

# TRANSLATING RESEARCH INTO CLINICAL PRACTICE

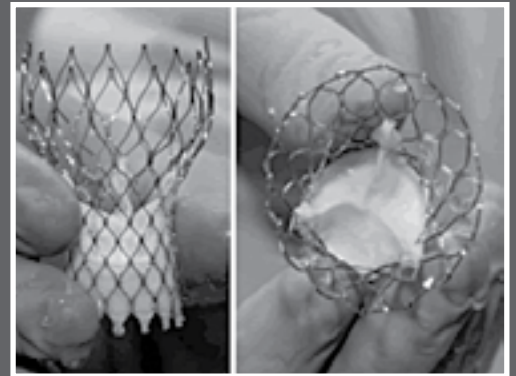
Translation of research findings into sustainable improvements in clinical practice and patient outcomes is the major goal of clinical research. Described here are some examples of changes to clinical practice resulting directly from research conducted recently within the Alfred Medical Research and Education Precinct.

## Cardiovascular medicine

Several of the projects within the Department of Cardiovascular Medicine translate the findings of biomedical research and development into clinical practice. Three studies undertaken during the past year illustrate different aspects of the translational process. Studies from Dr James Shaw and colleagues have demonstrated that the infusion of HDL (good) cholesterol can reduce inflammation in atherosclerotic plaque given several days prior to plaque removal by percutaneous atherectomy. These studies paved the way for future investigations of the effects of such therapy on clinical end-points.

Research by Professor Murray Esler and Dr Tony Walton have demonstrated that interrupting the sympathetic nervous supply of the kidneys in subjects with high blood pressure can be done safely through a percutaneous catheter, and appears to result in worthwhile gains in blood pressure reduction in subjects who are poorly controlled with medical therapy. These studies have been published in *The Lancet* and will form the basis for a definitive clinical trial to establish the place of this novel therapy.

A third example relates to the study within the department of an innovation developed by Professor David Kaye to make it possible to more safely undertake coronary angiography in subjects with renal failure. The research builds on Professor Kaye's extensive experience with similar techniques in both clinical and experimental animal research, and uses a catheter based device to extract radio-opaque dye used in cardiac angiography before it has circulated through the body and potentially caused further kidney damage.



*The CoreValve ReValving System™ is currently under evaluation through research at The Alfred. It consists of a porcine pericardial bioprosthetic valve mounted and sutured in a multi-level self-expanding Nitinol frame. The bioprosthesis is housed in a collapsed position for percutaneous delivery via a catheter-based technique, and implanted within the diseased aortic valve. The procedure is performed utilising local anaesthesia (with or without conscious sedation).*

## The accuracy and completeness of patient reported medication histories compared with those obtained by a pharmacist in a preadmission clinic

The aim of this study was to prospectively evaluate the accuracy and completeness of a patient-completed questionnaire (PAQ) completed by patients attending the preadmission clinic (PAC) compared with a pharmacist's preadmission assessment.

The study was conducted over a three-week period in August 2007 with patients attending a preadmission surgical clinic. Consecutive patients had a preadmission assessment with the PAC pharmacist. Comparison was made regarding the accuracy of medication information between the PAQ and preadmission assessment by the PAC pharmacist. Of the 150 patients enrolled in the study, 33 (22.0%) had a PAQ that was totally correct. There was an average of 3.9 drug discrepancies per PAQ. The discrepancies were related to drug omitted (317), incorrect dose (24), dose omitted (110), frequency incorrect (24) or frequency omitted (63). The patient's adverse drug reaction status was recorded correctly on the PAQ for 84.7% patients.

This study has shown that a PAQ used in the setting of a preadmission surgical assessment is not accurate in four out of five patients. This highlights the positive contribution of a pharmacist working in a PAC in ensuring that an accurate medication history is available.



*Sharon Selvanayakam, Senior Clinical Pharmacist, completes a patient medication history in the preadmission clinic.*

## Pure gold in the prostate ensures our aim is true!

Investigators: J Millar, L Obesekera, M Brown, T Morgan, S Paule, L Lord, S Booth



*From left: Dr Michelle Brown, Associate Professor Jeremy Millar, Dr Bronwyn Matheson and Leah Lord, four of the large team involved in the prostate marker project.*

necessary to place a marker into the prostate. This concept was tested in a pilot study in 2005–6, where tiny gold ‘fiducial markers’ were placed in the prostate prior to treatment of men for prostate cancer. These were looked at with EPI each day before turning on the treatment beam.

This study demonstrated that gold markers could safely be placed in the prostate, visualised on a daily basis during treatment, and the beam aim adjusted correctly using this information. Higher doses of radiation can be more accurately delivered to the prostate, with a decrease in the side-effects of treatment. As a direct result of this research, in 2008 the WBRC introduced a program termed ‘Our Aim is True’, placing gold markers to ensure the most accurate targeting in all men with prostate cancer undergoing radiation treatment.

Radiation treatments to cure cancer are, in theory, simple. All that is required is a large enough dose of radiation to the tumour. This then rapidly gets complicated, since in situations like the curative treatment for prostate cancer, it is necessary to get very high doses precisely to the prostate gland consistently over an eight-week period, while avoiding high doses to the nearby bowel, bladder, nerves and blood vessels.

This problem was addressed by applying new imaging and computing technology. The William Buckland Radiotherapy Centre (WBRC) was among the first radiation departments in Australia to use Electronic Portal Imaging (EPI) to allow visualisation each day, prior to turning on the beam, to ascertain and confirm the radiation field placement. The method allows visualisation of bony landmarks near a tumour, but to see the prostate gland on a standard X-ray, it was

## Factors contributing to bleeding risk in patients receiving warfarin therapy

Investigators: J McNeil, P Cameron, M Dooley, R Wolfe, S Evans, E Maxwell, L Piterman, A Street, B Diug, J Lowthian



*Standing, from left: Basia Diug (PhD student), Judy Lowthian (PhD student) and Dr Sue Evans (Associate Director, Centre of Research Excellence in Patient Safety). Seated: Professor Peter Cameron (Director, Centre of Research Excellence in Patient Safety).*

Warfarin is the mainstay of prophylaxis against stroke in atrial fibrillation and valve replacement. Warfarin’s narrow therapeutic window necessitates close monitoring of the International Normalised Ratio (INR) as numerous factors are recognised to increase or reduce its anticoagulation effect. Despite its efficacy, warfarin remains one of the most common drug-related causes of death and morbidity, with increased bleeding tendency as its major adverse effect.

The aim of this project is to reduce the amount of unnecessary bleeding due to warfarin, by identifying predisposing factors and potential system of care issues amongst patients with significantly elevated INR levels, and to develop a preliminary risk profile of patients being treated with warfarin who record elevated INR levels in the blood. We hypothesise that people with an elevated INR level will have a different profile than those who maintain an INR level within a therapeutic range.

Based in metropolitan Melbourne, this project is being conducted in collaboration with Melbourne Pathology, and consists of two phases. The pilot study was completed in 2007; 40 patients with INRs  $\geq 6$  and their primary treating doctors were interviewed. The current case control study comprises 450 patients: 150 cases and 300 controls. Patients are eligible if they are aged  $\geq 18$  years, reside in the community, provide informed consent and have been on warfarin for a minimum of six months. Additionally, cases have recently developed an INR  $\geq 6.0$ , whilst controls have been well stabilised for a minimum of three months. Patient interviews investigate potential predisposing factors, including demographic and clinical characteristics, comorbidities, diet, medication and warfarin knowledge. Standardised measures evaluate cognition, mood, social support, functional independence, and adherence and medication complexity.

A major outcome of this study will be an improved ability to ‘risk-stratify’ patients given warfarin therapy into those at high and low risk of bleeding. Ultimately, it may reduce the significant burden of harm attributable to warfarin and improve the ratio of benefit to harm achieved with this agent. The project is funded by NHMRC Project Grant ID 436763.