-Pacific region – four at Mercy Hospital in Auckland and five at Waikato DHB (the latter funded by the Waikato Heart Trust and an individual who gifted more than $300,000 for the valves).</td>
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<tr>
<td>December 2008</td>
<td>Waikato DHB's Department of Cardiology put a proposal forward to NSTR for the introduction of a TAVI programme for high-risk surgical candidates in the public sector.</td>
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<tr>
<td>March 2009</td>
<td>NSTR assesses that the TAVI proposal, at this stage, should not proceed to the development of a full business case through the SPNIA framework as it was an emerging technology with low levels of evidence. Recommends that TAVI should not be publicly funded but that it should be reconsidered once evidence of benefit had been established. Also recommends that “new technologies without evidence from published randomised control trials are best implemented by DHBs as part of a formal clinical trial that includes utility analysis, before consideration of public funding”.</td>
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<tr>
<td>April 2009</td>
<td>Ministry of Health accepted NSTR’s recommendations but also agreed that ‘funding with evidence’ concepts should be explored to support clinical innovation and objective analysis in the developmental phase of emergent technologies.</td>
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<tr>
<td>August 2009</td>
<td>Ministry of Health supports Waikato DHB progressing TAVI initiative as a pilot.</td>
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<tr>
<td>March 2010</td>
<td>CE Mark for its Edwards Sapien XT valve, as well as its NovaFlex transfemoral and Ascenda 2 transapical delivery systems, receive CE mark.</td>
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<tr>
<td>September 2010</td>
<td>Waikato DHB pilot results on 42 patients provided to Ministry of Health. First randomised TAVI trial initial results presented in United States (PARTNER on Sapien).</td>
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<tr>
<td>December 2010</td>
<td>Auckland DHB’s CPC review TAVI at the request of the NHB and recommend interim funding.</td>
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<tr>
<td>March 2011</td>
<td>Minister of Health approves access to publicly funded TAVI for high risk surgical candidates.</td>
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<tr>
<td>April 2011</td>
<td>NHB advises DHBs that TAVI is approved for publicly funded cardiac surgery patients and could be included in cardiac surgery targets. Signals that cardiac clinical groups will review and recommend parameter guidelines and the patient selection process.</td>
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<tr>
<td>Date</td>
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<tr>
<td>October 2011</td>
<td>NHB advises DHBs of the cardiac clinical group developed parameter guidelines and the patient selection process. Signals that the NCSCN will undertake an analysis of outcomes and review the TAVI selection criteria and pathway in early 2012.</td>
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<tr>
<td>November 2011</td>
<td>Sapien gains FDA approval for transfemoral approach in non-surgical candidates. CoreValve recieves CE mark for transapical approach.</td>
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<tr>
<td>May 2012</td>
<td>NCSCN informs DHBs that it has started a review of the TAVI patient selection criteria and pathway and seeks their input, toward making recommendations to the NHB. Signals that a review of outcomes pends agreement between the centres performing TAVI on the dataset to be collected and submissions of data.</td>
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<tr>
<td>June 2012</td>
<td>FDA panel recommends Sapien for high-risk surgical candidates, including transapical approach (note: not FDA approval).</td>
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<tr>
<td>July 2012</td>
<td>NCSCN gathers DHB feedback on cardiac unit TAVI experiences.</td>
</tr>
<tr>
<td>August 2012</td>
<td>Recent TAVI evidence discussed at HealthPACT. NHC led review of TAVI proposed.</td>
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References


National Health Committee (NHC) and Executive

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