HealthPACT emerging health technology **Bulletin**

Health Policy Advisory Committee on Technology, Australia and New Zealand

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Issue 28

Inside this issue:

From the Chair ...

HealthPACT Chair Prof Brendon Kearney

Welcome to the June 2017 edition of the HealthPACT Bulletin. 30 June 2017 will see significant changes in the way in which HealthPACT operates following an AHMAC review of committees. At this stage, it is proposed that all administrative functions of HealthPACT will be located within the AHMAC Secretariat office in Adelaide, with the horizon scanning and technical functions still under consideration.

Over the last six years, with the support of Queensland Health, HealthPACT has made tremendous gains, with the combination of in-house and contracted evaluator expertise proving to be an effective and efficient way of managing HealthPACT's work program. HealthPACT has been at the forefront of horizon scanning for new and emerging healthcare technologies internationally and has made a significant contribution to all healthcare jurisdictions, as well as the TGA, DVA, MSAC and the Safety and Quality Commission. The provision of timely HealthPACT advice has assisted in the rational introduction of new technologies with significant savings to the Australian and New Zealand public healthcare systems.

HealthPACT's work has been made possible by a dedicated Secretariat, currently led by Queensland Health staff: Linda Mundy, Paul Hassed and Jenene Tull. However, the success of the HealthPACT Secretariat is largely due to the commitment, leadership and drive of Kaye Hewson, especially in securing in-kind support from Queensland Health. The Secretariat has worked efficiently and smoothly, responding to jurisdictional needs, and I wish to thank all those involved for their contribution over the last six years.

Although the detail of the AHMAC committees review will not be finalised and implemented until August 2017, I wish to pay tribute to the Queensland Health HealthPACT Secretariat and their willingness to contribute to the new arrangements. It is hoped that this transition will be smooth and as effective as possible in order to maintain the continuity of the HealthPACT work program. HealthPACT welcomes the opportunity to change and embrace the new arrangements as determined by AHMAC.

With best wishes

Brendon Kearney

HEART FAILURE TECHNOLOGIES

Heart failure (HF) is a condition characterised by an underlying structural abnormality or cardiac dysfunction causing inability of the heart ventricle to maintain sufficient blood flow. Usually a chronic, long-term condition, HF has a number of causes including heart attack, high blood pressure, primary heart muscle weakness (various causes) or a damaged heart valve. In 2011–2012, the Australian Bureau of Statistics reported 297,800 people in Australia had HF or symptoms related to HF.

Current standard care in HF involves physical activity programs and dietary management (e.g. fluid intake advice), medical therapy (e.g. ACE inhibitors and beta blockers), supportive devices and post-discharge HF management programs (e.g. home based interventions).

For patients with HF subclass II or III at the time of hospital discharge, a structured multidisciplinary HF management program with 12 week follow-up care is recommended. This i ncludes self-monitoring of their weight daily and a personalised HF action plan.

Six technologies of interest were identified by HealthPACT for inclusion in this rapid compendium on HF therapies and diagnostic interventions: intracoronary gene transfer using an adenovirus vector for HF patients with low left ventricular ejection fraction (LVEF), interatrial shunt devices for chronic HF patients with preserved left ventricular ejection fraction (pLVEF), left ventricular parachute devices for ischaemic HF, mesenchymal stem cell therapy (MSCT) for advanced HF, and the Edema Guard and CardioMEMS^{TM} devices for monitoring lung oedema and pulmonary arterial pressure, respectively.

Intracoronary gene transfer for congestive heart failure with low left ventricular ejection fraction such as RT-100 are being investigated as an alternative to standard HF treatments. RT-100 is administered by an intracoronary infusion to deliver a gene which encodes for human adenylyl cyclase type 6 (AC6) protein.

Based on an RCT of 86 patients, the RT-100 to increase the heart function (left ventricular ejection fraction) among HF patients with low LVEF showed no difference when compared to placebo. Sub-analysis suggested that patients with HF of non-ischaemic origin may be more likely to benefit from RT-100, but this was based on a sample of only 34 patients.

The clinical importance of this technology remains unclear at this time. An informed decision on the adoption of RT-100 into clinical practice will require further clinical trial evidence. Further investigation of RT-100 dosing below 3.2×10^{11} virus particles appears unwarranted.

InterAtrial Shunt Device (IASD) for heart failure patients with preserved ejection fraction has been designed to directly alleviate the pulmonary congestion experienced by HF patients with preserved LVEF due to elevated left atrial pressure. The IASD is implanted using a percutaneous catheter procedure and works by redistributing blood from the higher pressure left atrium to the lower pressure right atrium.

One series of 64 HF preserved LVEF patients (non-comparative evidence) assessed the safety and effectiveness of IASD. Overall, the findings suggested that patients experienced clinically significant improvements and overall survival was 95 per cent.

No comparative evidence was identified. Therefore conclusions regarding comparative safety and effectiveness cannot be made. Decisions on uptake of the technology will be aided when and if comparative data become available.

Parachute implant for ischaemic heart failure is a ventricular restoration device. Following a heart attack, many patients experience remodelling of the left ventricle (LV), which leads to decreased cardiac output and typical HF symptoms, including shortness of breath. Using a catheter procedure, the parachute partitions the damaged heart muscle segment from the remaining functional segment of the LV, restoring overall volume and geometry. This is claimed to improve function.

HEART FAILURE TECHNOLOGIES

(CONTINUED)

Three relevant publications were identified and included for the assessment of the Parachute implant. However conclusions regarding the comparative safety and effectiveness were not possible for all three case series.

The Parachute remains investigational. No comparative evidence was identified. Data from a randomised comparison with 560 patients with optimal medical therapy, due to be completed in July 2017, may provide data to inform whether or not the Parachute device is likely to be of clinical benefit.

Mesenchymal stem cell therapy (MSCT) for advanced heart failure use a mix of cardiogenic growth factors and are intended as direct substitutes for ventricular assist devices (VADs), and heart transplantation. MSCTs use mesoderm-derived multipotent stromal cells found in various adult tissues, but commonly isolated from bone marrow. The mesenchymal stem cells (MSCs), which are claimed to restore heart cells lost due to progression of HF and secrete beneficial growth factors, are delivered using specialised catheters.

HealthPACT assessed two RCTs conducted in Europe and the US both funded by industry, as well as one Chinese RCT.

Reduction in overall cardiac events among HF patients attributed to Ixymyelocel-T are based on an industry funded RCT. Bias due to funding from industry cannot be ruled out. RCTs with complete outcome reporting based on individually measured endpoints would be helpful to more clearly determine the potential clinical benefit of this therapy.

Findings that C-Cure improves LVEF and six-minute walk test outcomes compared to standard care alone should be interpreted with caution, given that the relevant RCT was funded by the developer of C-Cure. Reporting of other outcomes was incomplete. A larger, more highly powered RCT with full and accurate data reporting would likely help in assessing the clinical value of C-Cure.

Other RCT evidence not funded by industry found that one unnamed MSCT failed to demonstrate additional benefits for HF patients beyond the improvements observed among placebo patients. A larger RCT may be required to determine the clinical benefit of this therapy. The RCT investigating an MSCT based on Wharton's jelly versus placebo reported promising outcomes on LVEF among MSCT patients. Further investigation of this technology including additional patient relevant outcomes appears warranted.

Edema Guard to monitor lung oedema in heart failure is intended to measure lung impedance, or resistance to electrical current, to monitor fluid accumulation in the lungs. It is claimed that the data provided by Edema Guard can be used to commence necessary treatment long before a patient has symptoms of pulmonary oedema.

Evidence for the safety and effectiveness included one large RCT with 256 patients reporting on NYHA class II-IV HF patients with low LVEF (≤35%). HF-related mortality was reduced by two thirds in the Edema Guard group compared to the standard group ($p<0.001$). Based on these encouraging results another RCT is underway with completion expected in January 2020.

Consideration of this new evidence is warranted to inform a decision on the clinical use of the technology in Australia and New Zealand, if the technology becomes available outside of Israel.

CardioMEMS™ for monitoring pulmonary arterial pressure in heart failure functions by permanent implantation of a sensor in the far end of the pulmonary artery during a right heart catheterisation procedure via the femoral vein.

Based on one RCT, it would appear that this technology is associated with adverse events in less than three per cent of patients and may reduce the risk of hospitalisation by up to 30 per cent, compared to patient management initiated on the basis of clinical guidelines alone.

However, the RCT was funded by the developer and CardioMEMS™ was rejected for public funding by the MSAC.

More details about the report can be found at the HealthPACT website.

Email us at HealthPACT@health.qld.gov.au

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ARE DOCTOR BIASES LEADING TO LOW-VALUE INTERVENTIONS?

The Royal Australasian College of Physicians, the Menzies Centre for Health Policy and NPS MedicineWise collaborated on a review published in the Medical Journal of Australia concerning the potential reason doctors continue to provide treatments that are known to be of low value.

This is care that confers little or no benefit and may instead cause patient harm, is not aligned with patient preferences, or yields marginal benefits at a disproportionately high cost.

The narrative review titled "Countering cognitive biases in minimising low value care" recently published in the Medical Journal of Australia, states that doctors have been warned to be aware that psychological factors could lead them to suggest medical interventions of little or no value to patients, despite campaigns aimed at eliminating unnecessary tests, treatments and procedures.

Lead author Associate Professor Ian Scott, who heads the Department of Internal Medicine and Clinical Epidemiology at Brisbane's Princess Alexandra Hospital, said that the problem of cognitive bias cuts across all medical disciplines and concerns GPs and specialists alike.

"In most situations this intuition generates the correct decision, but in some circumstances doctors can fall prey to cognitive biases which generate the wrong decision," Dr Scott said.

"These cognitive biases, or psychological factors that influence thinking, can come from formal education and training and from peer opinion, personal experience, societal norms and from socialising with colleagues.

"These biases are inclinations a person can have based on one's preferences or beliefs, and can steer clinicians towards continuing to believe in, and deliver, care that robust evidence has shown to confer little or no benefit.

Professionally led national campaigns, such as the Choosing Wisely Australia campaign and EVOLVE (Evaluating Evidence, Enhancing Efficiencies), aim to raise awareness of, and reduce the frequency of low value care and interventions.

In a review of articles on clinical decision-making, Dr Scott has found the effectiveness of such campaigns could be limited by common forms of cognitive bias. Biases need to be understood and addressed if campaigns such as Choosing Wisely and EVOLVE are to achieve their full potential.

Dr Scott said sharing case studies of what could be seen in hindsight as low-value care with colleagues and disclosing one's reasoning for such decisions could help expose and reduce cognitive bias, but further research was needed.

Dr Scott was also recently a guest on ABC Radio National's Health Report discussing this issue in more detail. Click here for the transcript.

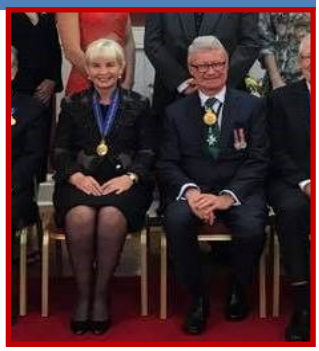
CONGRATULATIONS TO ...

Prof Lizbeth Kenny

As many of you know from our March edition of the HealthPACT Bulletin, Prof Lizbeth Kenny, Queensland Clinical Advisor to HealthPACT was the recipient of an **Officer of the Order of Australia** award earlier this year.

In early May, Prof Kenny was presented with the AO medal at the Investiture Ceremony at Queensland Government House by His Excellency the Honourable Paul De Jersey AC, Governor of Queensland for distinguished service to medicine as a clinician and researcher in the field of radiation oncology, and to executive roles with professional organisations nationally and internationally.

Prof Kenny is a Senior Radiation Oncologist at the Royal Brisbane and Women's Hospital and Medical Director – Central Integrated Regional Cancer Service and is committed to improving Cancer Services in Queensland. Her main areas of specialty interest are Head and Neck Cancer and Breast Cancer.



Prof Liz Kenny with His Excellency the Honourable Paul De Jersey AC, Governor of Queensland

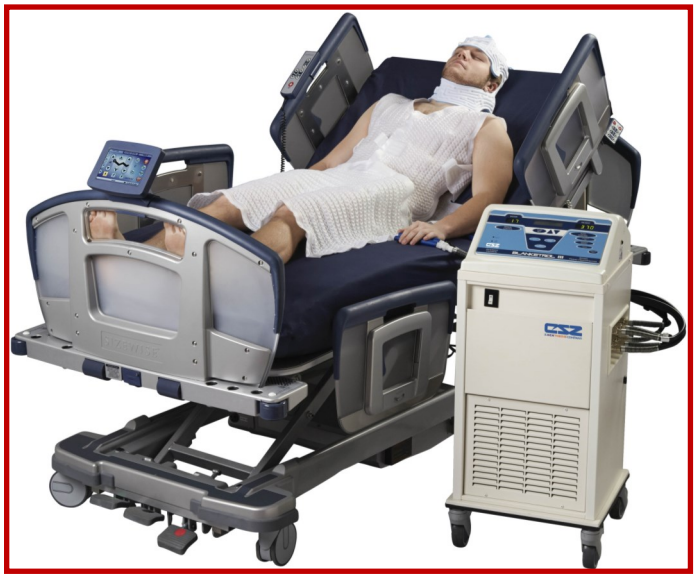
THERAPEUTIC HYPOTHERMIA FOR INTRACRANIAL HYPERTENSION FOLLOWING TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) may be caused by a variety of mechanisms. TBI ranges in severity from mild to severe, and in addition to short-term impairment, those who sustain TBI often suffer from persistent symptoms. Symptoms may be lifelong and have a substantial impact on quality of life. Owing to advances in critical care medicine, mortality from TBI is declining. However, a high proportion of TBI survivors require ongoing rehabilitation for long-term physical, cognitive and psychological sequelae.

Intracranial hypertension (IH) is an important cause of secondary brain injury. The severity and duration of IH are associated with functional outcomes after TBI. Monitoring of intracranial pressure using different devices is necessary to prevent IH and maintain cerebral perfusion pressure, the fundamental therapeutic goals after TBI.

Identified conventional therapies for traumatic IH include hyperventilation, osmotic diuresis, ventricular cerebrospinal fluid (CSF) drainage, barbiturate coma or less severe sedation and pharmacological neuromuscular paralysis. More recently treatments have also included hypertonic saline, lumbar CSF drainage and decompressive craniectomy.

Therapeutic hypothermia has been used as a direct substitute for, or alongside, conventional therapies to treat IH following TBI.



An example of a whole body cooling system for applications designed to induce hypothermia.
(Image reprinted with permission from Cincinnati Sub-Zero [CSZ])

A variety of methods may be used to induce hypothermia in patients with IH following TBI. These include, but are not limited to, simple surface cooling approaches traditionally achieved with ice packs, ice baths and head fanning, or with more complex methods using cooling caps and helmets. Besides the surface cooling approaches, the literature describes the use of intranasal selective hypothermia (using cold air), trans-arterial or trans-venous endovascular cooling (using cooled saline or the patient's own blood), extra-luminal vascular cooling (involving a cooling cuff, with cold circulating water, wrapped around the common carotid arteries) and epidural cerebral cooling (cold saline infused in the epidural space).

HealthPACT identified a high-level but inconsistent body of evidence on the topic of therapeutic hypothermia for patients with traumatic brain injury (TBI) compared to standard normothermic care. Older evidence (pre-2009) in a relatively limited sample of patients suggests better functional outcomes for patients treated using hypothermia. Evidence limited to patients requiring craniotomy suggests that rapid cooling to 35˚C within 1.5 hours of craniotomy is associated with better functional outcomes compared to cooling to 35˚C beyond 1.5 hours post-craniotomy. The largest and most recent RCT identified, including 387 TBI patients recruited from across Europe suggests that avoiding hypothermia results in better functional outcome after TBI. Given this RCT was the largest study and represented the highest level of evidence identified, its findings should be given precedence over the other identified studies for informing the decision for or against disinvestment from therapeutic hypothermia in the TBI population.

Recent evidence suggests that therapeutic hypothermia for traumatic brain injury is inferior to standard clinical care. Indeed, there is some evidence that therapeutic hypothermia may result in poorer neurological outcomes.

HealthPACT recommends that therapeutic hypothermia should not be routinely used to treat patients with traumatic brain injury.

For further information about this technology, please contact HealthPACT.

GETTING TO KNOW …

Dr Stephen Munn, New Zealand

How long have you been a member of HealthPACT?

A little over 10 years.

Do you have a nickname?

No, but a few years ago a telephone operator was uncertain she had heard my surname correctly and asked if my name was 'Mud'! I had the presence of mind to say "Not yet".

What would your alternate career be?

I've had several interests including Physics (especially nuclear physics), Actuarial work (I enjoyed mathematics at high school and university), and Writing (I write short stories for fun – nothing published yet).

What is the one thing you can't live without?

That's pretty easy – my wife Glenys to whom I've been happily married for over 40 years and with whom I've had six children.

Do you have any phobias?

I'm not too keen on confined spaces (claustrophobia) but have recently had to have MRI scans that are not ideal for people like me. I got through those pretty well so maybe I'm getting more mellow with age.

Where is your next holiday destination?

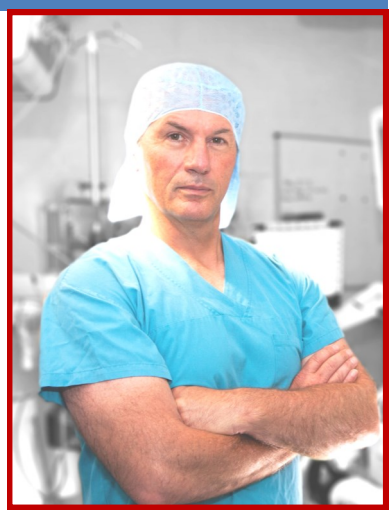
I'm going to a Health Technology Assessment (HTA) conference in Rome so Glenys and I will be spending around 10 days in Sorrento before getting to Rome. We love the Amalfi coast area of Italy.

What is left to do on your 'bucket list'?

I've travelled to close to 50 countries but never made it to Russia. I'd like to see St Petersburg in particular. I enjoy Russian writers – Tolstoy, Dostoevsky, Solzhenitsyn etc. and to see places that they write about would be great.

What is your specialty dish to cook?

I'm not a flash cook but I like preparing a big roast beef dinner for my tribe of kids and grandkids and then sitting at the head of the table with them all around and chatting – it's a great feeling!



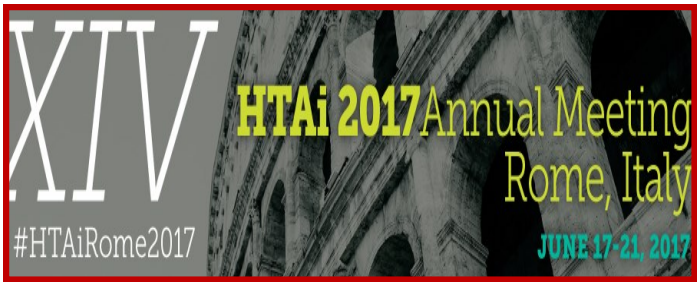
Dr Stephen Munn, Auckland District Health Board, New Zealand - Clinical Advisor, HealthPACT

When and where are you at your happiest?

Whilst I love my family to bits, I'm most at peace when all is quiet and still and I can concentrate on reading or writing. An ideal scenario is a warm, sunny, leafy place either in solitude or just with Glenys and plenty of uninterrupted time to spare.

And finally, you've just been appointed as the Health Minister, what will your first priority be?

Well, obviously the first thing to do would be to get a psychiatric opinion because taking on such a task would clearly be a sign of mental instability. After checking that out I can say that, without a doubt, I'd wish to go from a reactive stance (just putting out fires) to a careful, strategic one whereby, over a long period of time, each medical service, drug, medical device and diagnostic test came under scrutiny to see if it truly added value and, if so, at what cost. I believe that, eventually, that would both save money and improve the quality of healthcare we deliver. A long view for sure but a crucial one in my opinion.



MONARCH™ EXTERNAL TRIGEMINAL NERVE STIMULATION SYSTEM FOR DRUG-REFRACTORY EPILEPSY

Epilepsy is a term used to describe a group of brain disorders in which clusters of nerve cells signal abnormally, causing repeated, unpredictable seizures. Seizures can vary in frequency from less than one per year to hundreds each day. They can also vary in their intensity from brief lapses in awareness, unusual movements or muscle jerks to severe and prolonged convulsions with loss of consciousness. Epilepsy affects men and women of all ages.

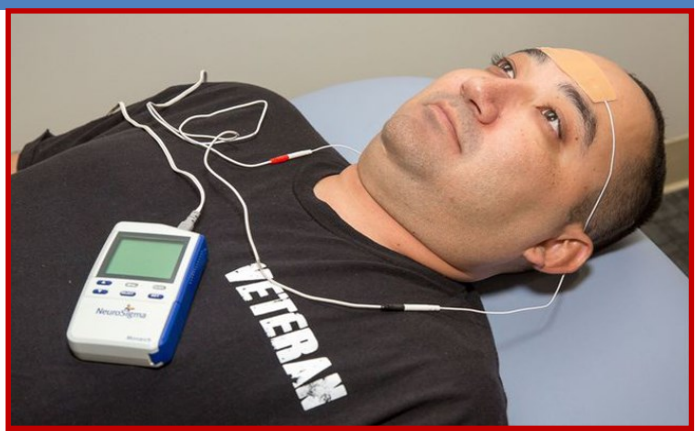
The Monarch™ external Trigeminal Nerve Stimulation (eTNS) System is a non-invasive adjunct therapy for drug-refractory epilepsy (DRE). DRE is diagnosed when adequate trials of two antiepileptic drugs, taken singularly or in combination, have failed to achieve sustained freedom from seizures.

Current treatment options for DRE include surgery or vagus nerve stimulation. Both options, however, require invasive and complicated surgery. The Monarch eTNS System is a novel, non-invasive therapy for DRE that is less complicated and potentially less expensive than current treatments.

The Monarch eTNS System consists of a small external pulse generator connected to a single-use adhesive patch which is placed on the patient's forehead, delivers a low-intensity electrical current that stimulates the ophthalmic branch (referred to as V1) of the trigeminal nerve. The stimulation is confined to the surface of the forehead and does not penetrate into the brain. The initial level of stimulation is set in consultation with a physician and can be manually adjusted.

HealthPACT assessed two randomised controlled trials (RCTs) and one prospective case series. The first RCT compared patients receiving active eTNS treatment to those receiving an active control pulse. The second RCT was a continuation of the first RCT where all patients who agreed to continue with long-term treatment were converted to effective treatments settings. Follow-up in all three studies ranged from 18 weeks to 12 months. All three studies had low patient numbers (≤50) and large losses to follow-up, particularly the second RCT which had losses to follow-up of 81 percent in the control group and 58 per cent in the treatment group.

Adverse events from the use of eTNS were mild in all three studies (anxiety, headache and skin irritation). With respect to effectiveness, the only significant differences that occurred in the first RCT were between the treatment group and the control group was with respect to mood, which improved with eTNS treatment, and with 50 per cent responder rate for the treatment group, which increased from 18 per cent at six weeks to 41 per cent at 18 weeks. In the second RCT with long-term follow-up, significant reductions in median seizure frequency occurred in the original treatment group at the 3-, 6- and 12-month follow-ups and for both groups combined at the 6- and 12-month follow-ups. In the case series, a statistically significant reduction in mean seizure frequency was observed at the 3-month follow-up, but not at the 6- or 12-months follow-ups.



A patient demonstrating the use of the Monarch™ eTNS System

Based on the three included studies, the Monarch eTNS System seems to be safe with relatively minor adverse events reported. However, the effectiveness of the device is still unclear with no significant effects on seizure frequency reported in one of the RCTs and small patient numbers and large losses to follow-up reported in all three studies.

HealthPACT noted that although the Monarch™ eTNS™ System is approved by the TGA as an adjunctive treatment for patients nine years and older with drug-resistant epilepsy, the evidence base to date only describes results in adult patients. HealthPACT noted that efficacy of the Monarch™ system was not demonstrated by the current evidence base, with no significant difference in seizure frequency between the control and intervention groups. HealthPACT does not support public investment in this technology in clinical practice at this time.

For further information about this technology, please contact HealthPACT.

NEXT MEETING ...

9 June 2017

The HealthPACT meeting held on Friday, 9 June in Brisbane discussed the following topics:

- High-throughput non-invasive prenatal testing for fetal rhesus D genotype
- Close contact casting versus surgery for initial treatment of unstable ankle fractures in older adults
- Allogeneic mesenchymal stem cell and autologous T-cell therapies for the treatment of refractory Crohn's disease
- Haemorrhoidal artery ligation versus rubber band ligation for the management of symptomatic haemorrhoids
- Behavioural activation versus cognitive behavioural therapy for depression
- Prostatic artery embolisation to treat benign prostatic hyperplasia
- Hysterectomy, endometrial ablation and hormone-releasing intrauterine devices for heavy menstrual bleeding
- Exablate Neuro (MR-guided focused ultrasound) for neurologic movement disorders
- Lutetium-177, Actinium-225 and Bismuth-213 prostate-specific membrane antigen radiopharmaceuticals for metastatic castration-resistant prostate cancer
- Overview of 3D printing in Australia and New Zealand
- Overview of CRISPR - genome editing technology

HAZARD ALERT

Bioresorbable Vascular Scaffold System

On 2 May 2017, Abbott Vascular Australia and the Therapeutic Goods Administration (TGA) issued a hazard alert for Absorb Bioresorbable Vascular Scaffold (BVS) System. Abbott has now undertaken the task of recalling all unused stock of the device and it has now been removed from the Australian Register of Therapeutic Goods (ARTG).

This move has been in response to recent data showing elevated rates heart attacks and blood clots.

HealthPACT assessed this technology in both July 2015 and again in December 2016 and concluded that there was insufficient evidence to determine whether patient outcomes with the BVS technology were equivalent, or inferior to, those in patients treated with conventional drug eluting stents. It was noted that " HealthPACT does not support public investment in this technology in clinical practice at this time, and not until after consideration of published results of studies demonstrating clinical equivalence or superiority with long-term patient outcome data."

If you have any questions or concerns about this issue, contact Abbott Vascular Australia on 1800 550 939.

UPCOMING EVENTS ...

17-21 June 2017	HTAi 2017 Annual Meeting	Rome, Italy
17-19 July 2017	10th Asia Pacific Conference on Medical and Biological Engineering (APCBME)	Sydney
1-3 August 2017	69th AACC Annual Scientific Meeting and Clinical Lab Expo	San Diego, USA
5-8 August 2017	HGSA 41st Annual Scientific Meeting - Next Generation: Coming of Age	Brisbane
10-13 August 2017	CSANZ 2017: 65th Annual Scientific Meeting and the 41st Annual Scientific Meeting of the International Society for Heart Research	Perth
30 Aug - 1 Sep 2017	Neurosurgical Society of Australasia Annual Scientific Meeting	Adelaide
12-14 September 2017	AACB 55th Annual Scientfic Conference	Melbourne
29 Sep - 1 Oct 2017	GSA Annual Scientific Meeting – Abdominal Wall: Access and Repair	Canberra
9-13 October 2017	33rd Patient Classification Systems International Conference	Sydney
11-13 October 2017	42nd Australian and New Zealand Annual Scientific Meeting on Intensive Care and the 23rd Annual Paediatric and Neonatal Intensive Care Conference	Gold Coast
13-16 October 2017	ANZSVS Scientific Conference - Vascular Surgery in Times of Economic Pressure	Perth
18-21 October 2017	RACMA 2017 Annual Scientific Meeting: Past Reflections, Future Directions	Melbourne
19-22 October 2017	RANZCR 68th Annual Scientific Meeting	Perth
25-27 October 2017	AusBiotech 2017 - Australia's Life Sciences Conferences	Adelaide
1-3 November 2017	HSRAANZ 2017 10th Health Services and Policy Research Conference	Gold Coast
9-11 November 2017	iSMIT 29th Conference of the Society for Medical Inovation and Technology	Torino, Italy
12-14 November 2017	CSIRO and MIME International Conference on Medical 3D Printing	Melbourne
13-15 November 2017	2017 COSA ASM - Immunotherapy: Molecules and Mountains	Sydney
20-22 November 2017	Cutting Edge Science Symposium on Genome Engineering for Cancer Treatment	Canberra
21-22 November 2017	NFMRI Medical Research and Innovation Conference	Sydney
4-7 December 2017	Design 4 Health 2017	Melbourne

"There was no umbilical cord. These days, babies are connected by Bluetooth."