University of Otago, Christchurch
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2012 / 2013
Summer Studentship Programme
Lay Reports
COVER: Nicole Sycamore (student) with Tim Edmonds (Cure Kids Research & Innovation Manager) and Stephanie Moor (supervisor)
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Tom Wilkinson
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1. Introduction

Rau Rangatira ma, tena koutou, tena koutou, tena koutou katoa.

Nau mai haere mai Te Whare Wananga o Otago ki Otautahi. Piki mai kaki mai.

Each year the University of Otago, Christchurch (UOC) hosts a Summer Studentship Programme, allowing participating students to get an introduction to research methods in a field of interest to them, such as public health, clinical or laboratory-based research.

We had an impressive programme this year, in spite of the on-going challenges imposed by the closure of our main building since the 2011 earthquakes, with 53 students assigned to a wide variety of health related projects. This was only made possible through the continued efforts of our dedicated supervisors, the host departments and our generous sponsors. We continue to be grateful for the assistance of organisations such as Canterbury Scientific Ltd, the University of Canterbury and Lincoln University who provided laboratory space for our researchers and their students.

This booklet is a compilation of the reports submitted by the student participants in the 2012/2013 Summer Studentship Programme. The main objective of the Summer Studentship Programme is to give undergraduate medical and health science students an introduction to research. It is a regional programme that encourages participation from students and staff of the University of Otago, Christchurch; Canterbury District Health Board; University of Canterbury and Lincoln University. Any student who is enrolled at a New Zealand tertiary academic institution at a pre-doctoral level is eligible to apply for the studentships.

The summer studentship programme is heavily dependent on the financial generosity of external organisations that contribute an educational grant for each student. We offer our thanks to these sponsors who are listed in this report booklet. Thanks also to Carole Acheson, Professional Practice Fellow – Christchurch, for providing the students with the seminar ‘Presentation Skills and Dealing with the Media’ and to Tuari Potiki, University of Otago Director Maori Research Facilitation, for his introductions to the students’ presentations.

We are grateful to the following members of the Research Committee: Dr Gillian Abel, Professor Andrew Day, Professor Lisa Stamp and Professor Martin Kennedy, who undertook the difficult tasks of assessing the project applications and judging the students’ presentations.

Three prizes of $500 each for outstanding studentship presentations were awarded and a fourth prize of $500 was awarded for the ‘Best Overall Project’ this year.

- Best oral presentation in the ‘Laboratory’ category – Simon Hogg, ‘A 3D cell culture in a 96-well format for rapid drug screening in advanced ovarian cancer’. This prize was sponsored by Canterbury Scientific Limited.
- Best oral presentation in the ‘Clinical’ category – Harmony Thompson, ‘Does early variation in sample separation time affect plasma glucose analysis? Implications for glucose meter evaluation’. This prize was sponsored by the Christchurch Radiology Group.
- Best oral presentation in the ‘Community’ category – Lucy Peterson, ‘Reducing barriers to practice nurse involvement in general cervical screening and understanding effective methods of inviting and engaging priority women in cervical screening in general practice’. This prize was sponsored by the Lions Club of Selwyn.
- Best Overall Project – Angela Ballinger (student), Dr Suetonia Palmer (Supervisor), ‘Calcimimetic agents to improve clinical outcomes in people with chronic kidney disease: Meta-analysis of randomised, controlled trials’ This prize was sponsored by the Canterbury Branch Trust Board of the New Zealand Federation of Graduate Women (Inc.).
Our particular thanks go to all of the organisations for their support of these prizes. We wish to offer our congratulations to the winners and our thanks to all the students whose fine efforts made the selection process such a difficult one.

These reports are a small reflection of the enormous amount of work and commitment put into the projects by the students, staff, departments and sponsors. We hope that you will enjoy reading the reports and we look forward to your support of the 2013/2014 Programme.

Professor Margreet Vissers  
Associate Dean (Research)

Elizabeth Cunningham  
Research Manager-Maori

Virginia Irvine  
Research Manager

Research Office  
Department of the Dean  
University of Otago, Christchurch  
PO Box 4345  
Christchurch 8140  
New Zealand

Telephone: +64 3 364 3630  
Email: research.uoc@otago.ac.nz  
Web: www.otago.ac.nz/christchurch/research/researchoffice/
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- Older Persons Health, Orthopaedics & Rehabilitation, Canterbury District Health Board
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• The Canterbury Health Care of the Elderly Education Trust
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• The Royal New Zealand College of General Practitioners
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• University of Otago Health Sciences Divisional Summer Scholarships
3. Supervisors

Dr Gillian Abel
Dr Paul Abernethy
Ms Cerina Altenburg
Dr Nigel Anderson
Professor Tim Anderson
Associate Professor Nicola Austin
Dr Sue Bagshaw
Ms Karyn Balance
Associate Professor Lutz Beckert
Dr Caroline Bell
Dr Juliet Berkeley
Professor Stephen Brennan
Dr Kim Burgess
Dr Andrew Butler
Dr Anthony Butler
Dr Janet Carter
Professor Steven Chambers
Dr Peter Chapman
Professor J G Chase
Dr Kenny Chitcholland
Dr Lynley Cook
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Dr Birgit Dijkstra
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Mr Tim Eglinton
Dr Jane Elmslie
Dr Michael Epton
Professor John Evans
Associate Professor Chris Florkowski
Professor Chris Frampton
Dr Darryl Fry
Dr Peter Ganly
Dr Ashley Garrill
Associate Professor Richard Gearly
Dr Susan Gee
Professor Peter George
Dr Shayne Gooch
Dr Matthew Grayling
Dr Jo Gullam
Dr Gavin Harris
Mr Charles Hawes

Dr Michael Hlavac
Professor Gary Hooper
Dr Ben Hudson
Dr Ruth Hughes
Dr Jenny Jordan
Mr Paul Kelly
Professor Martin Kennedy
Associate Professor Ross Kennedy
Associate Professor Peter Larson
Dr Michael Lever
Ms Ramai Lord
Dr Helen Lunt
Dr Michael MacAskill
Associate Professor Dee Mangin
Ms Pip Mason
Mr Christopher McEntyre
Dr Virginia McIntosh
Dr Tracy Melzer
Mr Grant Moore
Dr Stephanie Moor
Ms Helen Morrin
Dr Hilda Mulligan
Ms Olivia Paku
Dr Suetonia Palmer
Ms Leigh Parsons
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Professor Mark Richards
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4. Summer Studentship Reports

Georgina Allison

The efficacy of home based non-invasive mechanical ventilation in patients with obesity hypoventilation syndrome

Supervisors: Mr Paul Kelly, Ms Sally Powell, Dr Michael Hlavac
Sponsor: Planning & Funding, Canterbury District Health Board

Background:
Obesity Hypoventilation Syndrome (OHS) is a condition defined by being obese (having a body mass index >30) and not breathing enough, therefore retaining carbon dioxide to a partial pressure in the blood greater than 45mmHg. OHS can lead to many problems including headaches, high blood pressure, chest pain and heart failure.

The ventilation disorder is exacerbated during sleep, when their breathing muscles relax the weight on the upper airway causes airway collapses. The solution lies in a machine which delivers a positive pressure of air to keep the airways open throughout the night. This is delivered through a tightly sealed mask which surrounds the nose or the nose and the mouth. Patients normally begin with a machine that delivers a continuous pressure of air (CPAP), but if they cannot ventilate adequately with CPAP they are shifted to BiPAP, a machine which delivers two pressures of air. There is a higher pressure during inspiration and a lower pressure during expiration.

The rise in obesity is fuelling the rise in OHS, in the CDHB service alone there are 77 patients with OHS, treated with BiPAP. Given the resources involved in the set up and maintenance of therapy in this group, it is important to assess the effectiveness of the current therapy.

Aims:
There are three main research questions to address.

1. Do patients with OHS meet BiPAP compliance expectations?
2. Is long term therapy an effective treatment modality and does it improve subjective symptoms?
3. What is the cost effectiveness of treatment in this group?

Method:
39 patients with OHS in Canterbury were reviewed during their annual BiPAP audit clinic. Mass, height, neck circumference, blood pressure, and other parameters were measured. Participants had a blood test and a lung function test, overnight sleep study, and completed a questionnaire to assess daytime sleepiness. The BiPAP machines were serviced, and data recording compliance was downloaded. Pre-BiPAP data was then compared with data from the present day. A clinical records search was undertaken looking for total admissions, and total relevant hospital admissions two years before and two years after commencing BiPAP.

Results:
39 patients were reviewed (24 males, 15 females), with an average age of 57 and body mass index (BMI) of 46.7 kg.m⁻².

1. Compliance data was retrieved from 36 patients. Mean BiPAP usage as a percentage of days analysed was 90.4%, ranging from 8.6-100. BiPAP was used for an average of 5.8 hours per night. 81% of patients meet CDHB compliance expectations for number of nights used.

2. The overnight sleep study data showed great improvements compared to before BiPAP. Blood oxygen levels were significantly higher during the night. The average percentage time spent with oxygen levels below 90% saturation reduced from 82.2% to 26.3%. Analysis of arterial blood gas during the day showed a significant improvement in oxygen and carbon dioxide levels. Mean carbon dioxide pressures in the blood dropped from 61.1 to 46.3mmHg. Mean oxygen pressures increased from 53.3 to 65.3mmHg. Subjective improvements were also seen through a reduction in the mean Epworth Sleepiness Score (ESS) from 11 to 7. Mean BMI also showed a significant reduction from 47.7 kg m⁻² to 45.1.
3. When comparing admissions of 38 patients two years before BiPAP initiation with two years after; total days spent in hospital reduced from 496 to 275 days. Relevant OHS related admissions reduced from a total of 140 days to 55 days.

**Conclusion:**
The majority of the patients met compliance expectations. The improvements in objective measures (arterial blood gas and overnight sleep studies) were highly significant. They showed that oxygen levels were higher and carbon dioxide levels were lower. This shows that ventilation has improved while on BiPAP. This alone serves as evidence that the BiPAP therapy is an effective treatment modality. The positive trend mirrors the subjective improvements in daytime sleepiness. In conclusion, patients are mostly complying with therapy, they are showing significant clinical improvements, and a reduction in subjective sleepiness. Additionally the study has shown that BiPAP therapy is a cost effective treatment given that it reduces the total number of bed days in hospital.
Jayden Ball  
Validation of Smoking Cessation Advice Recorded in Hospital Discharge Summaries  

Supervisors:  
Associate Professor Lutz Beckert, Ms Vivien Daley, Ms Sue Stevenson  

Sponsor:  
Planning & Funding, Canterbury District Health Board  

Background:  Smoking, despite being proven sixty-two years ago to be a cause of lung cancer by Sir Richard Doll is still prevalent within the New Zealand population with 1 in 5 adults identifying as current smokers. In late 2011, the Canterbury District Health Board introduced a new compulsory field into the hospital discharge summary to record the smoking status of each patient and whether smoking cessation advice was given. The target is that a “brief intervention is to be given to 95% of all smokers”. This field must be completed before the discharge summary can be released. A concern has been raised that this field was being marked as ‘advice -given’ while no evidence of this advice was mentioned in the medical notes.  

Aim:  The first aim of this study was to validate the discharge summary. We explored if “advice given” was an over-estimation or under-estimation of the true events. The second aim of this study was to identify ‘roadblocks’ stopping departments in reaching the health target of 95% coverage of receiving advice.  

Method:  
For aim one we searched the database of the CDHB for discrepancies in their record. Our study groups were patients admitted and coded as smokers. Our target group was patients, who had ‘advice given’ ticked on their discharge summary and no evidence documented in their clinical notes. Our control group was patient who had ‘advice given’ ticked and evidence of this advice documented in the clinical notes. The control group was matched by admission data, age and department to the study group. We called patients in each group to verify whether advice was given or not. For aim two we interviewed ward staff on wards that had not consistently achieved the health target: nurses, senior and junior doctors, allied health professionals and the ward clerks to gain an understanding of ‘roadblocks’ in smoking cessation advice given.  

Results:  Of 62144 patients admitted in 2012, 7750 were identified as smokers. In a total of 241 admissions (3.61%) ‘advice given’ was ticked in the discharge summary and no documentation was apparent in the clinical notes. We managed to reach 60 of these patients by telephone and 59 confirmed they were smokers at the time of admission. Of these 59 smokers 45 (76.3%) recalled receiving cessation advice and 27 (60%) felt the advice was helpful at the time. The control group contained 35 of 5102 (74.34%) patients where the discharge summary and the clinical records both agreed that smoking cessation advice was given. Of the 35 smokers 31 (88.6%) recalled receiving cessation advice and 15 (48.4%) felt the advice was helpful at the time.  

At the time of interview 44 of 59 patients of the target group were still smoking indicating a decrease of 25.4%. Of those who quit, 12 engaged with an outside support, with GP’s accounting for 75% and Quitline the remaining 25%. At the time of interview 29 of 35 patients in the control group were still smoking indicating a decrease of 17.1%. Of those who quit 3 also engaged with an outside support, with GP’s accounting for 2 patients (50%) and Quitline 2 patients (50%).  

Staff interviewed were generally aware of the health target (13 of 17, 76.5%) but only 11 of 17 (64.7%) were consciously aware that their ward was falling behind in the target. All Senior Medical Officers (SMO), Clinical Nurse Specialists and Charge Nurses were all aware of the performance of their ward. Only 14 of 17 (82.35%) regularly offered patients brief cessation advice, and only 12 of 17 (70.58%) regularly assessed the smoking status of patients. Allied Health workers and ward clerks didn’t feel empowered to assess smoking status or offer brief cessation advice. Many believed that the key reasons as to why the health target is not being met included recurrence of patients who had been assessed at their previous admission. The second reason was that time and documentation were an issue in that either there was not enough time with the patient to properly assess and offer an intervention, or that there was not enough time to accurately document the intervention they did offer, stating that they felt they had to document the intervention in its entirety. Opinions were divided as to whether the advice was being given accurately.  

Conclusions:  Our research validates the information recorded in the discharge summary as accurate. It shows a good effect of smoking cessation advice on stopping smoking. Reassurance about the documentation may empower more staff to engage in giving smoking cessation advice.
Angela Ballinger
Calcimimetic agents to improve clinical outcomes in people with chronic kidney disease: Meta-analysis of randomised, controlled trials

Supervisor: Dr Suetonia Palmer
Sponsor: Canterbury Medical Research Foundation

Kidney disease is increasing in prevalence and people with chronic kidney disease are almost three times more likely to suffer from a sudden heart attack than the general population. In people with severe kidney disease, the kidneys do not remove toxins sufficiently, resulting in a build up of toxins that have harmful effects on the body. The body reacts to this build up using a complex feedback system to counteract these harmful effects. Unfortunately, this feedback system causes accumulation of calcium that gets deposited on blood vessels making them harder and narrower. This accelerates risks of stroke or heart attack. Currently there are no drugs proven to prolong survival or prevent heart disease for people who have severely damaged kidney function. Drugs that work in the general population such as aspirin and statins are less effective for people with kidney disease because the processes that cause vascular damage are different. Cinacalcet is a new drug that can trick the body into thinking calcium levels are normal. By doing this, less calcium is laid down in the blood vessels. The hope is that cinacalcet might become the first drug to decrease the risk of heart disease in people who have advanced chronic kidney disease.

This project summarises the existing evidence in all available research trials that test the effects of cinacalcet in patients with chronic kidney disease using the methods of systematic review and meta-analysis. A systematic review is a complete literature review that brings together all the available evidence on a particular research question. A meta-analysis is a statistical method to combine the treatment effects of all studies into a single result.

Using systematic searching of the Cochrane and EMBASE databases in July 2012, we identified eighteen studies (comprising 7466 participants) that could be included in the systematic review. These studies compared cinacalcet plus standard therapy against placebo or no treatment plus standard therapy. Standard therapy generally included other treatments to prevent arterial disease in people with chronic kidney disease.

Overall, the results show that cinacalcet has little or no effect on the risk of death for people with advanced kidney disease but may prevent a small number of patients needing surgery. Side-effects including calcium abnormalities and nausea and vomiting were common. The evidence for people with advanced kidney disease treated with dialysis is currently high quality and reliable, suggesting new trials in the future are unlikely to change these results. Information for people with less severe kidney disease and those who have received a kidney transplant is sparse and new trials may help us understand the effects of cinacalcet treatment in these patients.
Annelise Basevi
Improving our clinical systems and care to help our patients have a better experience

Supervisors: Dr Andrew Richardson, Professor Les Toop, Dr Paul Abernethy

Sponsor: Pegasus Health (Charitable) Ltd

The 24 hour surgery was created 25 years ago as an after-hours service for General Practitioners (GPs). Since then it has grown to provide extra services for more complex patients. It is the only place in Christchurch, apart from the Emergency Department, that is able to provide 24 hour medical care, 7 days a week. There are over 320 GPs in Christchurch who are enrolled with the surgery and recommend the after-hours services. This means there are 380,000 patients that can use the healthcare provided at the 24 Hour Surgery. Patient numbers at the surgery can be very unpredictable which may result in long waiting times. The focus of my summer studentship is working with a project team at the 24 Hour Surgery to try and improve patient flow within the surgery.

Now the 24 Hour Surgery has such a broad range of services, the patients who just need a quick doctor consult arrive at reception mixed together with the patients that need complex consults. These patients are triaged as non-urgent. They spend a long time waiting yet they only need to spend a short amount of time with the doctor. What we are doing is trying to identify patients who will only require a short consult. We will then stream them separately from the other patients arriving at the surgery. This patient stream will be called the “Green Stream”. The focus of the Green Stream will be to try and move these patients in and out of the surgery more quickly.

The Green Stream is made up of a doctor, nurse and healthcare assistant (HCA) working as a team. Patients arrive at reception and are then seen by the triage nurse. Patients likely to have a quick consult with the doctor are put into the Green Stream by the nurse. The patients are then seen by a HCA who does some basic tests before seeing the Green Stream doctor.

The Green Stream pilot began on Saturday the 24th of November and has been run every weekend since. It was also run most days over the Christmas and New Year period. Data was collected and analysed each week allowing us to make changes as needed.

Overall the project was a success. The average time in facility for a Green Stream patient was 35 minutes. The feedback collected from staff and patients was generally positive. The total time in facility for all patients at the 24 hour surgery was reduced by 10% during the time the project was running. This suggests that all patients, not just those in the Green Stream, had shorter waiting times because of an improvement in patient flow.

The results of this study show that the Green Stream is a success however it has been suggested that that the full potential of the project has not been reached. Further analysis of the Green Stream is recommended before the 24 Hour Surgery permanently adopts the project as a tool to improve patient flow.
Betaine and secondary events in an acute coronary syndrome cohort: 4 year follow up

Supervisors: Professor Steven Chambers, Professor Peter George, Dr Jo Young, Dr Michael Lever, Dr Sandy Slow, Dr Jane Elmslie, Associate Professor Richard Troughton, Professor Mark Richards, Professor Chris Frampton

Sponsor: Canterbury Health Laboratories

Betaine is an essential chemical found in the human body. We get betaine from our diet, particularly from foods such as wheat products, beetroot and sugar beets or we can synthesize it from another nutrient we eat called choline, which is found in high levels in liver, eggs and wheat products. Betaine is accumulated to high levels in body tissues where it acts to maintain the fluid balance inside cells, preventing them from damage when there are changes in the saltiness of the surrounding fluid. Betaine also takes part in an important metabolic reaction where it is used to convert the chemical homocysteine into methionine. The breakdown product of betaine from this reaction is dimethylglycine. Homocysteine is a naturally occurring product in the body but if the levels in our blood get too high, because we are unable to remove it, then it can cause damage to blood vessels and lead to such events as blood clots, heart attacks and strokes. While most people’s bodies are very good at keeping betaine levels constant, some people may lose a lot of betaine in their urine. The people recorded with having extremely high betaine excretion include about a quarter of diabetics, a tenth of those with high fat and cholesterol levels and a fifth of those with a disorder called the metabolic syndrome. These people are at a risk of a betaine deficiency, which may have negative effects on their health. Studies have looked at different ways to reduce the levels of homocysteine in the blood but few have investigated the role of betaine, instead choosing to focus on an alternative pathway that uses folate and vitamin B12. Although some of these studies have shown that folate and B12 supplementation is effective for lowering homocysteine, none have shown any effect of supplementation for reducing the presence and consequences of coronary artery disease. The hypothesis we are investigating is that in some people, a betaine deficiency may be to blame for their high homocysteine and poor health.

We aimed to investigate if there is a relationship between blood and urine betaine levels and the risk of coronary events in a population of people with prior cardiovascular disease. In 2012 the paper Betaine and Secondary Events in an Acute Coronary Syndrome Cohort, authored by Michael Lever et al. was published. This study consisted of a group of 531 patients, who had been treated in hospital for angina or a heart attack. Relationships between their blood and urine betaine four months after discharge and the incidence of secondary events during a follow-up time period of two years on average were investigated and reported. The project I undertook is a continuation of this work, where I repeated the analyses with a longer follow-up time (4.5 years), and more secondary events.

In my analyses, I looked at 5 different potential markers for 5 different cardiovascular events. The markers were plasma and urine betaine concentrations, plasma and urine dimethylglycine concentrations and plasma homocysteine concentration. The events we recorded over the follow-up period included death, secondary heart attack, heart failure, unstable angina and all admissions to hospital for a cardiovascular disease. Statistical analyses were undertaken to find out whether the time taken for a given secondary event to occur was significantly shorter for those in either the top or bottom 20% for each of the markers, compared with the middle 60%.

The result produced in this study corroborated the earlier evidence that plasma betaine was a viable predictor of cardiovascular health. Once again, the data gave evidence that both high and low levels of plasma betaine indicated a greater level of risk of a secondary event; however, more events over a longer follow-up period also allowed us to conclude that the presence of type 2 diabetes plays an important role, where those without diabetes showed worse outcomes with low plasma betaine while those with diabetes showed worse outcomes with high plasma betaine.

As could be expected, our results were consistent with prior findings in regards to homocysteine, where those in the top 20% of homocysteine levels had a dramatically increased risk of a serious event. This group had 2.3 times the risk of having a heart attack and 1.9 times the risk of both getting heart failure and of having an earlier death, when compared to those with homocysteine levels in the middle 60%. In addition, in accordance with the previous study, there was also evidence that the top 20% of the population in terms of plasma dimethylglycine was also at a higher risk of some events, such as having 1.6 times the risk of having a heart attack compared to those with plasma dimethylglycine levels in the middle 60%. Unfortunately neither of the urine measurements proved to be a useful determinant of coronary risk.
The fact that the results of the current paper support the previously drawn conclusions is promising. The current thought behind why plasma betaine is a good marker for coronary disease is that both high and low levels of betaine in the blood are representative of low levels in the tissue, either because large amounts of betaine are leaking from the tissue or because poor dietary choices or defective metabolism are causing low betaine stores in the body. This theory may also explain the differences between diabetics and non-diabetics as disease processes in diabetes could quite probably lead to a decreased retention of betaine in cells in accordance with our finding that high levels of plasma betaine are especially concerning for diabetics.

The evidence for dimethylglycine, betaine's break down product, being associated with negative outcomes is also interesting and one theory is that high levels of this metabolite slow down the action of the enzyme that removes homocysteine, thereby indirectly raising homocysteine levels. Alternatively this may also be explained by the fact that dimethylglycine levels are raised in response to increased homocysteine levels, so it may just reflect the same disease process that leads to raised homocysteine.

Our results have given stronger weight to the theory that betaine insufficiency may play a key role in coronary risk; however, these results do not imply causation. In addition the population studied was a previously at risk one and these results may not generalize to a healthy population. Nevertheless, there is enough evidence here that further investigation should be undertaken into the benefit of betaine supplementation, especially in at-risk populations and those who may be betaine deficient, in the hopes that this might solve the ‘homocysteine controversy’ and succeed in lowering homocysteine while also preventing coronary events.
Heidi Blackburne  
Quantifying the surgical impact factor in colorectal surgery: A pilot study  

Supervisor: Dr Matthew Grayling  
Sponsors: Helen Poole & Ian McDonald Memorial Summer Studentship / Canterbury Medical Research Foundation  

Background:  
Colorectal cancer is a malignant growth which starts in the large bowel and rectum. It can spread beyond the bowel wall to the liver and lungs. The World Health Organisation (WHO) estimates that the Australia/New Zealand region has the highest rates of colorectal cancer (CRC) out of all the regions they monitor. In 2009 alone 2837 people in New Zealand were diagnosed with CRC and in the same time period 1244 people died of the disease.  

Standard curative treatment is primarily surgery with chemotherapy and/or radiation therapy. It is important to understand that this treatment itself has risks associated with it. Everyone has a baseline risk of dying within 30 days, surgery however can temporarily increase this risk, and this amount by which this risk is increased is termed the surgical impact factor. Patients need to be assessed and told of the risks of the surgery in order for them to decide whether this treatment is appropriate. Health professionals need a way of calculating the likelihood of certain outcomes (in this case death from post-operative complications), in order to correctly inform patients and enable them to decide whether to undergo surgery.  

Aim:  
Using the Bi-National Colorectal Cancer Audit database we propose calculating a procedural specific surgical impact factor to use in individualised risk assessments for future patients.  

Methods:  
We selected all the patients in the pre-existing database who had undergone elective (planned) surgery in Christchurch from July 2008 to October 2012. From computer based notes we collected data on co-morbidities specifically, previous heart attacks, strokes, peripheral artery disease, heart failure, and transient ischaemic attacks for each patient, as well as renal function. Patients were said to have the co-morbidity if they had a hospital admission relating it or if the co-morbidity was stated on at least 2 sets of clinical notes. Then using a previously developed calculator based on data collected from the UK census we calculated their risk of death within 30 days without surgery. We then compared the calculated risk of death within 30 days without surgery with the rate of mortality in the patients undergoing surgery.  

Results:  
In the chosen time frame there were 563 patients who we included in our study after non-elective surgery and patients with incomplete notes were excluded. 7 of these patients died within 30-days of surgery. The average estimated “without surgery” 30-day mortality risk was 0.399%. The actual post-operative 30-day mortality rate was 1.24%, this gives us a surgical impact factor of 3.11.  

Discussion:  
The surgical impact factor found in this study needs to be verified with a larger study. Due to the complexity of the calculations the researchers were unable to calculate the number of patients needed to get the most accurate number. However the researchers have agreed that the current number of participants is too small. Further larger studies may also be able to separate rectal cancers from the other cancers giving two surgical impact factors.  

Getting a bigger sample set involves recruiting patients from outside the Christchurch area and may lead to the development of a hospital impact factor. This hospital impact factor may take into account levels of before, during and after surgery care, as well as staff experience and facilities available as these can impact on patients’ mortality rates. A larger data set may also allow for identification of high risk patients. Indicators for high risk patients may include older patients and those with more co-morbidities, it is likely that the cut off points will differ depending on gender as males had higher risks than females with the same age and co-morbidities. High risk patients may then be referred for further testing to judge their suitability for surgery. This testing may include looking at lung function and exercise tolerance. High risk patients that undergo surgery may need higher levels of during and after surgery care, identifying patients and planning for it may lead to better outcomes. Identifying a high risk patient’s risk of dying of non-cancer causes may help the patient’s understanding of the true benefit of undergoing surgery. This calculator has previously been used to design...
a decision aid for patients undergoing elective abdominal aortic aneurysm (AAA) repairs, and with further research this decision aid could be used for patient’s deciding on surgical treatment for CRC.

Low risk patients are the least likely to benefit from this surgical impact factor. Younger and fitter patients have a small without surgery 30 day mortality and a large surgical impact factor would still result in a negligible risk. The life-limiting process in these patients is more likely to be the CRC and therefore the vast majority of the time they will choose curative surgery. This study included the younger age groups in order to increase the study population; however due to the lack of benefit and relevance follow on studies may look to only include older patients.

None of our study underwent lung function and exercise testing. Lung function and exercise tolerance were therefore not factored into our without surgery calculations, however previous studies using this calculator have also used individual patient values gained from this testing. Given the number of patients who undergo surgery for CRC, and the mortality rate in Christchurch it is not economical to put every patient through lung function and exercise testing. Using a select group of higher risk patients it may be possible to get a more accurate without surgery calculation and therefore a more accurate surgical impact factor.

This study also serves to remind clinicians that all patients will have a risk of dying within 30 days with and without surgery. Care must be taken not to dismiss other health conditions that are also potentially life limiting as chemotherapy and radiation therapy alone may be enough to prevent CRC symptoms without exposing them to the risks associated with surgery.

**Conclusion:**
Using the mean we were able to get a surgical impact factor of 3.11. There was however a small sample size in this study and more research using a larger number of patients may be able verify or correct this. More research may also lead to the identification of higher risk groups and the separation of rectal cancers from the rest of the CRC. Including more hospitals not only allows for a bigger sample size and a more accurate surgical impact factor but it also may raise the idea of a hospital impact factor.
Analyses of the pre and post arthroplasty Oxford 12 outcome scores in patients undergoing hip and knee replacement

Supervisors: Professor Alastair Rothwell, Professor Gary Hooper, Professor Chris Frampton

Sponsors: University of Otago Health Sciences Divisional Summer Scholarships

Background: Total hip arthroplasty (THA, hip joint replacement) and total knee arthroplasty (TKA, knee joint replacement) are procedures that improve quality of life and decrease pain in patients with end-stage joint disease. An aging population combined with technology allowing arthroplasty in younger and older patients has greatly increased the population of patients requiring joint replacement. To understand how best to meet these demands, large national registries have been established in several countries. These allow the long-term surveillance and ultimately improvement of arthroplasty service delivery. Formed in 1998, the New Zealand Joint Registry (NZJR) now has an immense amount of information, consistently capturing data from greater than 96% of joint replacements across the country. Oxford scores and ASA classes (described below), and information about revision surgeries (procedures undertaken when joint replacements fail) make up some of the data available for the 165,737 registered joint replacements in the NZJR at the end of 2011.

ASA Background: The American Society of Anesthesiologists (ASA) physical rating system, performed by an anaesthetist, divides patients into one of 5 classes based on their systemic health. While the system has been criticised for its subjective nature, which leads to poor inter-observer reliability, the ASA is still a useful and widely used tool.

Oxford 12 Background: Patient Reported Outcome Measures (PROMs) are standardised and internationally validated questionnaires that help patients to communicate their level of function or disability. The Oxford Hip Score and the Oxford Knee Score are twelve item PROMs that were developed to assess function after hip and knee arthroplasty. To achieve a 20% sample of NZJR patients, a random selection of 28% of THA and TKA patients are sent an Oxford questionnaire six months after surgery. The scores from each question in the PROM are added, giving a total score of 0 to 48; a higher score reflects higher function. Previous analysis of the 20% sample has shown that low Oxford 12 six month scores are associated with a higher risk of early revision (defined as revision within two years of the primary procedure). Higher six month Oxford 12 scores are predictive of good medium-term outcome. While the NZJR sample is randomly selected, it is thus far unknown how the response rate affects this randomisation. Without this knowledge, we do not know if the Oxford 12 associations with revision risk and medium-term function also apply to the NZJR patient base. To assess this, we first looked at the Burwood patient database. The Burwood cohort has two distinct advantages over the wider NZJR. Firstly, all Burwood patients are given a pre-surgery Oxford 12 questionnaire. Secondly, all patients are sent six month Oxford questionnaires, with a response rate of about 95%. The excellent response rate allows the Burwood group to act as a suitable comparison for researching the Oxford 12 associations.

Statistical methods: Statistical analysis was performed with statistical program SPSS version 18, Microsoft Excel, and an online Chi-square calculator. T-tests; Chi-square tests and Mann-Whitney U tests were used, as appropriate. A p-value of less than 0.05 was deemed statistically significant.

Burwood Database: There were 719 patients in the Burwood THA group; 3229 in the NZJR 20% THA group (including 1304 were public patients); 494 in the Burwood TKA group; and 3177 in the NZJR 20% group (including 1209 public patients). Burwood THA and TKA patient groups showed significant differences to their respective 20% NZJR group in key areas of age, gender, ASA, and primary diagnosis. The NZJR group includes public and private hospitals; the Burwood group only public. Assuming that this could account for some of the difference between groups, we also performed analyses with only public patients. This removed many of the statistically significant differences. Notable, however, were the differences in distribution of ASA classes, evident in hip and knee analyses. Burwood patients had higher ASA classes, representing higher levels of systemic disease. This is of particular interest, in light of recent NZJR research that linked higher ASA classes with early mortality, early revision, and worse functional outcome. Part of the ASA difference is likely to be a result of inter-observer variation, described above. Differences in arthroplasty eligibility criteria may also contribute to the difference.

Oxford 12 Scores: Mean pre-surgery Oxford 12 scores were 17.7 for Burwood THA and 19.5 for Burwood TKA. Six month scores for THA were 39.7 for Burwood patients; compared to 40.1 for NZJR 20%. The public-only NZJR patients
actually had a slightly lower average Oxford 12 score, indicating Burwood patients have better function six months after surgery. Six month scores for TKA were 35.8 for Burwood patients; with significantly higher scores for NZJR 20% (38.2) and NZJR 20% public groups (37.0), probably related to the small age difference in these groups.

**Revisions:** Access to Burwood patient notes allowed descriptive analysis of reasons for revision. Revision was uncommon in the Burwood patient group. Only six THA patients and four TKA patients in our analysis required a revision; of these, only three THA patients and a single TKA patient were early revisions. We compared the reasons for revision in patient notes stored at Burwood Hospital to the reasons stated on the database. THA patient notes revealed six different reasons for revision, matching the database. All TKA patients had pain cited as a reason, three also had other reasons. There was almost complete agreement between TKA notes and the database.

**NZJR 20% and 80%:** Insufficient Burwood revisions meant that we could not calculate the predictive value of the pre-surgical Oxford score. Additionally, underlying differences between Burwood and NZJR patients meant the Burwood database was also an unsuitable comparison group. Our next step was to investigate how well the 20% sample represented the NZJR patient base. We compared the 20% with Oxford scores to the rest of the NZJR across a wider time period. There were 49,640 THA patients and 35,346 TKA patients in the 80% groups; and 12,390 THA and 11,630 TKA in the 20% samples. The 20% sample of THA was 0.3 years younger than the 80% THA group, while TKA patients in the 20% sample were 0.2 years older than the 80% TKA sample. Both of these age differences were statistically significant, a function of very large sample sizes, but are too small to be clinically relevant. Hip and knee analysis showed that the 20% groups had lower than expected numbers of women and publicly funded procedures, with statistically different distributions of each. Because the Oxford 12 scores are sent out to a random sample, any statistical difference between the 20% and 80% groups represent differences in questionnaire return rates.

**Summary:** We investigated data from total hip arthroplasty and total knee arthroplasty patients in Burwood and New Zealand Joint Registry databases. We found differences between Burwood patients and the 20% of NZJR patients for whom an Oxford 12 PROM score was available. While the differences appeared to be largely due to the privately funded procedures in the NZJR databases, removal of these patients showed that differences in ASA class remained. Unfortunately there were too few revisions in the Burwood database to assess the predictive power of Oxford 12 scores for this population. Analysis of the wider NZJR group found that the 20% was only very slightly different to the rest of the NZJR patients. This shows the associations between Oxford 12 scores with early revision and with medium-term function can be applied to all New Zealand patients undergoing total hip or knee replacement. That being said, we found that males and privately funded patients were somewhat more likely to return the Oxford 12 PROMs. Further research could therefore analyse reasons for this discrepancy; how to address these differences; and how Oxford 12 associations differ in NZJR subpopulations.
Jonathan Bong

Measurement and motion analysis of knee function in patients following anterior cruciate ligament (ACL) injury

Supervisors: Professor Gary Hooper, Dr Shayne Gooch, Dr Tim Woodfield
Sponsor: Canterbury Orthopaedic Services Trust

The anterior cruciate ligament (ACL) injury is one of the most common causes of anterior knee instability and the majority of ACL injuries are sports related. The ACL consists of two bundles, the anteromedial and posterolateral bundles. The anteromedial and posterolateral bundles together restrain forward movement of the tibia relative to the femur; they also have a secondary role in stabilizing the knee and preventing excessive rotation. A complete rupture of the ACL can lead to recurrent knee instability, meniscal tears, and articular cartilage degeneration. The ACL does not heal once it is torn and surgical reconstruction is the standard treatment.

Conventional ACL reconstruction techniques have been primarily focused on restoring the static anterior-posterior (AP) translation stability while the native ACL constrains not only AP translation but also internal-external rotation of the tibia. There have been marked differences particularly in the type of rotational changes following ACL reconstruction surgery reported in the literature. Accordingly, several studies have shown that the motion or kinematics of the ACL reconstructed knee remains abnormal when compared to the contralateral side or when compared to healthy control knees. In addition, it also has been reported that a significant portion of patients with ACL reconstruction do not return to their previous level of sporting activity. Hence although ACL reconstruction results in good short term results, recent postoperative studies suggest that the ability of ACL reconstruction to protect long-term joint health may be limited.

This is significant because if the normal function of the ACL is not fully restored in the ACL deficient knee, it can lead to a change in the distribution of load in the reconstructed knee and this has been correlated to the early development of osteoarthritis. While there are many factors that may contribute to the development of osteoarthritis following ACL injury or reconstruction, abnormal rotatory kinematics is believed to have an important role in contributing to joint degeneration. Given the importance of the ACL in stabilizing knee motion, there is a need for understanding how knee motion is affected following ACL reconstruction.

Measurements of anterior-posterior (AP) laxity are frequently used to document an ACL injury and to evaluate the success of ACL reconstruction. Several non-invasive devices, or arthrometers, have been developed that attach externally to the lower leg to objectively assess knee laxity. Most of these arthrometers provide a measure of tibial displacement relative to the femur; however the effect on the rotatory movement of the knee has yet to be investigated.

Therefore, in the present study, our aim was to design and build a non-invasive measurement device that allows us to objectively measure and identify the differences in tibial displacement as well as rotation between ACL deficient knees (pre and post-surgery) and healthy knees when a perpendicular anterior load, at the level of the tibial tuberosity is applied to the upper part of the tibia.

The test rig was designed to allow the flexion of the knee, as well as tibial rotation to be controlled while the anterior load is applied to the knee. The amount of anterior displacement and tibial rotation will be then quantified and compared to allow a better understanding of knee kinematics following ACL reconstructed surgery. The movement of the knee is to be measured using an electromagnetic device (FASTRAK, Polhemus, Colchester Vt) which measures movement in 6 degrees of freedom and allows the accurately quantification of the static movement of the knee.

The data collected using the device can then be used to quantify the AP and rotational stability of the knee following ACL reconstructive surgery and used clinically to evaluate the treatment or care following ACL reconstructive surgery.
Dietary betaine and choline intakes in patients with type 2 diabetes participating in a weight loss study

Melissa Butt

Supervisors: Dr Jane Elmslie, Dr Michael Lever, Dr Sandy Slow, Professor Peter George, Professor Steven Chambers

Sponsors: Guardian Trust / R G Bell Charitable Trust and the Diabetes Training & Research Trust

Dietary management of diabetes is essential to avoid both short (e.g. hyperglycemia) and long term (e.g. diabetic neuropathy) complications. Two essential nutrients found in the diet, betaine and choline, have recently become the focus of researchers, who wish to ascertain whether diabetics have a greater requirement for these nutrients than non diabetic individuals.

A deficiency in either Betaine or choline can result in liver damage, similar to that induced by severe alcoholism. The combination of low betaine intake and high choline intake has been associated with an increased risk of heart disease and stroke.

Both choline and betaine are found in our diet. Once consumed, choline can be transformed into betaine by the liver. Rich dietary sources of choline include eggs, liver, milk and peanuts. Foods rich in betaine comprise of beetroot, spinach, silver beet/ Swiss chard and shellfish.

Research has found that diabetic individuals lose more betaine in the urine than non-diabetic individuals. This suggests diabetics may need to consume more betaine and possibly choline in their diet to match the extra loses in urine and avoid deficiency.

To date, research has focused on the intake of choline or betaine in non-diabetics. Hence our study aimed to determine the average daily consumption of betaine and choline in diabetic individuals.

We analysed the diet of 158 adults with type 2 diabetes mellitus. The average amount of choline consumed daily by our diabetic population was 310mg/d (± 105mg/d); similar to that found in previous studies of non-diabetic individuals. The calculated amount in all studies is less than recommended for optimal liver function. However, these studies, including our own have probably underestimated the true value, due to currently limited dietary data. Therefore, the true value may be much higher and our study sample is unlikely to be at risk of liver damage.

Unfortunately we have not been able to calculate the betaine intakes of the people in our study yet. The software package we used to compute the study participants’ choline and betaine intakes needs to be modified to display the betaine values. They are in there we just can’t see them yet.

From the wealth of research to date, we can conclude that if dietary modification is necessary in this population, then increasing betaine, not choline intake will be the safest way to increase the body’s essential betaine levels.

Adding more betaine to the diet of diabetics could occur without negatively affecting blood glucose control. Wholegrains, for example, are high in Betaine and have a low glycaemic index, meaning they will increase betaine intake without causing a large rise and fall in blood sugar levels. For diabetics wholegrain foods already hold many benefits, so this is yet another reason to encourage wholegrain choices over more refined carbohydrates.

Wholegrains, green leafy vegetables and fish are all rich sources of betaine and key components of the Mediterranean diet, a diet which has long been praised for its heart healthy properties. In comparison a western diet, high in processed foods such as pizza with high concentrations of sugar and fat, contains less betaine and more choline than that of the Mediterranean dietary pattern.

A very low carbohydrate diet, such as the Atkins diet contains 2.5 times more choline than a typical low fat diet and less betaine containing foods. Remembering high choline alongside insufficient betaine status increases the risk for CVD, the Atkins diet would not be a suitable diet for betaine deficient diabetics, especially for overweight people with diabetes, who already have an increased risk of CVD.
For some people with diabetes, particularly those already making dietary alterations, betaine supplements may be a more realistic way of increasing betaine intake without having to make more dietary changes. Research into the use of supplements is on-going.

In conclusion, choline intakes in people with diabetes are likely to be similar to those in the general population. However, further research into the betaine intakes in people with diabetes is necessary to establish whether dietary modification and/or supplementation of betaine is beneficial for people with diabetes.
Matthew Chamberlain
Psychological impact of September 2010 and subsequent earthquakes on Christchurch general practice patients

Supervisors: Associate Professor Dee Mangin, Ms Cerina Altenburg
Sponsor: The Royal New Zealand College of General Practitioners

Introduction:
The Canterbury earthquakes caused injury, death and damage to homes and workplaces. Most Cantabrians had a normal stress response but recovered with time and support. A smaller group experienced more distress for longer and saw mental health workers. High distress levels can be shown by a high score on a Kessler questionnaire. There are risk factors that might make some people have higher Kessler scores following natural disasters. So far there has been little research into this area, especially on natural disasters with an element of repetition, such as aftershocks.

Aims:
1. To describe the effect of the Canterbury earthquakes on the mental health of people seeing general practitioners.
2. To look at links between patient age, sex, ethnicity and other possible risk factors and levels of distress.
3. To see any changes in distress levels over time.
4. To compare our findings with worldwide research on natural disasters, especially those with an element of repetition.

Method:
Following the first earthquake in September 2010 a review of natural disaster research was done. This review identified five key risk factors for mental illness following natural disasters. These include past mental illness, past trauma, social support, other stressors and seeing death or injury. Information on these factors was collected by trained counsellors who saw people with earthquake stress. 1476 of the patient assessments were analysed and collected in a database. To check reliability 150 of the assessments were analysed a second time by other researchers.

Results:
The study is still in progress, but we have noticed several things so far. Distress levels were similar across genders and ages. Pacific Island and Asian people seemed to have distress levels one or two points higher than others. People from the Southern suburbs, including Sumner and Lyttleton had lower Kessler scores. If someone had none of the five risk factors their distress levels were around 25. If a person had four risk factors their distress levels averaged 34.

Conclusion:
Because the study is still in progress our conclusions are not definitive. It should also be noted that collecting data was difficult due to the chaos following the earthquake. But based on the study so far risk factors like poor social support may play a more important role than patient factors like age. However a big part of people’s distress could not be explained by these factors. This highlights the need for a model that takes many risk factors into account. This knowledge could be useful to guide the mental health response in future disasters.
Thomas Chima

**Randomised controlled trial of a consultation-based decision aid for hip fracture prevention**

*Supervisors:* Dr Ben Hudson, Ms Pip Mason

*Sponsor:* Pegasus Health (Charitable) Ltd

**Background:**
My project builds upon a summer studentship from last year. The student created and did a small trial on a decision aid (DA) for patients to help them decide whether to take medication that prevents hip fractures. A DA is used when it is difficult for patients to make a decision on the treatment options available.

The difficulty is in helping patients to understand the pros and cons of the treatment, a range of drugs called bisphosphonates. Hip fractures lower a patient’s quality of life and the risk of fracture may be reduced by using bisphosphonates. However the risk reduced by these drugs is typically small and they cause side effects. So the problem is that patients must weigh up the benefits of lowering the already low risk, with the cons of the potential side effects.

Before this decision aid can be used in practice, we need to find out how the DA will affect general practitioners (GPs) in the way they prescribe bisphosphonates.

**Aim:**
To trial the use of the DA with GPs to determine how the presentation of fracture risk in either written or visual form affects the likelihood of GPs’ recommending bisphosphonates.

**Method:**
GPs were sent questionnaires in which three clinical cases were presented. The cases included a patient at low, medium and high risk of hip fracture. For each case GPs were asked to show the strength of their recommendation for the patient to take a bisphosphonate. GPs were randomised to receive either a control or intervention questionnaire. In the control questionnaire fracture risk and its reduction with treatment was shown in a written format. The intervention questionnaire showed fracture risk and its reduction with treatment visually using a grid of 1000 squares each representing a person. Some demographic and professional details were also recorded.

**Results:**
720 GPs from the Christchurch and Auckland areas were randomised and sent the questionnaires and 179 were returned (response rate 24.9%). In all three cases GPs who received the intervention questionnaire were less likely to prescribe bisphosphonates than those who received the control questionnaire, but only in Case 2 was this difference statistically significant. Case 1 (low fracture risk) had an 18% prescription rate for controls and a 10% for interventions. Case 2 (medium risk) had a 52% prescription rate for controls and 35% for interventions. Case 3 (high risk) had a prescription rate of 81% for controls and 69% for interventions.

**Conclusion:**
GPs presented with fracture risk, and its reduction with treatment in a visual format, were less likely to prescribe in a medium fracture risk case. In cases of low and high fracture risk, likelihood of prescribing was lower when risk information was presented visually, but this difference may have been due to chance. DAs that include the visual representation of fracture risk may reduce GPs’ likelihood of prescribing bisphosphonates. This effect on physician behaviour suggests the need for further investigation and should be taken into account when creating DAs.
Haematopoietic stem cell transplants, also known as bone marrow transplants, are commonly employed in the treatment of life-threatening blood disorders such as multiple myeloma or acute leukaemia. In these diseases, the bone marrow mutates, causing a change to the function of the blood cells that it produces. Haematopoietic stem cell transplants (HSCTs) aim to repopulate the bone marrow with normal stem or ‘seeding’ cells from a donor free from disease, resulting in a possible cure for the blood disorder. Donors are often related to the patient, being chosen as they share specific immune-related genes with the patient so that the donor cells do not recognize the host cells as enemies and attack them, and vice versa.

Most patients receive a course of chemotherapy or radiotherapy prior to transplantation, in order to attack the diseased marrow and deplete it. This acts as a way of both treating the underlying disease and making room for the donor marrow to occupy. These therapies often have unpleasant side-effects and can only safely be used in fitter, younger patients, usually less than 40 years old. Older patients and those with other health problems are treated with ‘reduced-intensity conditioned’ (RIC) HSCTs. This procedure involves lessened chemotherapy or radiotherapy prior to transplantation, reducing the toxicity and the risk of harm.

HSCTs may cause ‘graft-versus-host disease’, whereby donor immune cells attack host tissues. This can cause significant illness and even death, but may also promote a ‘graft-versus-disease’ effect, whereby the donor cells aid in the treatment of the disorder by destroying the diseased cells, potentially being curative. In RIC transplants, this effect is relied upon, for it allows donor cells to populate the bone marrow space without the marrow needing to be destroyed by prior therapy.

Christchurch Hospital has been performing RIC and standard-conditioned transplants for the past 12 years. We investigated the outcomes of the patients involved in these procedures over this period until July 2012, in order to see if the trends were consistent between the two groups and if they were comparable to international data.

All patients who received these procedures from January 2000 to July 2012 were recognized through existing computerised databases. Additional information was obtained from clinical records, including patient age at time of transplant, main diagnosis requiring treatment, additional health issues, gender of recipient and donor, patient place of residence, current patient disease status, when patient was last known to be alive, cause of death (if applicable), if there were any transplant-related illnesses such as graft-versus-host disease, how long they survived post-transplant and if their disease had returned or progressed post-transplant. This data were then compared between the two groups (one being RIC and the other standard-conditioned), and assessed to determine whether there were any major discrepancies. If there were differences, we wanted to ascertain whether one procedure might be better, safer or more successful than the other. The collected data was also compared with data collected in other international transplant centres from similar studies. This comparison was to establish whether Christchurch Hospital’s procedures and standard of care are equivalent to those observed elsewhere, and to judge if we are keeping up with international trends.

The results showed that there were few major differences between the outcomes of RIC and standard-conditioned HSCTs performed at Christchurch Hospital over the 12 year period. Outcomes were comparable to those observed internationally. As expected, the main differences between the make-ups of the two groups were that RIC patients were around 20 years older than those receiving standard-conditioned procedures, and RIC patients often had more ‘other’ health problems. In both groups age of patient at time of treatment did, however, have a significant role in overall survival time post-transplant, with 55% of patients older than the median age for their procedure surviving to 2 years post-transplant, compared with 70% of those younger than median age. Patients deemed to be ‘low-risk’ pre-transplant, with respect to patient frailty and other health issues, had better survival outcomes than those categorized as ‘high-risk’. Similarly, patients who had a shorter projected survival, with respect to age, diagnosis, disease status pre-transplant, and donor/recipient matching, had poorer outcomes compared to those with a longer projected survival post-transplant. In both groups, a similar proportion developed graft-versus-host disease with a requirement for treatment. Risk of disease relapse was higher in the RIC group, although death from disease relapse was comparable to the MAC group.
RIC and standard-conditioned HSCTs are both relatively new procedures with little known about their downstream effects and effectiveness. This study will add to the growing knowledge about the outcomes both sooner and later after transplant. Our study confirms that the service provided at Christchurch Hospital is world-class, and adds to evidence internationally that RIC procedures should be more widely considered, as toxicity is lessened and patient safety may be improved without loss of treatment success. More detailed analysis is expected to enable this study to provide up-to-date and relevant information sufficient to create a decision tool for patients, so that they can more easily weigh up the risks versus benefits of these procedures. This will lead to better decision-making with increased patient involvement and satisfaction in their chosen treatment path, resulting in a healthier doctor-patient relationship overall.
Nicole Coman-Wright
*Long term urate lowering - how sustained is it after discharge from a clinical trial?*

Supervisors: Professor Lisa Stamp, Dr Peter Chapman
Sponsor: University of Otago Arthritis Research Theme

Gout is one of the most common forms of inflammatory arthritis. Symptoms are often self-limiting and are caused by the inflammatory response the body makes to the build-up of uric acid crystals in the body. Crystals are formed when urate levels in the blood (serum urate) reach high concentrations. Left untreated, recurrent gout attacks can lead to bone and joint damage causing disability. For this reason a major part of treatment of gout is using urate lowering therapies to reduce the level of serum urate (SU) and hence reduce the number of attacks patients’ experience.

Allopurinol is the most common medication used to lower SU levels. The dose that patients are prescribed is typically based on their kidney function. This is because the kidneys are responsible for excreting allopurinol. How well a patient’s kidneys are working is determined using creatinine clearance (CRCL), a laboratory measure that gives us a value indicating kidney functioning. In a previous clinical trial, the investigators wanted to see what would happen if patients were given doses of allopurinol higher than what was indicated by their CRCL levels in order to achieve the target SU concentration of less than 0.36mmol/L.

Previous trial data was collected during one year of monthly visits. Patients were then seen at two annual visits (year two and year three), during this time the patient’s general practitioner (GP) was advised to test SU every three months to ensure target SU was maintained.

Previous clinical trial data, laboratory computer systems and clinical notes were used to determine if patients continued on allopurinol, whether the reduction in SU was sustained for the two years of follow up and if advice about SU monitoring was followed after patients were discharged from a clinical trial setting.

**Results**

Of the 35 patients that completed year one, 29 completed the year two follow up and 26 completed the year three follow up. There were no significant differences in baseline demographics, clinical features, allopurinol dose and SU concentrations between the initial dose escalation group, those that completed year one visit and those that completed year 3 follow up.

Allopurinol was being used by all 35 patients at year one with a mean dose of 355.7 mg/day. All 29 patients who completed the year two visit were taking allopurinol at a mean dose of 353.45 mg/day, with four (13.8%) patients having their allopurinol dose changed before their year 2 follow up. Twenty five (96.2%) of the 26 patients that completed year three were still receiving allopurinol with a mean dose of 358 mg/day. Allopurinol had been stopped in one patient during a hospital admission and one patient had their dose decreased.

31/35 patients that completed year one achieved the target SU concentration of ≤0.36mmol/l, with a mean SU concentration of 0.32mmol/l. 24/29 patients that completed year two achieved the target SU concentration, with a mean SU of 0.29mmol/l. 23/26 patients that completed year three maintained the target SU, with a mean SU concentration of 0.32mmol/l. Of those patients that received three annual SU tests 19/28 (67.9%) remained below target for all three tests.

Three monthly testing plus the annual follow up testing meant that patients should have a minimum of four tests performed each year. During year two, 7/35 patients had ≥ 4 blood tests including SU. At year three, 4/35 patients had ≥ 4 blood tests including SU.

**Conclusion**

The majority of patients remained on allopurinol with 25/35 (71.4%) patients known to still be taking allopurinol at the end of the study period. Increasing the dose of allopurinol above CRCL based dose proved to be effective in reducing patients SU and sustaining SU long term with 67.9% of patients remaining below target for three annual SU tests. Advice about monitoring was followed in very few patients with only 3/35 (8.6%) patients receiving the recommended monitoring during both years of follow up.
**Tom Currie**

*Factors predicting successful treatment of Perianal Crohn's Disease with anti-TNF alpha therapy*

**Supervisors:** Mr Tim Eglinton, Mr Christopher Wakeman, Associate Professor Richard Geary

**Sponsor:** Warner and Patsy Mauger Summer Studentship

**Introduction:**
Crohn’s disease is a form of inflammatory bowel disease (IBD). It affects a large number of New Zealanders and its incidence is on the rise. It has a high prevalence in Canterbury compared with international rates. Crohn’s disease has a large impact on the health system in terms of the severity of the disease and the cost of treating it.

Approximately one in three of those with Crohn’s disease will have involvement of the anus (peri-anal disease). This can be in the form of an abscess, fissure or tract linking two parts of the body known as a fistula. There are many options to treat Crohn’s with medicines and/or surgery. The past ten years has seen increased use of a class of medicine known as anti-TNF alpha therapy to treat inflammatory diseases such as IBD. These medicines have been used with some success to treat peri-anal Crohn’s disease with response rates in large trials of up to 60%. Questions remain regarding their optimal use, in particular; which patients are more likely to respond to these agents, how long therapy should be continued in patients who do respond and how their use should be combined with other medical and surgical treatments. Anti-TNF alpha drugs are expensive and have some rare toxic side effects hence it is important to ensure they are used in a manner that will optimize the outcomes for the patient.

**Aim:**
To determine the outcomes of anti-TNFα therapy for perianal Crohn's disease in Canterbury.

**Method:**
We identified patients in Canterbury treated with anti-TNF alpha therapy that had peri-anal Crohn’s disease from January 2000 to November 2012 via the gastroenterology department, pharmacy and hospital coding databases. Data was collected retrospectively from hospital records. Data included: baseline demographics, treatment dose, duration, severity of disease, other medical treatments, surgical interventions, radiological follow up (MRI) and healing rates. The patient group that responded to anti-TNF alpha therapy was compared to those that did not to assess whether any factors predicted response.

**Results:**
75 patients were found to qualify for this study and were entered into the database. 41 were male and the median age was 31 years. The median length of follow up was 972 days. Some 55 patients (73%) responded to anti-TNF alpha therapy but only 15 (20%) healed the peri-anal disease completely. Of the 56 patients with perianal fistulas, 5 (9%) healed completely. All of those who didn’t respond had had an examination under anaesthetic and perianal abscess drainage. Responders were less likely to have been treated with antibiotics or receive major surgery such as a stoma bag.

**Conclusion:**
The majority of patients treated with anti-TNF alpha therapy in Canterbury demonstrated improvement in peri-anal disease, with response rates similar to those in large international trials. Response didn’t seem to be associated with any patient or disease factors. The patients who didn’t respond to therapy were more likely to have had concomitant antibiotics and a stoma bag. This is likely due to the fact these patients had more severe disease. Patients who didn’t respond to therapy were also more likely to require subsequent major surgery including removal of the rectum (the last part of the large bowel near the anus) and a permanent stoma bag.

The majority of patients had an examination of the anus under general anaesthetic or a Magnetic Resonance scan prior to initiation of therapy in keeping with guidelines from international specialist centers. Despite this, complete fistula healing occurred in only a small proportion of patients. Patients commencing treatment with these agents need to be made aware that they may help control the disease, but the chances of being free of fistulas is very low. To improve complete healing rates, further research is necessary into the optimal duration of therapy and its combination with other medical and surgical treatments for perianal Crohn’s disease.
Lydia Dockrill
The use of supplementary oxygen therapy in the acute hospital setting
Supervisors: Dr Hilda Mulligan, Ms Sarah Whitfield
Sponsor: Allied Health, Canterbury District Health Board

During their time in hospital, many patients may require additional oxygen for a number of reasons. These include aiding postoperative recovery, assisting with pain management and maintaining an appropriate level of oxygen in the blood for the body to work well and to prevent breathing problems. Oxygen therapy is one of the most widely used treatments in the hospital setting, and is most commonly delivered in the form of nasal prongs, but can also be administered in other ways.

Oxygen needs to be prescribed and administered safely, like any other medication or drug, as it can actually harm breathing or cause burns in some patients. Despite these risks, the stated protocols for oxygen therapy may not be strictly followed in the hospital setting. This mixed method study aimed to investigate the use and understanding of supplemental oxygen therapy on the acute orthopaedic wards at Christchurch Public Hospital (CPH), particularly in relation to the role and scope of physiotherapists.

Physiotherapists play a large part in the respiratory care of hospital patients. Assessing and making changes to supplemental oxygen therapy is within the scope of physiotherapy practice, but physiotherapists can only prescribe oxygen under a standing order in accordance with Ministry of Health guidelines. This would need to be workplace specific and individual to each physiotherapist. The Canterbury District Health Board (CDHB) has a written protocol regarding supplemental oxygen therapy prescription and administration.

We undertook two audits on wards 18 and 19 at CPH, a tertiary level hospital. The first audit investigated current administration of oxygen therapy over a period of seven consecutive days. The second audit investigated how physiotherapists working on these wards practice with regards to the management of oxygen supplementation. We also interviewed key health care team members individually about their understanding and perceptions of the use of supplemental oxygen therapy on these wards. We analysed the audit data with descriptive statistics, and identified the themes in the interview data.

361 samples were examined in the first audit and 15 in the second audit. The 12 interviews included one consultant, three house officers, five nurses, one physiotherapist, one occupational therapist and one social worker. All participants understood that the purpose of protocols in clinical practice is to allow patients to be treated in line with safe standards of treatment. Despite this, 27% of patients sampled were administered oxygen without prescription. Further, half of the six patients prescribed oxygen failed to receive it in accordance with the prescription.

One third of the staff interviewed for this study reported knowing about situations where oxygen had been administered unsafely, most often to patients for whom high levels of supplementary oxygen could have serious health effects. The safety problems were seen as due to factors such as: a lack of clear reporting processes about oxygen therapy, poor communication between team members on the ward about individual patients, and a lack of education to enable sufficient clinical reasoning by some team members. In addition, supplemental oxygen was perceived to be over-administered.

Eight of the twelve participants believed physiotherapists have the skills to manage the administration of supplemental oxygen therapy to patients. We also found that physiotherapists routinely make changes to patients’ supplemental oxygen therapy in an independent manner, without consultation, indicating that they perceive themselves as competent to do so. This was shown in 13 out of 15 samples of our second audit.

Our research showed that although all participants knew about the intent of protocols, many staff members were not familiar with the protocol surrounding oxygen therapy. It is essential for any District Health Board (DHB) to have user-friendly, practical protocols, which are written from a clinical perspective and make sense to those who are expected to follow the protocol. Otherwise, staff may not access the protocols because they find that they are unclear or vague and therefore not useful. Our research discovered that health professionals on these CDHB wards are either not familiar with the particular protocol for oxygen therapy, or had not bothered to read the protocol because previous experience of other protocols had not been useful to them.
Our research demonstrated a lack of accountability amongst the multidisciplinary team as to whose responsibility it is to make decisions surrounding patients’ supplemental oxygen therapy. In conjunction with this, it also demonstrated that physiotherapists competently administer supplemental oxygen without prescription daily. While the Physiotherapy Board of New Zealand states that the assessment and modification of supplemental oxygen therapy fits within the scope of practice for a physiotherapist, the prescription of oxygen can only be carried out under a standing order in accordance with the Ministry of Health guidelines. To make physiotherapists accountable for the prescription of supplemental oxygen therapy in the CDHB, it would need to further develop its own protocol to guide physiotherapists and other health professionals for the safe and effective use of supplemental oxygen therapy.

Poor communication between members of a multidisciplinary team can lead to decreased patient safety, specifically for high risk patient populations. We suggest that a method of identifying patients at risk from oxygen therapy be established within the CDHB, either through the use of coloured arm bracelets (much like patients who are at risk of falling are identified), via colour coded stickers in patient notes, or via written documentation in handover sheets.

In addition to keeping patients safe, identification strategies such as the ones suggested above and the detailed use of prescription charts may lead to the more efficient and effective use of resources. Our research shows that many participants feel that supplemental oxygen is overused on the wards, which wastes valuable resources and money.

In conclusion, oxygen supplementation is currently poorly prescribed and administered on wards 18 and 19 at CPH. This is, in part, due to a lack of accountability for the prescription of oxygen as a drug. Lack of education and poor clinical reasoning by some health professionals is leading to oxygen being unsafely administered, sometimes to high risk patient groups. As well as risks to patient safety, unnecessary administration of oxygen therapy wastes valuable resources for the DHB. Members of the health care team believe that physiotherapists have the skills to take on the role of prescription for oxygen therapy, but a standing order would be required in accordance with Ministry of Health guidelines for this to occur.

Because this study investigated the use of oxygen therapy on two wards in one DHB, the findings cannot necessarily be generalized to other parts of the hospital, nor to other DHBs without further investigation. Nevertheless, this study provides a useful snapshot of the use and understanding of oxygen therapy in an acute setting.
Josie Ganly  
**Does identification with the therapy model reduce dropout in psychotherapy for depression?**

**Supervisor:** Dr Jenny Jordan  
**Sponsor:** Edith Tripp Trust Summer Studentship

Depression is a common psychiatric disorder which has serious and widespread implications for the individual, their family and society. Although treatments are effective for many, up to half do not respond and a proportion of depressed patients prematurely drop out of treatment. This means that they leave before having received an adequate dose of therapy. In order to improve the outcomes for patients, we need to know more about the many and complex factors that affect how a patient responds to treatment, which in turn may affect whether they remain in treatment to receive an adequate does of therapy.

Two effective ‘talking’ or psychological treatments for depression are cognitive therapy (CT) and metacognitive therapy (MCT). CT focusses on challenging the content of depressive thoughts a depressed person has in order to help them change how they think, which in turn helps how they feel. Often these unhelpful thoughts pop into your head and are known as automatic thoughts. MCT does not look at the content of the thoughts, but addresses the unhelpful thinking styles (for example worry), which are believed to maintain psychological distress. By challenging and changing these patterns of thinking, a person’s mood can completely shift.

Previous researchers have suggested that how much a patient identifies with the therapy and how much they have adopted skills and knowledge from therapy into their daily lives, predicts the risk of relapse. One way of measuring patient identification with CT therapy is with the Ways of Responding Scale (WORS). We have adapted this scale and created a new subscale so that we could measure patient identification with the other therapy we have been trialling, MCT. In order to measure identification with therapy, trained raters listen to audiotapes of the therapy sessions and use the scale to rate the way the patient talks about specific aspects of therapy. If patients exhibit knowledge of the model, skills and language taught in therapy, then they get high ratings on the WORS. For example, a patient who identifies well with MCT may be able to recognise when they are worrying, that their worrying is not helpful, and understand and use the techniques which allow them to interrupt and refrain from worry or rumination. Similarly, identification with CT may be scored highly for a patient who can recognise his or her automatic thoughts in a situation, understand the impact of these on his or her feelings and can rationally challenge and come up with a more helpful or accurate thought in response to that situation.

The aim of our project was to understand whether the extent a patient identifies with the therapy model to which they were randomised can predict dropout from therapy.

**Method**

We recruited 48 participants with depression, referred for outpatient psychotherapy treatment. Participants were informed about the study and consented to be audiotaped. They were randomly assigned to one of two therapy groups; either CT or MCT. Participants were to receive between 8-15 therapy sessions over 12 weeks from a skilled therapist. A minimum of eight sessions was deemed necessary to have achieved an adequate ‘dose’ of therapy. Those participants who did not complete the final assessment for whatever reason, were called ‘non-completers’. The therapy sessions were audio recorded and a single middle therapy session from each participant was chosen for rating, on the basis that patient adoption of the therapy model would be most easily rated at this stage. For those who completed the course of therapy (n=37), this was usually between sessions 6-9. For non-completers (n=9), a session around the middle of their treatment course was selected. Rater reliability was checked to ensure that all raters were using the scale in a similar way. All data were analysed using a statistical program called SPSS.

**Results**

The WORS score for the therapy the participant received did not predict whether or not participants dropped out of therapy early. We identified four components or factors within the WORS score and found that one of these factors did predict drop out from CT, however no equivalent result was found for predicting dropout for the other therapy (MCT).
Discussion
This project examined the ability of our measure of patients’ adoption of therapy, to predict dropout from therapy for depression. The ability of a specific factor within the CT subscale to predict dropout, when the CT and MCT WORS subscale totals did not, suggests that further refinement of this measure is warranted.

Existing literature suggests that dropout is associated with more divergence between therapist and patient in the tasks of therapy and is associated with worse symptom ratings. In this study though, reasons for not completing therapy were varied; a sizable proportion of non-completers had improved depressive symptoms and were rating well in their adoption of the therapy when last seen. Given the diversity within the dropout group, the difficulty in predicting dropout status is not surprising.

The small sample size and in particular, the small dropout numbers mean that significant differences between completers and non-completers was not able to be detected. It is possible that choosing a single session per participant may not have accurately captured the extent of identification. Including ratings from more sessions per participant would give a more robust representation of the extent each participant identifies with the therapy.

Future research will apply the refined WORS to establish whether it can predict relapse over the two year follow-up phase. Examining the relationship between this refined scale and established predictors of dropout and outcome may improve understanding about factors which predict retention in treatment and improve the likelihood of a good treatment outcome.
Ian Glass  
*Gating of physiological monitors in MARS scanner for small animal research*

**Supervisors:** Dr Anthony Butler, Dr Nigel Anderson  
**Sponsor:** Canterbury Medical Research Foundation

The ability to monitor and study biological responses to drug treatment in small animals has always been an invaluable process for progression in medicine; however producing static internal reconstructions of living specimens becomes difficult. Due to organ displacement of live animals during scanning processes, signal and consequently image artifacts are produced requiring some method of image correction. One such method in CT, MRI and PET scanners is to provide gating driven by physiological signals. The motivation for the project was to be able to produce non-distorted CT imaging of live animals. This will allow researchers to monitor cancer progression and responses to drugs in live animals most closely representing human physiology.

In particular this involved providing software and hardware interfacing of ECG, respiratory, temperature and Po2 monitoring for physiological gating of the MARS CT scanner using small animal monitoring equipment. The CT scanner works by emitting and then acquiring the attenuated and scattered X-Rays off an incident sample. Due to the discrepancies in energy bands and atomic mass and scattering mechanisms, wide variations in X-Ray energies are observed producing a characteristic energy spectrum. The characteristic energy spectrum is intrinsic to a specific material which allows the user to identify material composition of the specimen in a 3-dimensional image.

To produce image correction, two gating options were proposed, prospective and retrospective gating. Unfortunately neither of the two gating protocols has been fully implemented; however the specifics on how they would be achieved were planned out. Prospective gating will be done by constantly exposing the specimen to X-rays and regulating a shutter which exposes the medipix chip (the sensor) to the attenuated X-rays. It will be driven by the ECG and respiratory signals obtained from the on board small animal monitoring equipment.

Physiological parameters will be acquired and sent to the gating module. The gating module will then wait for preset cardiac and respiratory phases at which point a gating trigger will be sent to the PC. This will trigger the medipix shutter to open for an average time of 1 millisecond and cause a sample to be collected. Once this is done the gantry (equipment housing) will reposition itself at a different angle ready to receive the next gating trigger. After a few iterations of the scanning process enough data will be collected to be reconstructed using the image reconstruction software.

Retrospective gating will be performed by constantly scanning and saving the cardiac and respiratory phases with each data set. After scanning a program will sort through the data and match image sets which correspond to each cardiac and respiratory phase. Retrospective scanning will allow a 3-dimension image to be reconstructed with the added benefit of a real time image. This will allow researchers to study the flow of flow and muscle contraction within the living specimen.

The results of this project have provided the basis for completing the development of both prospective and retrospective scanning. It has also opened doors for further research and development, which in time will hopefully allow similar scanning protocols to be implemented on live human specimens. Due to the relatively short exposure time, large numbers of samples will be required to accurately reconstruct an image. This results in long scan times; however this is still comparable with standard MRI used in hospitals today. The next step is to develop retrospective scanning and develop Linux based software to display physiological waveforms for operators in real time. The future plans are to eventually design and develop our own hardware to measure physiological parameters and to integrate this directly into the CT scanners. The results of this project have opened doors for further research and development, which in time will hopefully allow similar scanning protocols to be implemented on live human patients.
Measure 5 year wear rates in total hip joint replacement patients receiving a new low wear (X3) polymer

Supervisors: Professor Gary Hooper, Dr Tim Woodfield, Dr Elango Selvarajah
Sponsor: Canterbury Medical Research Foundation

Total hip joint replacement surgery is an operation in which a diseased hip is replaced with a prosthetic implant. The procedure has long been known as a suitable treatment for osteoarthritis, but the long term results, however, are limited by many factors, the most common being polyethylene wear debris causing osteolysis and resultant component loosening. The polyethylene wear debris are produced due to wear at the weight bearing surfaces of the prosthesis.

Such complications are more common in younger patients, as not only are they more active, but they have to live with the prostheses for a longer period of time, thus are prone to earlier failure and subsequent revision.

The most common cause for early failure is surgical revision for recurrent dislocations. Surgeons have found that the use of larger diameter femoral heads decreases the risk for recurrent dislocation. A further advantage is that the patient experiences a greater ROM of the associated limb as well. The use of larger femoral heads thus seems the appropriate solution to preventing early failure due to recurrent dislocations.

There is, however, concern that using a femoral head with a larger diameter may increase the rate of volumetric wear of the polyethylene, resulting in increased osteolysis and early failure. This is where the new generation highly cross-linked X3 polyethylene may have a role to play. The X3 polymer undergoes a series of preparatory modifications such as annealing and irradiation, to increase the amount of cross-linking and decrease the amount of free radicals present, providing a polyethylene layer with increased resistance to oxidation and improved wear properties. Annealing involves heating the polyethylene to a temperature below its melting point, maintaining it at that temperature for a fixed time and then cooling at a predetermined rate. Other highly cross linked polyethylenes, which are melted, have observed changes in the mechanical strength of the polyethylene which have occasionally presented as fracture of the acetabular rim in steeply positioned cups. In the preparation of the X3 polymer, annealing, rather than melting, follows 3 Rad of gamma irradiation of the polyethylene and the process is repeated three times.

Current research in the University of Otago’s Department of Orthopaedic Surgery and Muskuloskeletal Medicine aims to determine whether there is an advantage in using X3 polyethylene in total hip joint replacement surgery by allowing the use of larger sized femoral heads without jeopardizing wear rates. In vitro studies of the X3 polymer already show lower wear rates and better resistance to fatigue and oxidation.

The Study aims to assess wear rates in younger patients with X3 polyethylene and 36 mm femoral heads. It is a prospective study that started in 2006, in which 100 total hip joint replacement operations were performed by two surgeons in Christchurch, both using the posterior approach. All operations were standardized, in which Ceramtec 36mm ceramic heads and X3 polyethylene were used. All used Stryker Trident Cup and ABG II Stem. Follow up with standardized x-rays took place immediately post-op, at 2 months, 1 year, 18 months, 2 years and 5 years.

A prospective group of 100 patients with X3 polyethylene with early wear rates recorded at 1 and 2 years had already been analysed. My role in the study was to re-measure the wear rate at 5 years to determine whether the early low wear rates were maintained. I was mainly involved in wear measurement, where I examined all the x-rays using 3D edge detection software known as PolyWare Auto. PolyWare eliminates human input from the wear measurement and has been shown to increase accuracy and reproducibility between investigators. A review by McCalden et al reports that PolyWare compares well with other computer wear measurement techniques in terms of precision and accuracy.

With PolyWare we were able to measure wear rates of the polyethylene. Of the 96 hips remaining in the study, 7 were lost to follow-up. Unsatisfactory x-rays of 3 hips were excluded by the software, 1 hip had been revised before 5 years and 1 patient was deceased. The remaining 85 THA in 79 patients had adequate radiological and clinical evaluation at a mean follow up of 5.08 years. The mean 2D linear femoral head penetration rate at five years was 0.21mm/year. The mean 3D femoral head penetration rate was 0.23mm/year and the mean volumetric wear rate was 90.45mm³/year for the same time period. These results are consistent with the low wear rates calculated after two years follow-up, where
mean 2D linear femoral head penetration rate at two years was 0.20mm/year. The mean 3D femoral head penetration rate was 0.25mm/year and the mean volumetric wear rate was 117.0mm³/year for the same time period.

Wear rates in thin polyethylene liners have been a significant concern, and with the increasing trend towards larger femoral heads, particularly in younger more active patients, the potential to accelerate wear in these thinner liners has increased. However, to date we have found no evidence for increased wear rates at five years in these patients. The benefits of stability and range of movement with the use of 36mm femoral heads could be offset by increased volumetric wear, however at five years we found a low mean volumetric wear rate confirming that the size of the femoral head had little effect. These results were independent of age and as this study focused on younger patients (average age 60 years), who potentially had higher physical demands; these results give some reassurance to the current trend of implanting larger diameter femoral heads.

The results of the study should offer reassurance to surgeons wishing to use larger femoral heads with the X3 polymer.
(Margaret) Qiao He

*Tolerability and efficacy of Rosuvastatin in a Lipid Clinic Outpatient Cohort*

Supervisors: Dr Jo Young, Professor Russell Scott, Professor Peter George
Sponsor: Canterbury Health Laboratories

**Introduction:**

Rosuvastatin is a medication which belongs to a class of drugs called statins. Statins have been established as one of the most effective ways of lowering blood cholesterol since its introduction in the 1980s. Our blood cholesterol levels depend on how much our body produces and how much we absorb from our diet. Statins work by blocking our body’s own ability to make cholesterol by inhibiting a critical enzyme in the cholesterol synthesis pathway called HMG-CoA reductase. In humans the majority of our cholesterol is made by the body, therefore by blocking this pathway we can significantly reduce our total blood cholesterol (TBC).

The current health guidelines state to aim for a total blood cholesterol < 4mmol/L with the LDL cholesterol (LDL-C) (also known as the bad cholesterol) of <2mmol/L and a HDL cholesterol (HDL-C) (good cholesterol) of >1mmol/L. This is particularly important for patients who are at risk of cardiovascular disease as it can help to reduce their risk of heart attacks, strokes and peripheral vascular disease. Patients with a genetic condition called familial hypercholesterolaemia (FH) have very high levels of TBC and LDL cholesterol. They are put on statin therapy from an early age and this is a lifelong medication for them as adequate reduction in blood cholesterol puts their cardiovascular risk score to the same as that of the general population.

Muscle related side effects are a common complaint with myalgia (muscle aches) reported in up to 10-15% of patients on statin therapy. This often results in a reduction in dose or withdrawal from therapy which compromises the patient’s cardiovascular risk management. Rosuvastatin has been reported as a more potent statin meaning a lower dose is needed. It is also broken down through a different metabolic pathway in comparison to the earlier statins and therefore has the potential to have less drug interactions and muscle related side effects.

**Method:**

In this study 56 patients who were enrolled in an Early Access Program were followed up over a time period of three years. These patients were started on Rosuvastatin based on the criteria that they were not reaching their target cholesterol levels or experiencing adverse side effects on prior statin therapy. 32 of our patient population were known to have FH. Hospital notes and GP follow up information was collected to assess how patients were tolerating Rosuvastatin. Laboratory data and concurrent use of other lipid lowering medication was collected prior to therapy, at 1month, 18 and 36months after commencing Rosuvastatin to assess its efficacy at lowering blood cholesterol. We also recorded blood glucose, liver function tests and kidney function tests to assess the safety of this medication.

**Results:**

**Tolerability:** 40 out of 56 (71.4%) patients remained on Rosuvastatin therapy at follow up. All of the patients in the not treated to target subgroup were able to tolerate Rosuvastatin whereas 23 out of 39 (59%) patients with prior statin intolerance tolerated therapy. Of the 16 who withdrew from therapy, 7 of these patients experienced myalgia, with only one of these patients not having had experienced myalgia on previous statin therapy. Other reasons for stopping included headaches, high liver function tests, abdominal discomfort, rash, dry cough, depression and difficulty accessing medication. The majority of patients who could not tolerate Rosuvastatin discontinued therapy within the first three months after initiation on Rosuvastatin with the median number of days on therapy being 103 days.

**Efficacy:** The mean TBC for our study population was 7.0mmol/L ± 1.6 (SD) with a LDL-cholesterol (LDL-C) of 4.8mmol/L ± 1.6. We found a statistically significant reduction in both TBC and LDL-C of 22.9% and 32.7% respectively in patients remaining on Rosuvastatin therapy. As expected there was no significant change in HDL-cholesterol and triglyceride levels. Levels of Apolipoprotein B were reduced by 25.7% reflecting the reduction in LDL. The improvement in lipid profiles could be observed within one month of initiating therapy and this level was maintained as long as patients continued therapy. Prior to therapy very few of our patients had been achieving their lipid targets as they were quite a hard to treat patient population. 1 patient had a TBC <4mmol/L and 1 had an LDL-C <2.0mmol/L. We found a significant increase in the number of patients achieving their LDL target after 36 months with 8 patients having a LDL-C <2.0mmol/L. The number of patients achieving a TBC < 4mmol/L also increased from 1 to 5 patients after 36 months but this was not deemed to be statistically significant.
**Safety:** There were no statistically significant changes in liver enzymes, renal function or blood glucose for patients on therapy in comparison to those who withdrew throughout the follow-up time period.

**Conclusion:**
Rosuvastatin appears to be a tolerable, efficacious and safe therapy for the treatment of hypercholesterolaemia. It has the potential to be a beneficial alternative in the management of cardiovascular disease for patients who are not able to tolerate or respond adequately to the alternative statins currently available in New Zealand.
Karen Hodge
3D printing of porous scaffolds for tissue engineering

Supervisors: Dr Tim Woodfield, Mr Ben Schon, Professor JG Chase
Sponsor: Christchurch Radiology Group Trust

Background:
3-Dimensional printing has the potential to become extremely useful in the field of medicine. The ability to print implants and replacement joints to meet the specific dimensions and needs of individual patients would mean greater compatibility and greater success for such procedures. The Christchurch Regenerative Medicine and Tissue Engineering (CReATE) team at the University of Otago Christchurch (UOC) has developed a 3-dimensional (3D) bioprinter – a printer specialised to work with living tissues – with which they are experimenting with printing replacement cartilage tissue.

Many different conditions can result in cartilage joint defects, such as trauma or arthritis, and such defects can be debilitating. With the system being developed at UOC, a patient’s cartilage defect can be scanned, and an appropriately proportioned piece of replacement tissue printed. This can then be implanted into the defect. An additional benefit of this process is that the cartilage cells can be harvested from the patient’s own cartilage tissue (i.e. from the nose), which helps eliminate graft rejection problems that would otherwise be present with tissue transplantation.

There are several different techniques for printing biological tissues. The general idea is that living cells are arranged in an approximation of the desired end result, and this will encourage them to grow accordingly. One technique is to print biopolymer scaffolds, (made of a biodegradable material similar to plastic) into which spheres of cells can be inserted. This is what the bioprinter at UOC has been used for in the past.

Summer Project – Hydrogel Printing:
This studentship focused on experimenting with a different printing technique. In collaboration with researchers from Queensland University of Technology (QUT), we’ve been exploring the properties of a newly developed hydrogel material. Hydrogels are an alternative means of printing with tissues, where the cells can be suspended in the printing medium. This simplifies the process by avoiding the need to print the scaffold and insert the cells separately.

The hydrogel we’re using has been developed at QUT. It is gelatin based (so similar to jelly) and has had methacrylamide groups added to it. These are molecules that join together (‘crosslink’) when exposed to UV light, which means that the printed structure can be given more strength and integrity, and allows control over the physical properties of the gel – swelling behaviour, degradation mechanics etc. In order to increase viscosity and make the gel easier to print, gellan gum (a naturally derived gum) has also been added to the mix.

Whether we’re printing with a biopolymer or the hydrogel, we still need tight control over the printing process to produce a defined 3D lattice structure. A porous lattice allows cells in the centre to receive nutrients and an adequate blood flow, necessary to ensure cell growth post printing / implantation. Having tight control over the printing also allows control over the shape and mechanical properties (such as strength) of the printed structure.

The aim of this project has been to assess the optimal printing conditions for the hydrogel on the UOC printing system. The group at QUT has already shown that cells can survive in the gel, so our aim was to verify that it could be used to create useful structures for implantation, in order to provide ‘proof of concept’ regarding the viability of the gel as a bioprintable material. This meant showing that it is practical to work with, and capable of maintaining the 3D shape that it is printed in.

In assessing the hydrogel, we needed to find a range of appropriate printing parameters. This meant assessing the ideal values for temperature, nozzle diameter, auger speed, pressure, and printhead speed to produce viable lattices. We also compared several different gellan concentrations.

Lattice assessment was carried out initially by visual inspection, giving a broad indication of the viability of the final product and the success of the print. Lattices were assessed for strand consistency as well as good overall structure. The aim was to produce strands of consistent thickness, with minimal bubbles or breaks. The strands needed to be capable of building a functional lattice, which meant that additional layers must traverse gaps without significant sagging – a significant problem with existing hydrogels – in order to maintain porosity.
Based on the melting points of the various components of the hydrogel mixture, the operating temperature was maintained between 32 and 40°C, with the best results returned between 34 and 36°C. Strand diameter could be controlled via nozzle diameter, in combination with manipulation of pressure and printing speed. 1mm spacing with a vertical stepping height of 0.2mm produced reasonable results with small diameter (27g) nozzles.

The biocompatibility of hydrogels makes them attractive as a printing medium for tissue manufacture. As well as cells, nutrients and growth factors can be included in the hydrogel, which can provide cells with a 3D environment similar to natural tissues. The ability to print with cells directly as part of a hydrogel will allow for greater complexity in printed shapes, with the ability to lay down multiple different cell types with high accuracy. As a result of this project, we have succeeded in producing a number of satisfactory lattices, providing further evidence of the viability of this hydrogel as a bioprintable material. The ability to accurately control the gel by manipulating printing parameters will allow for the creation of tissue scaffolds with precise physical properties. This enables the production of defined, individualised pieces of bioengineered tissue, suitable for tissue transplantation.
Ovarian cancer is the leading cause of gynaecological cancer death among New Zealand women. One important reason ovarian cancer becomes so lethal is because there are no effective ways to detect the disease at an early stage. The symptoms are often misinterpreted and clinicians have no suitable test to diagnose the disease. As a result, the majority of women are not diagnosed with ovarian cancer until the disease is in an advanced stage. Advanced ovarian cancer is a difficult disease to treat because it has a tendency to spread to other parts of the body (metastasize) and can become resistant to anticancer drugs. Women diagnosed with advanced ovarian cancer have a very poor prognosis, and there is an unmet need to improve the quality of life and survival of these patients.

Currently, a patient with advanced ovarian cancer is prescribed a course of chemotherapy based on the statistical likelihood of a response as determined by clinical trials. Most commonly, a combination of two anticancer drugs (paclitaxel and cisplatin) is given. However, this is not effective in all women and in fact only 71% of women will respond to this treatment. If the first round of treatment does not work, a clinician will then prescribe an alternative treatment based on the statistics, again that is the likelihood of a response rather than information relating to the patient. The pitfall of this practice is that the patient’s condition is likely to worsen and their quality of life decrease. Unfortunately, even when a treatment appears successful initially, patients frequently relapse. Thus, there is a problem in our oncology clinics in being unable to determine which drug, or drug combination, is best for an individual patient. To overcome this, we are attempting to bring this problem from the clinic into the lab. We aim to devise a rapid, reliable drug screening method, which could be used for determining which drug, or drug combination, is best suited for each individual patient. This would assist clinicians in optimizing the most effective treatment regimen. We believe this will provide the patient with maximal benefit and lead to improved patient outcomes.

Previous attempts to create a drug screening method for advanced ovarian cancer have been unsuccessful. We believe the reason these previous method has been unsuccessful is because of a fundamental flaw in their experiments: the cell model, or the way cancer cells were cultured in the lab. Previously, ovarian cancer cells have been grown as a flat layer across the surface of a flask and we call this a two dimensional (2D) monolayer. Clearly, this does not resemble a cancer growing inside a patient. More importantly, it has been shown there are important biochemical differences, which make this type of cell model irrelevant to be employed for preclinical drug screening purposes. In this project, we are testing a new and improved cell model. This cell model is based on mimicking the extracellular matrix (ECM). The ECM is the interlocking mesh-like structure, composed of complex carbohydrates and proteins, found on the outside of cells. Cancer cells grow through this ECM-like framework in a three dimensional (3D) manner. 3D culture methods are becoming increasingly popular as it is recognized these more accurately reflect the tumour microenvironmen observed in patients. Thus, 3D cell models are used to more precisely predict drug responses.

The aim of this project is to test and validate the novel methodology using ovarian cancer cells. This preliminary investigation will assess whether our novel 3D cell model is compatible with ovarian cancer cell lines. We hypothesized that cancer cells grown in 3D culture will respond differently to those grown in 2D culture.

To test this hypothesis, two different ovarian cancer cell lines (SKOV-3 and OVCAR-5) are grown in both 2D and 3D culture. Cancer cells are grown in 96-well plates, which will allow many different treatments to be tested in a single experiment, and the biochemical analysis can be carried out in short periods of time.

In this preliminary study, the anticancer drugs cisplatin, paclitaxel, and everolimus, as well as natural products, including compounds from green tea (EGCG) and red wine (resveratrol), along with seven novel combinations of anticancer drugs and natural products were tested. We allowed cancer cells to grow for 6 days to establish a sufficient sample before treating the cancer cells with drugs, or drug combinations, for a further 4 days. We then measured three different biochemical endpoints including cancer cell growth, cancer cell metabolic activity, and the secretion of a cancer cell angiogenic marker, namely VEGF. VEGF is important protein for the growth of new blood vessels, a process which is
critical for the development of solid tumours. We believe these biochemical analyses offer very important information for clinical prognostics as adequate and substantial information can be obtained from a single experiment.

Our results showed that two ovarian cancer cell lines behaved and responded to treatments in distinctive manner between 2D cell monolayers and 3D cell culture. As hypothesized, we found that the response of cancer cells grown in 3D cell model exhibited greater resistance to clinical anticancer drugs than 2D monolayers. This is important as we expect the response of cells grown in 3D culture to be more clinically relevant. Furthermore, the results showed that treatment with combinations of drug had a greater effect than with any single drug. We also noted that the responses were cell line-dependent that was while both cell lines were derived from ovarian cancer, they each responded differently. Interestingly, we observed a phenomenon called ‘epithelial-to-mesenchymal transition’ with the SKOV-3 cell line in 3D culture. This phenomenon involves cancer cells drastically changing shape, from a large, diffuse shape to a thin, pointy shape, and then becoming invasive. These thin, pointy extrusions grow through and invade the ECM gel. Epithelial-to-mesenchymal transition is a key process occurring during early metastasis of advanced ovarian cancer.

In conclusion, we have begun to validate this novel 3D culture method with encouraging results. Importantly, we have observed epithelial-to-mesenchymal transition and cancer cells that acquire an invasive phenotype. This is a relevant morphological adaptation seen in the early event of metastatic invasion, which is absent in 2D monolayers. This study adds to a growing body of knowledge that the response of cancer cells grown in 3D model is distinct from those grown in 2D monolayers. Importantly, we suggest that the responses to clinical drugs in 3D model will be more clinically relevant. The ultimate goal of this methodology is to provide clinicians with a rapid and reliable tool to determine the use of anticancer drugs and their combinations to maximize the likelihood clinical responses in each patient. Thus, this 3D culture model deserves further validation for translational research and evaluation of drug efficacy in ovarian cancer cells from patients.
Blood flow correlates of cognitive impairments in Parkinson’s disease

Hannah Janssens

Supervisors: Dr Tracy Melzer, Dr Michael MacAskill, Professor Tim Anderson

Sponsor: University of Otago Health Sciences Divisional Summer Scholarships

Parkinson’s disease (PD) is a chronic neurodegenerative disorder characterized by motor impairment. In addition, cognitive impairment presents another very important aspect of this common disease. As many as 80% of Parkinson’s disease patients will develop dementia throughout the course of their disease. PD patients with dementia exhibit difficulty with a number of mental tasks including executive functioning (planning, attention and problem solving), memory, visuospatial and verbal functioning. Early signs of impairments, known as mild cognitive impairment, can occur early in the disease process, prior to the development of dementia. This cognitive dysfunction can have a significant impact on PD individuals, greatly affecting their quality of life and that of their caregivers. Hence an approach to identify those individuals most at risk of developing dementia is greatly needed, giving the opportunity to intervene and slow cognitive decline. Research suggests that altered brain functioning (for example metabolism and blood flow) may underlie cognitive impairments in PD; thus there is potential for abnormal blood flow to provide a physiological marker of PD-related cognitive decline.

Magnetic Resonance Imaging is a non-invasive technique used to create detailed images of cerebral anatomy and function. Using a novel technique called arterial spin labelling we acquired blood flow images from 74 PD patients and 36 healthy controls. All PD participants completed extensive neuropsychological testing covering four cognitive domains – executive function; learning and memory; attention, working memory, processing speed; and visuospatial/visuoperceptual function. These scores enabled classification of PD patients into three groups: 38 with normal cognition (PD-N), 26 with mild cognitive impairment (PD-MCI) and 10 with dementia (PD-D). The controls underwent the same battery of neuropsychological tests to obtain an overall, global cognitive score used for comparison.

In this project I investigated the relationship, if any, between cerebral blood flow and cognitive impairment. To do so, I performed a statistical analysis that controlled for the effect of grey matter atrophy, age, sex and education as these factors are known to affect either cerebral blood flow or cognitive status. I investigated whether blood flow was significantly reduced in PD relative to healthy individuals, as well as if blood flow decreased with increasing cognitive impairment in PD. Further analysis looked at blood flow correlates of cognitive scores across multiple domains of cognition.

We were also interested in the role of white matter hyperintensities (WMH) in PD cognitive impairment. WMH are lesioned areas in the white matter of the brain that appear bright white on certain MRI images (a clinical scan called a T2 FLAIR image). These white matter lesions are thought to be vascular in origin, representing altered or diminished blood flow and occur with normal aging. Research suggests that increasing volume of WMH may be associated with cognitive dysfunction, and the effect may be greater in PD than that seen in normal aging. Thus WMH may be contributing to cognitive decline in PD.

Relative to controls, PD-N exhibited no significant reduction in blood flow. PD-MCI showed areas of significantly reduced perfusion in the posterior and midline regions of the cerebrum. PD-D patients showed widespread reductions in blood flow throughout the brain. Results are consistent with previous studies showing that PD individuals exhibit reduced cerebral perfusion compared to healthy controls in predominantly posterior regions.

Additionally we identified an association between cerebral blood flow and cognitive score when looking across all PD and control subjects. An extensive global reduction in perfusion was associated with lower cognitive scores, involving both hemispheres and all cerebral lobes. We also investigated this relationship with the individual cognitive domains mentioned above. An extensive global perfusion reduction was found to be associated with lower executive functioning scores and with lower scores in attention, working memory and processing speed. Lower learning and memory scores correlated with a reduction in posterior perfusion and no relationship was found between visuospatial/visuoperceptual score and blood flow.

We found a significant reduction in posterior blood flow with increasing volume of WMH in all participants suggesting WMH may be contributing to cognitive decline in PD.
Perfusion deficits are now well documented in Parkinson’s disease; however there are also many conflicting studies. My research supports the theory of reduced cerebral perfusion in PD and its association with cognitive decline, adding a potential explanation for impairment in different cognitive domains. More research needs to be conducted in order to determine the sequence of events contributing to cognitive decline in PD. Specifically, longitudinal studies are required to determine this sequence and the direction of the causal relationship between reduced perfusion and cognitive decline.
Radiotherapy is the use of focused radiation to kill cells and tissue that are harmful. It is generally used as a part of cancer treatment. While it is often quite effective it is not without risk, and new radiotherapeutic treatments and regimes are frequently being developed, in the hopes of improving current techniques.

The normal course of action in developing other new drugs and treatments is to test extensively in animals before any human testing begins. With radiotherapeutic treatments, animal testing is much less prevalent. A major reason for this is that small animals are much harder to accurately irradiate due to their size and disinclination to remain stationary. A dedicated small animal irradiation machine is usually required for radiotherapy to give any meaningful results. The MARS CT scanner – a small sized CT scanner currently in development – may be a solution to this problem. We set out to prove that the MARS micro CT is a viable tool for accurate radiotherapy of small animals, enabling wider testing of new radiotherapeutic cancer treatments.

The specific aim of this study was to use the MARS CT scanner to irradiate 2 specific regions of the hippocampus (a small part of the brain associated with learning) of several rats, in order to kill the stem cells located there. If that area could be successfully irradiated, with little damage to surrounding tissue then we would know the MARS CT scanner has been effective. The reason the hippocampus was our target was so that the rats could be used in a secondary study carried out by a PhD student. That study focuses on the role of hippocampal stem cells in forming and breaking addictions. While our focus remains on the capabilities of the MARS scanner, it is good that more than one conclusion can be drawn from these rats.

Before irradiation could begin we had to design collimators. Collimators are lead plates with a small strategically positioned aperture. The lead blocks the oncoming x-rays, and the aperture hones them into a precise beam. With the use of a rat brain atlas and bony landmarks on the exterior of the rat skull we were able to calculate the correct positioning for the aperture on the collimators.

To ensure the collimators were accurate we tested the setup with gafchromic film – a special film that shows a visible darkening when struck by x-rays. This allowed us to calibrate the CT scanner so that the x-ray source was in the correct location. It also gave us an indication of the dose that would be received in the hippocampus. By determining the relationship between the darkness of the gafchromic film and the dose received, we were able to find the dose the film received when placed behind different thicknesses of Perspex. The Perspex - meant to simulate tissue of the head – was equivalent to the depth at which the hippocampus is found. Thus the dose to the hippocampus could be approximated.

Rats were anaesthetized and placed in a specially designed holder to keep their head fixed and stationary. The holder was placed in the MARS micro CT scanner and x-rays were fired from each side of the rat for around half an hour. This dose of radiation was calculated in order to be sufficient to kill stem cells but to leave other tissue undamaged.

3 rats were given this dose initially. Their brains were dissected and several staining techniques were used on slices of the hippocampus. These give an indication of the extent of the damage to the stem cell population. When comparing the control rats to the irradiated rats, early results appear to show a decrease in stained cells found in the irradiated rats. This indicates that fewer stem cells are present and that the irradiation has successfully hit the hippocampus. The MARS CT scanner is able to be used for the precise irradiation of tissue in small animals.

In the future the MARS CT scanner can be a useful platform for not only imaging but also small animal irradiation. Cell removal - like we did with neural stem cells - is one application that is now more available to researchers. This research also opens the door for greater testing and trialling of new radiotherapeutic treatments.

Small animal irradiation is still a niche area of research. We hope this project will begin to remedy this by making the practice more accessible to researchers through the use of the MARS CT scanner.
Gabrielle Kemp
The epidemiology of inflammatory bowel diseases in Nelson, New Zealand - Project 1

Supervisors: Associate Professor Richard Gearry, Dr Darryl Fry
Sponsor: Nelson Medical Research Trust

Inflammatory Bowel Disease (IBD) is a complex collection of disorders which present with inflammation of the small intestine or colon. The bowel wall becomes red, swollen and may produce ulcers along with other pathology, all of which lead to disruption of the normal digestive process. Crohn’s disease (CD) and ulcerative colitis (UC) are both encompassed under the definition of IBD. Both CD and UC have common and unique disease characteristics. Patients often suffer from diarrhea, abdominal pain, abdominal bleeding, cramps and may have severe weight loss. CD can occur anywhere from the mouth to the anus, whereas UC is found only in the colon.

IBD is a significant health problem which is increasing worldwide. However, there are limited data on disease distribution described in terms of person, place and time (descriptive epidemiology). Canterbury is the only region of New Zealand which has results published on prevalence (proportion of people in a population who have a disease) and incidence (number of new cases per population in a given time period) of IBD comparing sex and age, which is not hospital-based.

The aim of this project is to determine the descriptive epidemiology of IBD in the Nelson Tasman region of New Zealand. Nelson is the ideal location for epidemiological research. The care of all IBD patients is undertaken by a limited number of practitioners. There is only one gastroenterologist working in the Nelson region. There is also very little migration in or out of the region for medical care, and, it has a relatively stable background population.

In this study an excel spreadsheet was kept prospectively by the local gastroenterologist, of all of new IBD diagnoses at Nelson Hospital from January 1, 2001 until January 1, 2013. From that list we screened and researched each patient individually. All relevant information was entered onto a specialized custom built IBD Access database. The population area was defined using the territorial authorities’ as defined in the 2001 and 2006 census from Statistics New Zealand. We only looked at individuals who resided in the Tasman Region and Nelson City areas. The data were extracted and analysed descriptively to determine the point prevalence, incidence and age at diagnosis.

The point prevalence of IBD was determined on January 1, 2013. The prevalence of IBD in Nelson Tasman per 100,000 was 451.6, for CD 245.3, and for UC 206.3. Age-standardized prevalence per 100,000 was 389.3 for IBD, 226.3 for CD, and 162.9 for UC. There is a rapid rise in IBD prevalence from the age of 15, peaking at the age of approximately 35, and from then on prevalence remains relatively stable. CD shows a steep rise in prevalence from age 15 to age 35. UC prevalence has a much more gradual incline, peaking at ages 75-79 years. IBD prevalence per 100,000 is 481.9 in males, compared to 422.0 females. The prevalence per 100,000 for CD in females and males was very similar, 243.3 and 247.3 respectively. However, the prevalence of UC per 100,000 is much higher in males, 234.5, compared to females, 178.8.

The incidence of IBD in Nelson Tasman was determined prospectively for every year between January 1, 2001 and December 31, 2012. The crude incidence rate for IBD per 100,000 was 11.7 in 2001 and 18.9 in 2012. The peak incidence rate for IBD per 100,000 was in 10 with 26.9. CD incidence was 4.7 in 2001 and 13.7 in 2012, compared with UC incidence per 100,000 of 7.0 in 2001 and 5.26 in 2012. CD incidence has been relatively stable peaking in 2010 with 18.3 per 100,000. UC incidence peaked in 2008 with 13.2 per 100,000.

For the entire cohort, the peak age of diagnosis for CD patients was approximately 20 years. The peak age of diagnosis for UC patients is slightly later at 25 years. For CD, the median ages of diagnosis were 30 and 31 for males and females, respectively, whereas for UC, the median age of diagnosis were 37 and 39, respectively.

Overall, this study has prospectively defined the descriptive epidemiology of IBD in the Nelson Tasman region of New Zealand. It was found that the prevalence of IBD in Nelson Tasman as of January 1, 2013 is comparable to that which has been found in Canterbury, NZ. In Nelson Tasman the prevalence of CD is higher than that of UC, with more male IBD patients compared to females. Canterbury was found to have one of the highest published rates of Crohn’s disease. The prevalence of CD in Nelson Tasman appears to be very similar. It has also been found that the annual incidence of IBD diagnoses has remained relatively stable over the years of data collection. No other study in New Zealand has
prospectively collected incidence of IBD over a decade like ours. The peak and median age of diagnosis was found to be lower in CD compared with UC. All of these findings are significantly useful to the Nelson community, local medical personnel, the district health board, and any further medical research on IBD in New Zealand. These results support a growing impression of an IBD epidemic throughout New Zealand. Hopefully this data will become useful for future policy and funding changes within the Nelson Tasman region and beyond.
Latitia Kench
Optimising drug delivery during recovery from anaesthesia

Supervisors: Associate Professor Ross Kennedy, Dr Jennifer Woods, Ms Leigh Parsons

Sponsor: Anaesthetists’ Instrument Pool Ltd

Opioids such as fentanyl and morphine are commonly used as pain relief during, and immediately after surgeries. The dosing of opioids is a very subjective process and anaesthetists have to predict the amount of opioids their patients will require in order to be comfortable as they recover from their surgeries.

We now have the technology to be able to model, in real time, the amount of opioids actually working on opioid receptors in the central nervous system (the effect site level). It is important to research how this new technology may improve the efficacy of opioid dosing and improve patients’ recovery from anaesthesia.

Doses of opioids given during surgery and in the Post Anaesthetic Care Unit (PACU, or the recovery room), were collected from 78 patients undergoing laparoscopic (keyhole) surgeries at Christchurch Public and Christchurch Women’s Hospital. All patients over 18 undergoing laparoscopic procedures were eligible to be entered into the study, but only one PACU could be monitored at any one time. Doses given in surgery were recorded from the anaesthetic chart on arrival to the PACU while doses given in the PACU were recorded as they were given. Doses were entered into Medvis PK/PD drug display software which created a real time graph of the patients’ effect site opioid levels. Patients’ pain scores were also recorded using a verbal 0-5 score.

Most patients required some form of IV opioid while in the PACU. 51 patients reached a peak, after which they no longer required pain relief in the form of opioids, while 6 required extra opioid pain relief after reaching a peak but becoming sore again as it wore off. 21 patients did not require any IV opioids in PACU. There was a moderately strong relationship between the effect site opioid level on arrival in PACU and the maximum effect site level post-operatively. There was no relationship between effect site level on arrival and the time taken to reach maximum effect site level.

The computer programme used allows us to model patients’ effect site opioid levels at different stages of their surgery and recovery and also predicts what it will be in the future. As there is a relationship between arrival effect site level and maximum effect site level, this programme could help improve patients’ recoveries as using the patients effect site level on arrival to the PACU, staff may be able to determine a range of effect site level at which the patient is likely to be comfortable while in recovery.

Overall, the majority of laparoscopic patients have straightforward post-operative opioid requirements. This limits our ability to assess the use of tools allowing for effect site guided dosing as the real time modelling gives no advantage to the PACU nurses over that of their experience. I would recommend that further research be done using patients undergoing procedures which have greater opioid requirements post-operatively.
Isabel Lee  
**Diabetic foot ulcers, investigating the impact that peripheral arterial disease, peripheral neuropathy and infection have on healing time**

**Supervisors:** Ms Karyn Balance, Ms Juliet Berkeley  
**Sponsor:** Don Beaven Summer Studentship

Diabetic foot ulcers are defined by the International Consensus on the Diabetic Foot as “a full thickness wound below the ankle in a patient with diabetes”. These ulcers occur as a complication of diabetes mellitus and are the most common foot-related cause of lower limb amputations globally. As a result of diabetes, one amputation occurs every 20 seconds worldwide and New Zealand faces an economic cost of between NZ$9,000 and $13,000 per diabetic foot ulcer. Where healing is delayed and amputation required, this cost may increase to as much as NZ$85,000. In addition to high amputation rates, diabetic foot ulcers are notoriously slow healing with an average healing time of six months. Most importantly, it is believed that up to 85% of amputations can be prevented with the support of well organised diabetic foot care teams, good diabetes control and well-informed self-care. Crucial to this is the ability for treatment providers to predict the severity of a presenting ulcer based on the ulcer’s characteristics and the patient risk factors.

So what is causing diabetic foot ulcers? A loss of pain and sensation in the feet (peripheral neuropathy) and reduced blood flow to the feet (peripheral arterial disease) have both been shown to worsen the outcomes of diabetic foot ulcers by increasing healing times and increasing amputation rates. The loss of pain and sensation renders the diabetic foot more at risk of undetected injury and a loss of motor control can lead to muscle weakness in the foot, and loss of fine motor control. The foot’s ability to sweat is also affected by peripheral neuropathy (PN), resulting in less sweat being produced leaving the skin dry and more prone to cracks, ulceration and infection. Peripheral arterial disease (PAD) is a progressive blockage of the large arteries in the legs which reduces blood supply to the feet leading to slower wound healing.

This project aimed to investigate the healing time of ulcers treated at the Diabetes Centre High Risk Foot Clinic at Christchurch Hospital and to identify the risk factors contributing to longer healing times and poorer ulcer outcomes. Firstly we wanted to evaluate the effect on healing due to the presence of PN and PAD. We also wanted to examine the impact that infection, both soft tissue and bone, may have on healing times. Glycaemic control was also examined using HbA1c (glycated haemoglobin) as a measure of this.

The sampling time frame began on August 1st 2011 and ran until June 26th 2012 by which time 85 patients had been recorded with a total of 114 ulcers. All patients that had a new foot ulceration within this period were included. Each ulcer was observed for six months from the date of presentation and at the end of the six months ulcers were classified as either chronic non healing ulcers, ulcers ending in amputation or healed ulcers (which were recorded with a healing time). Of the 114 ulcers, 111 ulcers from 82 patients were included in the final analysis.

Data from each patient was collected from the Diabetes Centre patient records, electronic patient notes and by examination of the ulcer by one of three podiatrists at the Diabetes Centre. Data was collected on the patient’s background, ulcer characteristics, HbA1c levels, kidney function, PN, PAD, appointments with other health professionals, infection and amputation.

The mean age of all included patients was 64.5 years (±14.9) and 72.8% of patients were male. Of the 82 patients, 26.83% had both PN and PAD, 51.22% had just PN, 12.20% had just PAD and 9.76% had neither.

When ulcer outcome was looked at after six months, 17.12% of ulcers had not healed while 7.21% required amputation within the six month period. The remaining 75.68% healed within the six month period with an average healing time of 71.21 days.

On average, ulcers with PAD only and those with PAD+PN were more likely to be unhealed by six months (21.74% healed, 25% healed respectively). In comparison, those without PAD or PN (52.17%) or with PN only showed significantly better healing (51.14% healed).
The presence of PN and PAD had no significant effect on the likelihood of the ulcer presenting with, or developing, a soft tissue infection; however those with a soft tissue infection showed a prolonged healing time. Overall 63.96% of ulcers were associated with a soft tissue infection while only 17.12% of ulcers were complicated by a bone infection.

Glycaemic control and kidney function did not show any significant relationship to ulcer healing and it is likely this is a result of the small study size.

This study demonstrates that PN and PAD are very common in patients presenting with ulceration to the Diabetes Centre High Risk Foot Clinic, with only 9.76% of patients having neither of these diabetic complications. This may be in part due to diabetes patients seen at the clinic not being representative of all people with diabetes in New Zealand. This is because the Diabetes Centre High Risk Foot Clinic predominantly sees patients with harder to treat ulcers; compared to less complicated, quicker healing ulcers which are more likely to be seen in the community. The results demonstrate that PAD appears to have the greatest effect of the two on influencing an ulcer’s ability to heal within six months. This highlights the importance of prompt diagnosis early on in a patient’s treatment to determine whether peripheral neuropathy or PAD is present. This will allow for targeted treatment for these conditions. In addition, knowing the average time the ulcers are taking to heal will allow for improved planning of patients’ treatment and will aid in screening new patients who may be at risk of prolonged ulceration.

Identifying high risk patients early on will allow for more targeted care, thus helping to reduce more serious complications such as amputation further down the track.
Mild cognitive impairment (MCI) occurs when a person’s cognitive ability is less than what would be expected for their age. This has implications on a variety of cognitive functions and affects everyday lives. For example, some people with MCI in midlife will go on to experience dementia in late life.

Dementia is a debilitating condition with severe mental and emotional effects on the individual, their family and carers. Due to the ageing population in New Zealand, institutionalization and caring for those with dementia also causes a significant economic burden. Research into dementia often examines ways to prevent and treat the condition. Some studies have looked into conditions related to cardiovascular disease such as high cholesterol and high blood pressure, in relation to MCI and/or dementia. Studies have also investigated whether nutrient intake from food is associated with the risk of dementia and/or MCI as some nutrients (such as saturated fat) have negative effects on the body, especially the cardiovascular system.

This study aims to investigate the risk of MCI in a group of 50 year olds residing in Canterbury, New Zealand. It was hoped that some clues as to why people might have mild cognitive impairment would be discovered and that this would help to understand why some people are on an early path to dementia. The aim of this project is to use cardiovascular, cognitive and nutrition data from participants enrolled in the Canterbury Health, Ageing and Lifecourse study (CHALICE) to answer the following questions:

- Is cardiovascular risk at age 50 predictive of mild cognitive impairment (MCI) at age 50?
- Are the New Zealand Cardiovascular risk charts providing a good measure of heart health and cognitive function at age 50?
- Can nutrients play a role in cognition in this sample of 50 year old Cantabrians?

A five year cardiovascular disease risk profile (using the ‘New Zealand Cardiovascular Risk Charts’) was assessed and compared to cognitive function and nutrient intake. Mild cognitive impairment was assessed using the ‘Montreal Cognitive Assessment’ - a quick and easy tool to assess domains of cognition. Both MCI and cardiovascular disease risks were compared to intakes of fats and alcohol. Saturated, monounsaturated and polyunsaturated fat intakes were assessed using the average intake over four days and alcohol intake was calculated from the ‘Alcohol Use Disorders Identification Test’. Other factors affecting cognitive function such as depression and education were assessed and compared to risk of MCI and cardiovascular risk. Statistical tests were used to determine if there were significant relationships between factors.

Those with a higher cardiovascular disease risk score are at increased risk of MCI at age 50, probably due to blood vessel damage in the brain. There was no relationship between nutrients and risk of MCI or cardiovascular disease in this study, either because the study did not have enough people to show a significant relationship, or that fats and alcohol are having no effect on cardiovascular risk or cognitive function in this group. Depression and lower education are significantly associated with a higher risk of MCI. This is an expected result as it has been shown previously. Lower level of education was also associated with higher risk of cardiovascular disease.

This study has shown that increased cardiovascular disease risk at age 50 can predict an increased risk of MCI, and that the New Zealand cardiovascular risk charts are useful in this prediction.

This study was not able to show that nutrients play a role in altering cognition. Future studies should use more participants and concentrate on other factors that may predict the association between cardiovascular disease risk and cognitive function. Increasing education level is likely to have positive effects on both heart health and cognitive health, but implications on health and the mechanisms for this in the body need to be examined. Further investigations looking at nutrients, physical activity and other lifestyle factors should be undertaken.
Michelle Lindsay  
*Endometrial Cancer outcomes and follow up*

**Supervisors:** Dr Bryony Simcock, Associate Professor Peter Sykes  
**Sponsors:** Cancer Society of New Zealand, Canterbury/West Coast Division and joint funding by Cancer Society Amberley Group and Cancer Society Hurunui Group

**Introduction:**  
Endometrial cancer is the most common gynaecological cancer in New Zealand. Approximately 315 new cases are diagnosed annually and this incidence is increasing. The management of endometrial cancer, like that of most malignancies, involves follow up after treatment with the intention of diagnosing relapses early and therefore increasing survival. Relapse of endometrial cancer occurs in approximately 13% of cases. Follow up in New Zealand generally consists of vaginal smears and physical examinations, with or without imaging such as x-ray and CT, every 3 months, 6 months and then annually for a total of 5 years, though this varies depending on patient and disease characteristics, and the type of treatment used.

Recent literature has challenged the efficacy of intensive and prolonged follow up procedures such as this for three main reasons. Firstly, it has been observed that a high proportion of recurrences are detected through the presentation of symptoms, rather than as a result of follow up procedures such as smears and imaging. Secondly, a recent study has indicated that intensive follow up is not associated with increased survival when relapse occurs. In addition, the vast majority of relapses (found to be 70-100% in some studies) occur within 2-3 years following initial treatment. This brings into question the appropriateness of follow up exceeding this time period. Follow up procedures are highly resource intensive and so it is important that we evaluate their efficacy. In light of these developments the national recommendations for endometrial cancer follow up are currently being reviewed.

Literature has also begun to develop which indicates that women who have had endometrial cancer are at increased risk of other diseases such as cardiovascular disease (CVD), diabetes, breast and ovarian cancer. These associations need further investigation but, if validated, need to be addressed through patient education and interventions.

**Aims:**  
The purpose of this research was to investigate endometrial cancer survival and relapse with regard to age at diagnosis, the stage and grade of the tumour, and the type of treatment received. We also sought to investigate how relapses are most commonly detected. We aimed to consolidate this information into a report which will help inform the development of new national guidelines regarding endometrial cancer management and follow up.

In addition, we aimed to investigate if women who have had endometrial cancer have an increased risk of hypertension and diabetes, and increased risk of death from cardiovascular disease. If these associations are identified then this information can be used to develop educational tools and interventions to decrease these risks.

**Methods:**  
This research involved completing an existing database of 461 women who were diagnosed with endometrial cancer and treated at Christchurch Hospital or Christchurch Women's Hospital between 1997 and 2007. This database was recently used for an international study, but was incomplete for the purposes of this research. Data concerning treatment, relapse, grade and stage was collected from patient notes and the Oncology Register. Cause of death information was obtained from death records held by the Christchurch Hospital Mortality Office and the Department of Internal Affairs. Comorbidity information was obtained from the Christchurch Hospital Clinical Coding Office and patient notes.

The data was consolidated in Excel. It was analysed, with the help of a statistician, using SPSS Kaplan-Meier survival analysis.

**Results and Conclusions:**  
The mean follow up was 5.4 years. The 3 year overall survival was 84.5%, the 5 year overall survival was 78.5%. In accordance with other studies, our analysis found that 3 and 5 year survival decreased with increasing stage, grade and age at diagnosis. No meaningful association between survival and treatment method was observed. This is most likely a consequence of the relationship between severity of disease and the type of treatment used.
Analysis of relapse regarding its association with stage, grade, age at diagnosis and treatment could not be undertaken due to excessive loss to follow up. Analysis of how relapses were detected was also difficult as this information was unknown in 30% of cases. However, of the remainder, 63.6% of relapses were symptomatic at diagnosis, while 36.4% were detected through follow up procedure. This is an interesting result but more complete data is needed to draw conclusions regarding the need for follow up in detecting relapses. Furthermore, relapse survival needs to be analysed according to method of presentation to establish if follow up procedure leads not only to early detection, but to better patient outcomes.

The prevalence of diabetes in a sample of our cohort was 17.8%. This does not exceed that of women in the general New Zealand population (22.1%) as was hypothesised. In contrast, the prevalence of hypertension in our sample was 39.3%, this is significantly greater than the prevalence in women in the general population which is 12.1%. These results do not support that women who have had endometrial cancer are at greater risk of diabetes, but do indicate that they are likely to be at greater risk of hypertension. This is a risk factor for stroke and heart disease, and therefore education and interventions to decrease this risk in women who have had endometrial cancer are needed.

Endometrial cancer was the cause of death in 55.8% of cases; cardiovascular disease was the next most common cause of death and accounted for 24.8% of cases. The mortality rate from CVD in the general population is 27.3%. Our results do not support that women who have had endometrial cancer are at increased risk of mortality from CVD. However, other studies have shown that the risk of death from cardiovascular disease exceeds the risk of death from endometrial cancer 5 years after diagnosis, and it is the leading cause of death in the long term. Longer follow up of our cohort is needed to investigate the association between endometrial cancer and death from CVD.
Rachel Lines  
Outcomes of patients returned to GP coordinated care after assessment via the Sleep Disorders Clinical Pathway  

Supervisor: Dr Michael Epton  
Sponsor: Asthma Foundation  

Sleep disorders are a significant health problem in New Zealand. It is estimated that between 5,000 and 20,000 adults in the Canterbury region suffer from symptomatic sleep-disordered breathing. Obstructive Sleep Apnoea (OSA) is a form of sleep disordered breathing which is characterised by oxygen desaturations and arousal from sleep due to repetitive airway obstruction. The categorisation of OSA as mild, moderate or severe is determined by the number of these desaturation events per hour and the presence or absence of excessive daytime sleepiness. Even in the mild form, OSA is associated with morbidity. These morbidities include increased cardiovascular mortality, obesity, excessive daytime sleepiness, impaired concentration, motor vehicle collisions and strokes.

Prior to 2008, there were long delays in patients who were suspected to have Sleep Disordered Breathing/Obstructive Sleep Apnoea (OSA) being assessed by the Christchurch Hospital Sleep Unit. This delay time would frequently be around 18 months from the time of referral to an implementation of treatment. In 2008, the Sleep Apnoea Community Assessment Pathway was developed and an Obstructive Sleep Apnoea Screening Assessment Tool was developed to address this delayed time of patient treatment. It involves assessment of these patients in the community by approved providers and the results of this are reviewed at a Sleep Multi-disciplinary Meeting (MDM). Approximately 1500 patients are assessed annually in Canterbury through the Sleep Disorders Clinical Pathway (SDCP). A significant proportion of these patients (35% in 2012) are referred back for coordinated care by their GP as they either have; a) no significant sleep disorder, b) a sleep disorder which can be managed by primary care or c) OSA of a degree which does not qualify for hospital funded treatment.

The patients and their GP receive a letter detailing the outcomes of their sleep assessment and advice about treatment options. However, the outcomes of these patients are not monitored and in order to have a whole picture of the OSA Assessment Tool, we need to be able to understand what happens to these patients. It is vital to inform future treatment and funding discussions that the impact of this management process is understood. In addition, it is important that the patient’s response and understanding to this management are also evaluated in order to assess where improvements can be made.

The aims of this project were to (1) Assess the outcomes of the patients returned to GP coordinated care, (2) Assess the SDCP patient satisfaction and (3) Identify areas/aspects for improvement in the SDCP and develop strategies to improve these.

In order to assess these outcomes and satisfaction, an audit in the form of a survey was generated and sent out to a random sample of 300 patients by the Sleep Clinical Pathway and returned to GP coordinated care in 2012. The questions in this survey addressed aspects of time to assessment and outcome, communication of results to the patient, subsequent contact/activity by community health care providers and outcomes, including use of private providers of care. In assessment of quality of service and patient satisfaction, questions were also asked related to this.

Once surveys were returned, the data from these were entered into an Excel Spreadsheet, along with relevant information attained from patient data bases. This information included scores from sleep assessments, GP clinics, ethnicity, diagnosis given and other relevant information relating to the letter sent to their GP and the patient. Once all the data was collected, it was analysed through the statistical package Epi Info.

Results:
Of the 300 surveys that were sent out, a total of 119 (40%) were completed after both the due date and phone reminders were carried out. The results of these surveys showed that of these 119 people, 58 (49%) were seen by their GPs following their assessment. 51% of these patients had initiated this contact. Analysis of this data showed that the patients who were not followed up by their GPs felt less satisfied about the service compared with the patients who were followed up by their GPs.
It was also important to look at what treatment or advice was given to those who are followed up and the results showed that many had not received any advice or treatment from them (43%). The most common form of advice that was given was lifestyle measures such as weight-loss, decreasing alcohol and caffeine intake and having better sleeping behaviours with 42% of respondents receiving one or more of these. Three people had received private CPAP treatment and none had received any other form of private treatment e.g. a dental splint. The patients who were not followed up felt that they were less informed about available treatment options compared to those who were followed up.

The patients who were followed up felt that the coordination of their care (between the Sleep Clinic and their GP) was more acceptable than those who were not followed up, and their overall satisfaction of the SDCP was also higher.

**Conclusion:**

Through this study we were able to identify key areas of improvement in the SDCP involved with returning patients to GP coordinated care.

**Areas for improvement:**

- A significant amount of patients returned to GP coordinated care are not followed up after their sleep assessment (43%)
- 50% of the patients returned to GP coordinated care are able to be treated, therefore these patients may be missing out on possible improvements in their sleep quality
- Patients who are not followed up are less satisfied with the SDCP
- 43% of those who are followed up haven’t received any treatment or advice from their GP. This may indicate a gap in the education of the GPs in how to manage these patients

**Potential solutions:**

- GP education in terms of treatment following patients being returned to their care
- Keeping these patients in the SDCP and following them up through the Hospital System
- Electronically sending assessment letters to GPs with prompts to follow-up patient.
- Mandatory phone calls from staff in the SDCP following assessments
- Templates for Assessment letters.
- Clinics in the community setting for patient follow-up

These potential solutions will be discussed and explored thoroughly with the appropriate people. A strategy will then be implemented in order to improve these areas identified through this study and aim to improve the overall outcomes of the patients returned to GP-coordinated care.
Thomas Loan  
*Development of the molecular detection of chromosomal and genetic abnormalities using BACs on Beads (Bobs) and molecular karyotyping*

**Supervisor:** Dr Kit Doudney  
**Sponsor:** Canterbury Health Laboratories

Much of molecular genetics in the last thirty years has concerned short segments of DNA sequence; the pattern of base pairs (A, T, G and C) that make up DNA. Identifying changes (mutations) in this sequence have helped us explain a huge number of inherited diseases. In a genome of 3 billion base pairs (bp), these are small changes, but when mutations occur in critical gene regions, they can cause big disruptions to the protein they code for, resulting in diseases like cystic fibrosis.

Another angle from which to examine the human genome is at the chromosomal level, where we can measure DNA copy number differences that can also cause disease (Down syndrome, for example, is caused by having three copies of chromosome 21, instead of the usual two). In the past, looking at patients’ chromosomes by light microscopy (karyotyping), has allowed us to see large changes to their structure; ranging from the presence of extra whole chromosomes to extra or missing ‘segments’ of a chromosome. These are termed copy number changes. A relatively new technique has vastly improved our ability to see much smaller disease-causing copy number changes in chromosomes – molecular karyotyping, also called microarray or array comparative genome hybridisation. Molecular karyotyping enables a much more detailed examination of chromosomes, allowing us to characterize changes on a much smaller scale. We can detect differences of 50,000bp as opposed to the older light microscopy resolution of 5 million bp.

There are two main areas where studies of chromosomes are particularly important; firstly in patients (usually in childhood) with developmental delay, learning disabilities, autism or schizophrenia, often accompanied by dysmorphic features; secondly in cancer patients, where the chromosomes of cancer cells can be very abnormal, or show only a few small, yet critical, abnormalities. Studying how different chromosome abnormalities affect risk, prognosis and treatment response has played a major role in the fight against cancer. Notably roughly 80% of childhood acute lymphoblastic leukemia (a cancer of the blood and bone marrow) cases are treated effectively, with different treatments guided in part by the karyotype of the affected bone marrow.

In this study we have applied molecular karyotyping to 43 consecutively analysed patients with dysmorphic and developmental syndromes referred to the Canterbury Health Laboratories by NZ paediatricians and specialist genetics doctors. We have identified a range of subtle and gross deletions and duplications that may help explain a range of clinical symptoms. In the cohort of samples analysed, we detected clinically significant abnormalities in 2 of the patients, unclear significance (but likely detrimental) in 12 patients and detected no abnormal chromosomes in 29 patients. Many of these changes would be invisible to normal karyotyping.

In seventeen cancer samples, we have uncovered some interesting patterns of variation, with some common features across patient groups and some results that may help bring new insights into the biology of these cancers.

The great advantage of this technique is it allows a survey of the whole genome for these types of abnormalities in a single experiment. This generates a dizzyingly large amount of data which in some cases can be difficult to interpret, but already this information is becoming critical in a clinical setting and as more and more of these types of studies are done we will continue to develop our understanding of the underlying biology in some of the more complex genetic diseases.
Health literacy in general practice: describing practice nurses' understanding of health literacy

Supervisors: Dr Gillian Abel, Dr Lynley Cook, Professor Philip Schluter, Ms Ramai Lord, Ms Maria Pasene

Sponsor: Partnership Health Canterbury PHO

Introduction:
Health literacy is “the way in which individuals have the ability to find, process and understand basic health information and services in order to make informed and appropriate health decisions”. This means first, a patient needs to be able to access health information such as a discussion with a doctor or nurse. Secondly, they need to be able to understand that information. And lastly, they need to be able to make a decision based on the information.

Research has shown that over half of New Zealand adults have low levels of health literacy meaning they cannot understand basic health information to make important health decisions such as choosing treatment options or starting a new medication. In addition, the lowest levels of health literacy are amongst Maori, Pacific people and high deprivation populations; the same populations that are also affected the most by long term and costly conditions such as diabetes and asthma in New Zealand.

This is a problem because research has shown people with low health literacy are less likely to use preventive services (e.g. visit a GP), less likely to self-manage their long term conditions (e.g. monitor blood sugar levels in diabetes) and are more likely to be hospitalised due to long term conditions (e.g. having later complications of diabetes).

Aim:
The aim of this research was to describe practice nurses’ understanding of the concept of health literacy, the problems and impact associated with low health literacy in their practice and to identify strategies they use to overcome low health literacy.

Method:
Three focus groups were conducted with fifteen practice nurses from purposively selected Christchurch general practices. The nurses were asked to discuss topics around pre-planned questions associated with health literacy in New Zealand. Their discussions were audio recorded and the transcripts were analysed to draw out important themes or topics that emerged from the analysis of the focus groups.

Results:
Four key themes were identified by practice nurses: the types of people they identify as having the biggest challenges with health literacy, difficulties with managing long term health conditions, tools that they find effective to overcome these difficulties and other issues that might have a bearing on health literacy.

1. Vulnerable Populations
The nurses identified three key populations they considered in their experience as struggling with health literacy in their practices. They found the combination of hearing impairment and the general obliging nature of the elderly as contributing factors to their challenges with understanding health information. Young people were also an identified group and the nurses attributed this to the challenges with forming trusting relationships with them. The last group identified was people where English was their second language and the challenges associated with language barriers.

2. Difficulties managing long term conditions
The nurses thought managing long-term conditions such as diabetes and asthma were a considerable challenge for people. They thought some possible reasons for this could be a combination of the complexity of the conditions and medications themselves and the lack of understanding around the use of medication as prevention for later complications.

3. Tools nurses find effective for improving health literacy
Health pamphlets and web based resources were some of the most favoured health resources the nurses used to assist their patients in understanding health information. The nurses however were concerned over the lack of availability of
these resources in other languages such as Maori and Pacific. They also made valuable suggestions on how to increase the use and availability of such resources such as putting more computers with simple and reliable health resources in general practice waiting areas and public facilities such as libraries to be used by the public.

4. Other issues that have a bearing on health literacy
Nurses placed emphasis on the importance of a trusting professional relationship as central to improving health literacy and commented on specific communication skills and techniques that they identified as helpful ways to achieve this. Consistency in health information was highlighted as important for patients to understand their illnesses such as seeing the same doctor and receiving the same key messages each visit. Specific challenges nurses identified as a barrier to improving health literacy included the difficult language used in common screening questionnaires and they felt that many people, particularly when English was their second language, had considerable difficulties in understanding the questions asked of them.

Conclusion:
The results of this study demonstrate a variety of important issues raised by nurses in New Zealand practices that can be used to improve our primary care professionals’ skills around addressing health literacy. The information collected provides valuable evidence and direction for the development of new and innovative ways to improve health literacy in general practice. The study also emphasises an appreciation of addressing health literacy challenges as a vital step to improve many health outcomes in New Zealand.
Campbell MacLachlan

Review of the Cancer Society Tissue Bank: 10 years of donations

Supervisors: Ms Helen Morrin, Professor Bridget Robinson (special thanks to Dr Margaret Currie)

Sponsors: Cancer Society of New Zealand, Canterbury/West Coast Division and Cancer Society Ellesmere Group

Background:
The Cancer Society Tissue Bank (CSTB) was established to collect tissue samples from donors undergoing surgery for cancer at Christchurch public hospital, in order to facilitate high-quality cancer research. It had its beginnings in 1996, becoming an established bank in 2000, with on-going Cancer Society support from 2004. The establishment of the bank, its procedures and early experiences were reviewed and published in 2005. The bank’s storage procedures have developed as a result of advancements in scientific methods, and sample collection targets have responded to reflect changes in patient clinical management. The Information and Consent form has also evolved in response to a changing ethical environment. Information is now routinely collected on: Donor ethnicity, with separate consent sought for use of the sample overseas, or in a commercial project. There is also now the option at the completion of a project for the final disposal of the sample with a karakia (blessing). CSTB samples have been used in health research projects throughout NZ, and in several international collaborations.

Aims:
The overall aim of this project was to review Tissue Banking for research from 2000-2010, to (1) determine the value of the bank to all stakeholders, including: donors, researchers, charity funding bodies, the University of Otago, and the CDHB, and (2) identify the relevance of the bank’s collection to date, identifying any specimen gaps or redundancies, to direct future sample collection.

Methods:
There were three main components to the audit:

- Extracting information on donated sample types and numbers, as well as analysing donor consent form options.
- Analysing research applications to use samples, and release of samples for research.
- Web searching for publications resulting from CSTB sample use.

Results:
At the end of 2010, samples had been banked from over 6500 donors, with multiple samples taken from each donor. Sample types including fresh-frozen tissue, DNA preparations, serum, plasma, and paraffin blocks, with the predominant tissues banked from donors with breast (1169 donors), bowel (1080 donors), and prostate (507 donors) cancers. The majority of specimens utilised in research were: Bowel, breast, prostate, and uterine, so thus far utilisation of Bank resources has correlated with collection. From our 6500 donors, 6846 samples have been utilised, however over 70% have remaining tissues held by the bank and available for future projects.

In terms of consent form options, the vast majority of donors consented to: Access to medical records (97.0%), samples being sent overseas (97.5%), and the use of samples in commercial research collaborations (95.0%). A further 36.1% of donors requested disposal of their sample with a karakia. The majority (77.4%) of donors have identified as NZ European, 4.7% as Māori, and 2.5% as Asian, with the remainder identifying as another ethnicity, or not recording their ethnicity.

To date, 34 clinically-relevant journal articles have been published in high-impact peer-reviewed international journals using CSTB samples, as well as 8 theses, 2 commercial patents, and numerous other publications (including, summer studentship reports, and conference presentations).

Discussion:
In terms of the value of the bank to its stakeholders, the bank’s sample collection to date has been hugely valuable to researchers; large numbers of pre-collected samples allow shorter timeframes for research projects, and the ethnicity of donors being consistent with that of the region, ensuring that samples are representative of the Canterbury population.
Donors can be reassured that their donation is enabling important research; while funding bodies can be confident that the bank is facilitating good quality research with its diverse collection, and is functioning at maximum levels for its resources. Clinicians supporting the CSTB are involved in research projects they might otherwise not have been have undertaken.

The consent option response rates show strong donor faith in the Bank’s processes, and these results are consistent with those from the 2005 audit of the bank, meaning that that the percentage of donors consenting to these options has remained consistently high even as sample size increases. As more donors consent to these options, specimens become available for a more diverse range of projects.

The *karakia* was developed by the University of Otago, Christchurch to encourage people of all ethnicities (in particular, Māori) to participate in research, and this audit suggests the Bank may be achieving this goal, as 4.7% of donors identified themselves as Māori, yet the percentage taking up the *karakia* is much higher. This shows that the blessing is of value to donors of varying ethnic backgrounds. The ethnicity figures are relatively consistent with those of the 2006 census of Canterbury, ensuring that samples are representative of the Canterbury population.

The value of the CSTB can be best measured by the use of its samples and research outputs leading to improved healthcare outcomes. Research output resulting from the use of tissue banks follows a classical pattern in the first ten years of their operation, due to a lag phase where samples are being collected to provide the large cohorts required for quality research. During this period they tend to be able to only support home-institution based research. This is clearly shown in the case of the CSTB, with the majority of research outputs occurring from 2006 onwards.

**Conclusions:**
This audit confirms that the CSTB is collecting samples that are relevant to researchers’ experimental requirements, and is a resource of national importance. The CSTB is in a position to continue to fulfil its founding aim, facilitating high quality cancer research.
Georgie Malcolm

Developing an evidence based pathway for UTI management in the primary/urgent care setting

Supervisors: Associate Professor Dee Mangin, Ms Louisa Sullivan, Dr Andrew Richardson

Sponsor: Pegasus Health (Charitable) Ltd

What is the 24 Hour Surgery?
The 24 Hour Surgery is on Bealey Avenue in Christchurch. It provides 24-hour urgent medical and accident care. It can be very busy and sees more patients than the local emergency department. It is run by Pegasus Health, which is an organisation of general practitioners [GPs] in Christchurch. The team at the 24 Hour Surgery are a mixture of permanent staff and the 320 Christchurch GPs required to do regular shifts.

What are Urinary Tract Infections?
Urinary Tract Infections [UTIs] occur when bacteria infect and irritate the bladder. This can cause a burning pain when urinating, a feeling of needing to urinate more often, blood in the urine and lower abdominal discomfort. Half of women will get at least one UTI during their lifetime, with many getting regular UTIs.

What did this project address?
Primary care in Christchurch has a team-based approach with doctors and nurses sharing care according to their expertise and skills. However, the largest proportion of wait time at the 24 Hour Surgery involves waiting to see a doctor. Increasing the role of primary care nurses at the after-hours clinic has been identified as one way to improve efficiency and patient satisfaction. At the 24 Hour Surgery, UTIs were selected as a suitable condition for nurse treatment. Many women with UTIs come in to the 24 Hour Surgery. As their condition is classed as non-urgent, they often experience long waiting times, especially when the surgery is busy. This project aimed to test whether the length of time that patients spend at the clinic could be reduced if experienced 24 Hour Surgery Nurses provided treatment for women with UTIs.

What did this project find?
Nurse treatment for women with UTIs reduced the average time spent at the 24 Hour Surgery by an average of 15 minutes from 56 minutes to 41 minutes. This was not shown to increase the time spent at 24 Hour Surgery for other patients attending the facility.

Could Nurses at the 24 Hour Surgery treat other conditions?
It is thought that there are a number of other illnesses suitable for nurse treatment. The results of this study suggest that at the 24 Hour Surgery, waiting times could be reduced by the introduction of nurse treatment for other conditions. This could help to increase the efficiency of the service, while maintaining or increasing patient satisfaction.
Leila Marie
The effect of the Canterbury earthquakes on alcohol, substance and psychotropic medication use

Supervisors: Dr Caroline Bell, Dr Virginia McIntosh, Dr Janet Carter
Sponsor: University of Otago Health Sciences Divisional Summer Scholarships

Since September 4th, 2010, earthquakes and aftershocks have become an on-going reality for the residents of Canterbury. The series of seismic events have had devastating consequences for many residents, including injury, death of family and friends, and widespread property and infrastructure damage. The mental health sequelae of natural disasters are varied, especially when the events are unpredictable and on-going, as is the nature of aftershocks in this earthquake sequence.

Most individuals are exposed to trauma or significant adversity at some point in their lifetime, and many individuals manage to cope with the traumatic life events they experience. Psychological resilience is a term used to describe a person’s ability to positively adapt to or recover from a traumatic experience and has been associated with positive mental health post-disaster. Even though most individuals do not develop mental illness as a result of exposure to trauma, it has been well documented that exposure to traumatic events such as natural disasters is associated with negative psychological and behavioural outcomes, including symptoms of severe stress, depression, anxiety and increased alcohol and drug use.

Alcohol is currently the recreational drug most commonly consumed by adults in New Zealand, and research shows that people tend to drink more following a traumatic event. Alcohol consumption is related to over 60 disorders, having the potential to exert both acute and chronic negative effects on physical and mental health. Motivations for consuming alcohol are highly variable, however a common motivation observed among those who have experienced trauma, is drinking to cope. Coping in this sense refers to consuming alcohol or drugs in an attempt to manage unpleasant symptoms and to reduce negative emotional states such as sadness, anxiety or anger.

The Canterbury earthquake sequence provides an opportunity to examine alcohol and drug use in the community after a mass trauma, and how drug use might relate to psychological resilience and pathology. The current study examined changes in alcohol, drug and medication use since the earthquake sequence began, and whether patterns of ‘drinking to cope’ exist among Cantabrians who report coping well with the earthquakes and their effects. Such knowledge is important not only to promote psychological health among the residents of Canterbury, but also to identify warning signs among those more likely to be at risk of developing problematic patterns of drinking.

Based on past research, it was expected that participants would report drinking more since the earthquake sequence began, and that higher levels of current substance use would be associated with the severity of traumatic exposure experienced, as well as increased psychological distress and coping-oriented motives for drinking. Whether self-reported psychological resilience is related to patterns of substance use and motivations for drinking was also investigated.

In order to test these expectations, 39 individuals who experienced one of more of the major Canterbury earthquakes since September 2010, and who self-identified as coping reasonably well, were recruited for this study from the wider community using advertisements in local newspapers, flyers, newspaper articles and word of mouth. Those who exhibited significant levels of earthquake related distress were referred for appropriate treatment and those who had previously sought treatment for such distress were excluded from the study to ensure that this sample was comprised of people who were indeed ‘coping well’ with the earthquakes.

Information about participants’ demographics and psychological, emotional and behavioural symptoms was gathered by conducting a clinical interview and asking participants to complete a series of questionnaires. Contrary to expectations, results did not show that participants were drinking more since the earthquakes began, and level of substance use was not associated with the severity of traumatic exposure experienced or with psychological distress.

Interestingly, a large proportion of participants reported drinking to cope with symptoms of anxiety and depression, despite self-identifying as coping well with the earthquakes and their effects. Participants’ current alcohol consumption was related to coping-related motives for drinking, which suggests that those who endorse coping-related motivations for
drinking exhibit higher levels of alcohol consumption post-earthquake than those who do not drink to cope with symptoms of anxiety or depression. Self-reported psychological resilience was not associated with current substance use, however it was correlated with motivations for drinking. Higher levels of coping motives for drinking were related to lower levels of psychological resilience. Thus, it appears that those who have a lower capacity to positively adapt to or recover from a traumatic experience are more likely to consume alcohol to cope with negative affective states following exposure to a mass trauma than those who exhibit higher levels of psychological resilience.

Although these results are preliminary due to the small sample size and warrant further investigation, they do provide insight into the mental health and substance use patterns of our community after a devastating natural disaster, and have the potential to aid in the process of identifying factors that promote psychological resilience for the benefit of future survivors of trauma.
Rachel McDonald  
*Christchurch Youth Hub Evaluation*  

Supervisors: Dr Ria Schroder, Dr Sue Bagshaw  
Sponsor: Canterbury Branch Trust Board of the New Zealand Federation of Graduate Women (Inc.)

**Introduction**  
For many years, agencies have been looking for ways to improve the outcomes for young New Zealanders, and the Christchurch earthquakes provided youth services with a unique opportunity to explore new options, and ideas, for their future. The Youth Hub Barbadoes (YHB) is an innovative, collaborative, initiative made up of national and local government and non-government organizations that offer a variety of services for young people aged between 10 - 24 years.

**Aim**  
The purpose of the present study was to continue developing an initial assessment of service managers’ perceptions of, and their visions for, the YHB. The results from this project will also contribute to the on-going development and evaluation of the YHB.

**Method**  
Fifteen service managers working at the YHB were interviewed individually by students from the University of Canterbury, during March – December 2012. During these interviews managers were asked about their vision for the YHB, as well as current and future benefits and concerns about the YHB. Managers were also invited to discuss the positives and negatives of the ways in which they worked in the past and how that compared with how they were working at the YHB. The interviews were audio recorded, transcribed verbatim and analysed using thematic analysis. Thematic analysis emphasizes pinpointing, examining, and recording patterns (or "themes") within the data provided in the transcripts.

**Results**  
The interviews with managers provided an overview of the service managers’ perspectives of the YHB and how it was to work in a co-located service. Thematic analysis revealed five themes. These included the value of co-location, sustainability of the YHB, positive youth development, the YHB as a comprehensive, holistic service, and finally, management and direction. Due to space constraints, only three of these are presented in this report. The theme ‘the value of co-location’ indicated the high value that the service managers placed on the opportunities that being co-located with other services at YHB provided, especially in terms of collaboration. Co-location was valued because it provided opportunities for building relationships, networking, and working collaboratively. Specifically, the managers identified many examples where working together was more beneficial for themselves, their organization, and their young clients, than it was to work in isolation. For some the benefits related directly to how co-location made it easier for young people to connect with a range of services:

> Um, the benefit for the young person is that they can come to a place, and assuming there’s a connection made from the advisors here, that’s just as easy to make a connection with one of the advisors in one of the other sectors of services... and linking in, hand-holding, I guess if you like, to other support structures, so, yeah, making it easier, so making it easier in terms of a personal connection, but making it easier as well in terms of that geographical proximity, you don’t want them travelling to all corners of the city.

For others co-location provided an opportunity for services to work more closely together to improve their own knowledge of other services and in doing so improve the types of services they could provide for young people:

> Oh well I think for us, initially the work with children and youth it was very new, and I think you can always learn from those who know the area better, but also, to have knowledge of what Youth Health’s currently offering, Action Works, you know the Youth Shop and everything, that in our work, that shared knowledge, that we know what’s happening in here, and it’s just this natural transition as well for families, you know it doesn’t seem right to say ‘oh well if you ring this place or go there.’ We know this information now, and we can work together, so again, sort of trying to bridge all those gaps, and just make journeys for people easier, as they go through service, sort of linkup.
Co-location also provided an opportunity for smaller organisations to get together and provide a strengthened voice while also maintaining their own individuality. This was perceived to have benefits for the sector as a whole as well as providing improved opportunities for service funding.

... but additionally it offers the opportunity and I guess this is a benefit to us as well, but for the sector more so, of a stronger collective voice, and a stronger collective presence, um, I can see that being helpful in areas of efficacy, and ah, fundraising.

The second important theme was ‘sustainability of the YHB’. Managers expressed fears around how the YHB would develop if it did not secure adequate support and funding from outside bodies. In particular they noted the vulnerability of the concept without such funding and political support.

...um, so the worrying thing is about its [the Hub’s] sustainability, and so sustainability in terms of financial sustainability but sustainability in terms of, does the, does policy, government sector, support the hub? Support the hub as a concept, but equally and financially, to make us sustainable? Because if that doesn’t happen, then this has a huge risk of just toppling over, yeah.

The third major theme indicated the managers’ desire to encourage ‘positive youth development’. This involved providing opportunities for young people to have access to a range of developmental experiences.

Like, hoping to do youth development things like getting young people to decide what kind of competencies they’d like, so our ideas and things like cooking and growing vegie, but they might want something else, or maybe one of my patients is saying ‘can I help organize a youth food bank?’ another has said ‘can I help do Facebook?’ another one has said ‘I’d love to do DJ-ing’ so we can link them up with the radio station, or like White Elephant, I think they’ll come up with all sorts of things, young people in my experience, have loads of great ideas, and it’s about how to help them fulfil those ideas, and give them access to means for them to do that.

Managers also expressed the desire to see youth involved in the future development of the YHB, even if they weren’t sure how to make that happen. Firstly,

Actually maybe the most, the first important thing, is young people being involved in the vision, and being consulted, and I mean, it’d be great if more young people could be coming to meeting sometimes, or I’m not quite sure how we’d do that.

Some managers even went so far as to suggest that the YHB should be primarily run by young people.

Ideally what I would like is the hub actually run by youth so that every, all the people, running my service, all the young people, or the people that are running everything that there are young people and that um that would be the ideal, because that's the role model you're seeking. Um, instead of people my age wandering here, in here, and you know, we're well-meaning but I've got, I can only speak of the Facebook crew that I've got back in my office, and they're all pretty much 21 or 20 and they've made this, um, Facebook thing really work, because they understand it. I can see, I saw the possibilities and knew what I wanted, but they made it, and I think that's where I'd like to see it go is that, I mean surely you're not going to have a youth doctor you know, there are some professions that you're going to have scattered around, but ultimately wouldn't it look nice, be nice to greeted by your own, you know generation so to speak?

Conclusion
This study has identified five major themes in its analysis. These themes present the initial perceptions of managers involved with the YHB in its early developmental stages. As such they provide valuable information about the potential priority areas of focus in the future development of the YHB. They also provide important baseline information to form the foundation of an on-going, multi-methods, process and outcomes evaluation.
Inflammatory bowel disease (IBD) comprises Crohn's disease (CD) and ulcerative colitis (UC). These are conditions where, for reasons unknown, an overactive immune system causes inflammation of the bowel. This is a chronic disease causing diarrhea, abdominal pain and fatigue.

CD and UC differ in what portions of the bowel are involved and to what extent the bowel wall is inflamed. CD can affect any area of bowel whereas UC only affects the large bowel. Another key difference is that CD involves the entire thickness of the bowel wall, leaving patients at risk of rupturing their bowel. This event is an emergency that requires surgery and can lead to serious consequences. UC only involves a superficial layer of the bowel wall so bowel rupture is rarer. Both of these conditions are lifelong, causing suffering for many worldwide.

The purpose of this study is to look at the characteristics of CD and UC in the Nelson region. IBD research has never been performed in Nelson so this will be very useful to doctors treating patients in this region. We looked through a prospectively collected database kept by the specialist gastroenterology nurse. This had noted every patient in Nelson diagnosed with IBD in the last 6 years. We also used clinical notes to obtain information about how these people were managed. After collecting all the data, we were able to begin analysis.

What are people most commonly diagnosed with?
54% of IBD diagnosed in Nelson was CD, and 46% was diagnosed as UC. In Nelson over half of CD patients (56%) were diagnosed between the ages of 17 and 40. The most common location was in the large bowel only (40%). The vast majority of patients (64%) were diagnosed without any complications. In Nelson, UC is most commonly diagnosed between the ages of 17 and 40, however the average age of diagnosis is older in UC than in CD. The most common extent of inflammation was that involving the whole colon (37%).

What medications are most commonly used?
90% of CD patients and 91% of UC patients used 5-ASAs. Oral steroids were more commonly used by CD patients than UC (72% vs. 60%). There was a marked difference between CD and UC for use of immunomodulators (IMs) (azathioprine and 6_MPs). 65% of CD patients required IMs and only 39% of UC patients. For those who used Azathioprine, 50% tolerated the drug and stayed on it without any problems and 50% could not tolerate the drug or it was ineffective. 24% of all users of Azathioprine experienced side effects of the drug. The most common side effect of Azathioprine was nausea and vomiting. Biologics (infliximab and adalimumab) were more commonly used by CD (19%) than UC (4%) patients.

How many people require surgery?
The majority of surgery was undertaken on the CD patients, with 34% of patients requiring surgery on their bowel and 15% requiring perianal surgery. In the UC patients only 9.6% of patients required bowel surgery. The average time from diagnosis to first surgery in the CD patients was 4 years. The most common reason for CD patients to have a bowel operation was stricturing (or narrowing of the bowel) at 37%.

In summary, CD is more common than UC in Nelson. It is most often diagnosed in people aged 17-40 years, involving the large bowel and being uncomplicated. UC is also most commonly diagnosed in people aged 17-40 years, affecting the majority of the large bowel in the bulk cases. The 5-ASA drugs were commonly used in both conditions, as were oral steroids. The immunomodulators were used more frequently in CD patients as were the biologic medications. Azathioprine was used long term by half of its users and a quarter of all users experienced side effects, the most frequent being nausea and vomiting. Surgery was more common in CD. This study will give doctors working in Nelson insight in the pattern and treatment of IBD and should stimulate further research in the Nelson region.
Introduction
There is little doubt that diet affects your health, and we know that eating a good range and quantity of fruit and vegetables is good for you. Vitamin C is a well-known antioxidant that is present in a wide range of food that we eat. The human body is unable to make its own vitamin C, it is also cannot store it, which means all the necessary vitamin C must come from our daily diet. Despite being associated with health, the effects of vitamin C on cancer are controversial. It was first proposed to play a role in slowing cancer growth in the 1980’s, but the promising results could not be replicated in a major subsequent trial. However, there have been persistent case reports showing vitamin C to be of benefit in cancer which have continued to fuel the debate. Other studies showed no improvement in outcome with vitamin C treatment. Support for a role of vitamin C in cancer has come from recent studies in our group at the Department of Pathology. Analysis of human tumour samples from patients with endometrial and colorectal cancer has shown that low tumour vitamin C levels were associated with a more aggressive type of tumour. Vitamin C is important for the turnover of one of the most important regulatory proteins in cancer cells, and this connection may explain the role of the vitamin in cancer pathology.

Aims
1- To investigate the consumption of Vitamin C in cancer patients compared with healthy volunteers in and around Christchurch in relationship to national guidelines.

2- To determine whether levels of Vitamin C in tumours from patients with endometrial and colorectal cancer are related to patient outcome.

Methods
1- One hundred survey participants were recruited - 50 cancer patients and 50 healthy controls. Each participant was asked to complete a questionnaire, including food frequency (how often and how much fruit and vegetables were consumed), 24h diet recall (what they consumed the previous day) and a one week food diary, as well as a fatigue symptom survey. The questionnaire was approved by the University of Otago ethics committee, and ensured that no personal details were published. The data provided by the questionnaire was analysed using FoodWorks (dietetics computer programme) to calculate vitamin C levels. Comments around dietary change and use of vitamin supplements were also recorded.

2- A cohort of patients with colorectal (n=50) and endometrial (n=50) cancer, who had donated tissue to the Cancer Society Tissue Bank for research between 1998 and 2008 and who had given informed consent, were reviewed. The vitamin C levels of their tissue samples had been measured before the start of the summer student project (by PhD student Caroline Kuiper). Using a computer-based patient database, outcomes of all 100 patients were recorded (recurrence, metastasis and survival) from medical notes. We determined if there was a relationship between vitamin C levels in cancer tissue and length of time following cancer surgery without recurrence or metastasis (disease-free survival) and length of time until death (overall survival).

Results
1- The cohorts of cancer patients and healthy controls were relatively well matched: both cohorts contained an even number of women and men, with an average age of cancer patients of 58 years, and controls of 56 years. Participants were divided into 3 categories: below NZ recommended daily intake (RDI) (low, <315mg vitamin C/week), above RDI but below Suggested Dietary Target (SDT) levels for chronic diseases (medium, 315-1400mg vitamin C/week), and above SDT (high, >1400mg vitamin C/week). Between 12% and 28% of cancer patients consumed low, 54-71% medium, and 10-34% high vitamin C diets. Controls had a similar vitamin C intake: 14-20% low, 51-58% medium and 26-35% high. The food frequency and one week food diary tended to be similar across all participants. However, specifically in cancer
patients, the 24h dietary recall appeared different, showing a higher proportion of patients consuming low and a lower proportion consuming high amounts of vitamin C. A large number of the cancer patients were surveyed whilst undergoing therapy, and thus feeling unwell, which might explain this finding. Cancer patients reported higher levels of fatigue than controls. There did not seem to be a relationship between their vitamin C intake and their level of fatigue.

2- Vitamin C had no impact on overall cancer survival in either colorectal or endometrial cancer patients. In patients with colorectal cancer, high levels of vitamin C in their tumour samples appeared to be related to longer disease free survival. However, vitamin C levels in normal surrounding tissue from the same patients were not associated with survival, indicating a much more complex association between vitamin C consumption and cancer outcome. In patients with endometrial cancer, no relationship between vitamin C and disease-free survival was observed.

Conclusion
There are still many unanswered questions surrounding Vitamin C and its role in cancer. From the research we have done, it is clear that once diagnosed with cancer, many people seek to lead what they perceive to be healthier lifestyles, and this often leads to an increase in consumption of fruits and vegetables, and may lead to an increase in vitamin C intake. However, our data does not show any significant difference in the proportion of cancer patients vs. controls who are either below, at or above recommended vitamin C consumption. This was in spite of the fact that a greater number of cancer patients had changed their diet recently compared to controls. Doctors’ recommendations and advice are not taken lightly, and patients will take very seriously any passing comments made, that may impact their outcome.

We have seen the first evidence of a possible relationship between tumour levels of vitamin C and cancer recurrence and spread. It is important to note, that these are early data which need to be confirmed in more cancer patients in a controlled clinical trial. There is currently no evidence that taking vitamin C has any clinical benefits for cancer sufferers.
Imogen Nolan

Biological variation of markers for multiple myeloma: What constitutes a significant change?

Supervisors: Associate Professor Chris Florkowski, Dr Ruth Spearing, Professor Peter George, Jo Sanders, Jonathan Reid, Charles Hawes

Sponsor: University of Otago Health Sciences Divisional Summer Scholarships

Multiple myeloma is a cancerous condition affecting plasma cells in the bone marrow. Although in some cases it has a poor prognosis, it can be treated with chemotherapy. Plasma cells are a type of immune system cell that each produces a unique antibody. In multiple myeloma, these cells produce large amounts of a single type of antibody in an unregulated manner to the point where it can be detected in the blood. Measuring levels of this antibody and its components is the basis for disease monitoring. These markers include the antibody itself, a fragment called serum free light chains (SFLC) and the amount of tumour antibody, sometimes called the ‘M spike’ or paraprotein.

In order to decide whether the disease has progressed or responded to treatment, doctors will look at changes in these laboratory markers. An important consideration, however, is what constitutes a clinically significant change in results. For example, the difference between two results could be due to variations arising from repeated measurements in the laboratory. It could also be due to natural variations in the marker in any individual person, called biological variation. There are ways of assessing how much any marker needs to change in order to be certain that the change is not due to the combined effects of analytical and biological variation. This is called a “critical difference” or “reference change value”. At the present time, there is not a lot of information about biological variation of myeloma markers and none so far, in patients going forward in time. Our aim was thus to measure these markers in patients going forward and also comparing them with results from patients obtained previously and use these to derive critical differences for each marker. In that way, we aimed to be able to decide which is the most reliable.

Multiple myeloma patients with stable disease were identified who had at least 3 measurements of each of the markers. Another group of 22 patients had blood tests taken at weekly intervals for 4 weeks. Antibody and SFLC levels were measured as well as M-spike quantity on each patient sample. M-spike measurements were done both on laboratory instrument and manually using a dedicated gel and a machine called a densitometer which scans the gel and is then read by an observer. Retrospective data were obtained from a database and scanning available gels. Total variation was calculated for each myeloma marker in each group and used to calculate the critical difference. It was then possible to compare these with the changes set by guidelines for what indicates a response to treatment. We also investigated how reproducible the gel scanning technique was between different observers.

In the group going forward, critical difference for the antibody was 17.5% and 60% for SFLC. M-spike had a critical difference of 23%; and 41% by laboratory instrument. From the retrospective cohort we found the critical difference for antibody measurements was 46.6% and 105% for SFLC. Critical difference for M-spike was 69.6%. We also found up to 11.9% variation between observers in reading the gels.

For accurate monitoring of stable multiple myeloma, the antibody level is therefore the marker with the lowest variation and critical difference, compared with the M-spike measurements where the critical difference is higher; the 69.6% value obtained retrospectively exceeds the level of >50% reduction in M-spike considered to be a partial response to treatment by an expert international group.

While immunoglobulin measurement is automated on a machine, densitometry involves a lot of manual steps which introduce variation and make it less reliable. Variation in reading between different operators may also make this even less reliable. There is less variability in all markers in patients going forward and this needs to be confirmed in samples which we intend to obtain over a longer follow-up time period.
Lucy Peterson

Reducing barriers to practice nurse involvement in general cervical screening and understanding effective methods of inviting and engaging priority women in cervical screening in general practice

Supervisors: Dr Ruth Savage, Dr Kim Burgess, Jackie Cooper

Sponsor: Partnership Health Canterbury PHO

Introduction:
In 1990, the National Cervical Screening Programme (NCSP) was started in New Zealand. This programme tries to make sure women, aged 20-69 years, have a smear test to check for cervical cancer every three years. So far it has been successful in lowering the number of women who get cervical cancer and die from it. However, this has not been the same for all women in New Zealand.

Maori, Asian and Pacific Island women do not go for a smear test as often as other women. Some of these women are more likely to get cervical cancer and are also more likely to die from it. For these reasons, the New Zealand Government has called these women a ‘priority group’. General Practice has an important role in increasing the number of these women getting regular smear tests.

Another student project, done in 2007, showed that practices that have both a doctor and a nurse available to do smear tests have a high number of women getting checked. This study builds on the 2007 study and looks at what is helping or stopping nurses from being involved.

Aims:
• To understand what is helping or preventing nurses being involved in testing women for cervical cancer.
• To look at how practices are inviting women to come in for an appointment for a smear test
• To understand how practices are trying to increase the number of Asian, Maori and Pacific Island women getting checked, and how successful this is.

Method:
A survey was sent to nurses in Christchurch. This survey had two parts:
(1) Questions about the individual nurse (“are you a smear taker?” and “where were you trained?” etc)
(2) Questions about the General Practice that the nurse belongs to.

All answers were entered onto the computer to look for patterns. A statistical test was then done to see if there was anything that was similar about nurses or the practices they work in that led to a higher screening rate.

Interviews were also done with some GP’s. These GP’s came from practices that have a high number of Maori, Asian and Pacific women. This information was also collected and looked at for trends.

Results:
Two hundred and forty nurses from 97 different general practices around Canterbury completed the survey. Nearly half of those that responded were current smear takers. Of these nurses most were trained at the Family Planning Association, received funding from their employer to complete the training course and were given paid leave from work for this purpose.

The three main reasons why nurses were not smear takers were: “GP’s do their own cervical smears”, “other responsibilities within the practice” and “no opportunity provided by the practice.”

At a practice level three factors were identified that were linked with a higher screening rate:
• Offered smear taking outside of normal business hours
- The fee for a nurse to do a cervical smear was lower than for the GP
- Where women were contacted, using only one type of communication (i.e. only letters) to let them know they were due for another smear appointment.

Strategies for 'priority women', and referral to funded clinics were not associated with higher screening rates. However, they have mainly been used in practices that have a high proportion of Maori, Asian and Pacific women.

**Conclusion:**
This study has shown that many nurses were involved in cervical smear taking and were supported by their general practices. Low cost, out of hours access and simple, consistent invitations were associated with higher screening rates.

Because this study has shown that having a specific strategy for ‘priority women’ does not appear to correspond with an increased screening rate compared with other practices, the next step is to see if these strategies were effective within the practices in increasing screening rates in these women.
Yousif Rassam  
Pulmonary Arterial Hypertension – understanding our patient population. An audit of the Canterbury PAH clinic  

Supervisors: Dr Bronwen Rhodes, Associate Professor Lutz Beckert  
Sponsor: Maurice & Phyllis Paykel Trust  

Introduction:  
Pulmonary Arterial Hypertension (PAH) is a rare and progressive disease which has a devastating impact on a patient’s quality of life, as well as shortening their life expectancy. It develops when the vessels carrying blood from the heart to the lungs become narrowed and thickened increasing the work the heart has to do to pump blood, which can lead to heart failure. Patients with PAH are estimated to live an average of only three years following diagnosis, if left untreated. Thankfully, new treatments such as sildenafil and bosentan have recently become funded for PAH in New Zealand. With these new treatments now available, the need has arisen to review our specialist Canterbury PAH clinic (founded in December, 2005) and optimize its service delivery to patients.

Aims  
The aim of this study is to better understand our PAH population through assessment of disease severity, survival statistics, survival predictors, quality of life and patient satisfaction.

Method  
Our research involves a clinical notes audit of the 51 patients who have attended the clinic since its inception. There are four dimensions to this audit. The first dimension is determining a timeline of the patient journey i.e. how long were patients symptomatic, when were they diagnosed and when did they first attend the PAH clinic. The second dimension is looking at disease severity from the point at diagnosis, and then following their progress over months to years. The REVEAL score, a score which may predict a patient’s chance of survival based on a combination of clinical signs and investigation, was also calculated for each patient. The third dimension is looking at the quality of life of our patients through an internationally utilised CAMPHOR questionnaire. Finally, the fourth dimension of our audit is looking at patient satisfaction through a questionnaire formulated specifically for our Canterbury population.

Results  
The study population consists of 51 patients; 33 are females. As of December 2012, 26 are alive with an average age of 62 years. The predominant ethnic group identified by patients is New Zealand European, and five patients identified as Maori. 31 (60.8%) of PAH patients report being symptomatic for less than a year before a diagnosis of PAH was made. However, 9 (17.6%) were symptomatic for over two years before being diagnosed. It then took around 9.5 months for the provisional diagnosis of PAH to be confirmed by an invasive procedure known as a right heart catheter (RHC). On average, patients saw 2.8 doctors before seeing a PAH specialist.

A cause for PAH could not be found in 22 (43%) of our patients and so their condition was labelled ‘idiopathic’, while in 29% it was a result of a connective tissue disease (such as scleroderma). At diagnosis, 26 (51%) patients had a WHO functional class of III which meant they had marked limitation of physical activity. While they were comfortable at rest, less than ordinary activity caused severe shortness of breath, fatigue and chest pain. This is exemplified by the six-minute walk test, where patients are asked to walk around a set 30m track for six minutes as fast as they are able. The average distance covered by patients during this test is 303 meters, which is considerably less than the 600 meters that healthy individuals are expected to cover. 74% of patients who began treatment did so within six months following diagnosis with a RHC. 31 patients (63%) were only ever treated with sildenafil alone, while 7 (13%) were treated with two PAH-specific drugs.

Following treatment with sildenafil, our population group on average improved their six-minute walking distance. The mean percentage improvement of six minute walking distance is 10.6% (n=20) at six months and 24.34% (n=18) at one year of treatment. Our patients were found to have had around 2.2 admissions to hospital for cardiac or respiratory reasons, and had 1.33 RHCs performed. The average time of survival following diagnosis of those in our population who have died is just over two years (25 months). This ranges from as high as six years to as low as three months. 1, 3 and 5 year survival of our group was 85%, 50% and 21% respectively. We found that survival was worse in patients who had a REVEAL score of 8 and above, in those with the highest levels of a protein marker known as brain natriuretic peptide (BNP), and in patients with connective tissue disease.
We had 24 out of 31 CAMPHOR surveys returned, giving us a response rate of 77%. The CAMPHOR survey is divided into three parts assessing symptoms, activity and quality of life, with higher scores denoting worse outcomes. Patients with PAH due to connective tissue disease reported worse scores across all outcome measure, when compared to patients in the idiopathic and other category. The average total score for the CTD group was 37/80, compared to 31.4 for the ‘other’ group and 26.6 for the idiopathic category. We found that quality of life and activity scores were associated with six-minute walking distances. Patients with higher walking distances at diagnosis reported less impairment to activity and a better quality of life.

Finally, we had 15 out of 27 patient satisfaction surveys returned, giving us a response rate of 56%. The results from this survey indicate the PAH clinic is providing a good service to its patients. 73% (11/15) of patients strongly agreed that overall they were satisfied with the care they received in the PAH clinic, while 27% (4/15) agreed. Patients reported their experience with staff as extremely positive, particularly with regards to keeping patients informed on their progress.

**Conclusion**

The majority of patients were diagnosed within a year of symptoms developing and started treatment within 6 months of their RHC. However a significant number of our population presented late, with advanced symptoms, signifying a poorer prognosis. Introduction of therapy improved functional status in terms of walking distance, and longer walking distances were associated with better reported quality of life. Finally, patients have been extremely positive about their care at the clinic.
Rachel Sanders  
Substance abuse in pregnancy: Meconium analyses from infants born to a contemporary cohort of Canterbury women  

Supervisors: Dr Stephanie Moor, Dr Grant Moore, Carole Spencer, Professor Lianne Woodward, Associate Professor Nicola Austin  

Sponsor: Canterbury Health Laboratories  

In our society the media publicises the dangers of smoking and drinking during pregnancy. It is also assumed that once a woman becomes aware that she is pregnant she will stop using drugs in order to protect her developing fetus. However some women continue to use illicit substances when pregnant, which puts both the fetus and the mother at risk of complications. Of greatest concern for the fetus is a condition known as neonatal abstinence syndrome (NAS). This is when at birth a child has to withdraw from the substance that the mother was using during gestation. At birth the infant no longer relies on the mother for sustenance via the placenta, therefore the source of the drugs no longer exists and the infant may begin showing the physiological drug withdrawal.  

This study focused on the effects of maternal poly-substance abuse in pregnancy. Between 2003 and 2009, 109 pregnant women in Canterbury were recruited as community controls to participate in this prospective longitudinal study. This control group was matched on socioeconomic indices to represent the full range of household incomes in Canterbury. In order to measure the drug exposures of these women they were asked a series of questions about their habits surrounding drug use. We are however aware that self-report is not a very reliable indicator of drug use since women may be too embarrassed to divulge their recreational use to health professionals since society portrays use as being negative and it can carry negative repercussions. In order to get a more accurate sense of what the fetus was exposed to, meconium samples were collected at birth from 56 infants. Meconium is the first faeces passed by the infant after birth; it starts forming at 12-16 weeks of gestation and reflects cumulative second and third trimester substance exposure of the fetus. The aim of this study was to examine the extent of licit and illicit substances in fetal meconium and compare this with maternal self-reporting of drug use. Since the rates of drug abuse in Canterbury are unknown the exposure of this group of women will inform infant and obstetric care providers of the prevalence of substance abuse in the Canterbury region and help to better prepare them for infants born with NAS even when mothers have not admitted their use of harmful substances.  

Consent was obtained from the parents to collect a meconium sample. This sample was collected within the first 24 hours after birth, frozen and stored at minus 70 degrees Celsius. In the laboratory in December 2012, meconium samples were applied to a solid phase extraction cartridge (SPE) to extract the drugs and their products of breakdown. These were then analysed using a liquid chromatography mass spectrometry (LCMS) method to determine the presence or absence of a range of commonly abused substances.  

From the infants of the 109 consenting women in this study, meconium samples were collected from 56 although only 43 samples contained an adequate amount of meconium for testing. A total of 39 out of the 43 fetal meconium samples (91%) were positive for one or more substances. A total of 30 different substances were detected using the LCMS method.  

Of particular concern was the finding of 3 infant meconium samples positive for drugs of abuse which can induce withdrawal symptoms in the infant after birth: one positive for methadone, one positive for methamphetamine and one positive for three different benzodiazepines. None of the mothers had reported the use of these substances.  

Cigarettes: 7 of the 43 mothers reported that they smoked cigarettes during their pregnancy; however 21 of the meconium samples were positive for cotinine, a product of nicotine breakdown. This included all 7 self-reporters and another 14 who had denied use. We also looked at whether the mothers had reported that they lived in a household where there was a smoker as this may have exposed them to passive smoking. However the addition of this information did not account for the other positive results so we assume that the exposure was due to second hand smoking outside the home.  

Cannabis: In the control group only one mother reported the use of cannabis during her pregnancy although there were no meconium samples positive for cannabis or any of its products of breakdown. However there are methodological
problems with the detection of cannabis in meconium, we are not sure whether or not our negative results are reliable since the rates of cannabis use in New Zealand are known to be very high.

‘Over the counter’ drugs: All of the mothers in this control group denied using opiates during pregnancy; we did however discover that six of the meconium samples had positive opiate results. These results included the drugs codeine and buprenorphine which can be found in ‘over the counter’ cold remedies as well as pain medications. It is probable that these women were unaware that they were using potentially harmful substances during their pregnancy.

By extrapolating the data from our sample population we can see that at least 7% of pregnant women in Canterbury had exposed their fetus in-utero to drugs of abuse. Further research examining the neurodevelopmental outcome of these children is on-going. We assume that the high rate (49%) of meconium samples positive for nicotine and its products of breakdown is due to passive smoking and exposure outside the home. It is hoped that the changes in the law about public smoking, namely the Smoke- Fee legislation of 2004, which occurred during the course of the study will significantly reduce these rates. There are known problems with the detection of cannabis in meconium therefore our negative results may not be reliable since the rates of cannabis use in New Zealand are known to be very high.

Of concern is the 14% of pregnant women who have unknowingly used opiates during their pregnancy presumably due to the use of ‘over the counter’ cold remedies and pain medications. Improved labelling and better public education about the potential harmful effects of these medications is important.

In addition, there is the continuing development of new designer drugs in our society. In some cases these drugs are initially marketed as being safe recreational substances which are later found to be harmful and taken off the market. Due to the ever evolving nature of drugs and their associated culture research of this type will need to be conducted at regular intervals if we wish to apply the findings to the current population of pregnant women.
Katie Sleeman
One size does not fit all in rehabilitation: What do Maori perceive as important during their inpatient journey?

Supervisors:  Dr Debbie Snell, Ms Olivia Paku
Sponsors:  Rapaki Branch of the Maori Women’s Welfare League and Older Persons, Orthopaedics & Rehabilitation, Canterbury District Health Board

Background:
Burwood Hospital accepts patients from the south island and a big part of the north island for rehabilitation following brain injuries and spinal cord injuries (SCI) within New Zealand. Within this group according to the NZ census there is a relatively disproportionate statistic of Maori patients who are transferred as inpatients to either the Burwood Spinal Unit (BSU), or to the Brain injury Rehabilitation Services (BIRS), after a motor vehicle accident or stroke respectively. Within this scope of practice lie the services of Ranga Hauora, a service for Maori patients who are physically, mentally, and culturally impacted from their brain injury or SCI. This service remains a source of support, motivation and understanding within Maori, however it is unclear whether or not these services are what Maori patients deem important in their rehabilitation experience and if this support network makes a significant difference to outcomes of rehabilitation and quality of life.

Aims:
1. Examine the rehabilitation pathways of patients identifying as NZ Maori who are discharging from BSU or BIRS during 2011/2012 to understand what Maori believe is important in rehabilitation.
2. Investigate the nature of involvement of the Ranga Hauora services during the patients admission

Methods:
This was a small pilot study using a mixed methods approach to quantitative and qualitative data collection and analysis. Participants were eligible for inclusion if they identified as NZ Maori, were over 18 years of age, and were discharged from either BIRS or BSU within the last 12 months. Quantitative data was extracted from clinical records by file review for 20 patients and was analysed for demographic, clinical, and social characteristics. Prior ethical approval was sought for the qualitative phase, which involved two participants from each service who were interviewed in retrospect about their experience and their perspective (both BSU and BIRS patients were matched for gender and age). The interviews were based around questions pertaining to their rehabilitation perspective to cover a Maori viewpoint of their inpatient journey and what they perceived as important. The interviews were digitally recorded, transcribed, and analysed using a general inductive approach to thematic analysis. This involved close examination of transcripts and comparisons across the four interviews to determine patterns and themes in the data.

Results:
Quantitative findings:
File review from 20 BSU and BIRS patients discharging within the last 12 months, revealed an average age of 37 years (sd=13.9), and 51 years (sd=5.2) respectively. There were equal numbers of men and women identifying as NZ Maori, were over 18 years of age, and were discharged from either BIRS or BSU within the last 12 months. Quantitative data was extracted from clinical records by file review for 20 patients and was analysed for demographic, clinical, and social characteristics. Prior ethical approval was sought for the qualitative phase, which involved two participants from each service who were interviewed in retrospect about their experience and their perspective (both BSU and BIRS patients were matched for gender and age). The interviews were based around questions pertaining to their rehabilitation perspective to cover a Maori viewpoint of their inpatient journey and what they perceived as important. The interviews were digitally recorded, transcribed, and analysed using a general inductive approach to thematic analysis. This involved close examination of transcripts and comparisons across the four interviews to determine patterns and themes in the data.

Qualitative Findings:
1. Importance of a Maori Worldview:
An important message and superordinate theme that was conveyed by the four participants was the importance of a Maori worldview in rehabilitation. An example of a subtheme of this was the understanding of cultural issues within the Maori worldview, quality not quantity of time with patients was valued, and the importance of whanau and cultural connections whilst being away from home. Incorporating Maori activities such as poi and song allowed patients to stay connected to their physical, spiritual, and cultural beliefs.

“That’s not a Maori way, that’s your fellas way of looking at it. Our views are different” (Participant 1)
“I have no problem with working within both worlds, but you know ones got to complement the other” (Participant 1)
“They don’t always do things to a Maori worldview” (Participant 1)
Shared Kai was frequently mentioned by three participants as being an integral part of raising self-esteem and establishing insight into their injury because they were able to “share experiences” and reconnect with others who were in a similar situation but understood the significant of Maori culture.
“I never thought talking was my forte, now I’m into sitting down and yacking” “cos it helps me, need to talk about stuff” – “just gets me off the little sad notes”. (Participant 3)
“Its nice to meet other people, some of them are worse off then you are” (Participant 2)

2. Importance of relationships:
This emerged as another theme embodying the importance of being ‘listened to and treated as individuals’. Once connections through trust and respect were made participants said they were able to open up and explore support networks within the Ranga Hauora team.
“I just wish someone out there understood our journey” – “I was just lucky that I talked to the other people and they told me about xxx” [the Ranga Hauora Services worker]. “Yeah it was my security, if I couldn’t deal with anything there, there was someone there to help me, I go and see xxx” (Participant 3)
“They were my pathway to my whanau. They were my whanau when I was there” (Participant 1)

3. Advocacy
Advocacy and involvement from the Ranga Hauora team emerged for the need for someone to provide clear information, which could be understood.
“I don’t know how to work in a Pakeha system” “xxx [Ranga Hauora worker] helped me to, well make that journey” (Participant 3)
“Doing that for me actually got my life back on track” (Participant 3)
“Well they used to advocate on my behalf, if I needed something they were probably my first point of call” (Participant 1)
“I can’t say anything bad about them. They were always there when I wanted them” (Participant 2)
“If I didn’t come here, I don’t know if I would feel as good as what I feel now” (Participant 4)

The need for more Maori key workers was made clear as an important means of improvement within the Ranga Hauora services.

Conclusion:
Overall all this study highlighted what Maori believe is important in rehabilitation and in particular the power of understanding and working within the Maori worldview. The importance of support, trust, respect, dignity, advocacy, and cultural involvement were also important themes. These findings support the need for Maori key workers who are able to understand, empathise and establish a connection from within a cultural framework. Ranga Hauora continues to be an important source of support and our findings suggested increasing the number of available key workers could contribute to improved outcomes for Maori in rehabilitation. More research is required to explore these preliminary but important findings.
Rebekah Smith

**Thriving after trauma: a study of posttraumatic growth among Canterbury residents following the earthquake sequence since September 2010**

**Supervisors:** Dr Virginia McIntosh, Dr Caroline Bell, Dr Janet Carter

**Sponsor:** University of Otago Health Sciences Divisional Summer Scholarships

Traditionally, research following trauma has focused on the negative outcomes of the trauma. More recently researchers have noted that some people thrive in the wake of trauma. This phenomenon has been termed ‘posttraumatic growth’, and is theorized to emerge from the struggle after the trauma. Posttraumatic growth has been found to occur in survivors of war, serious illness, terrorism, and natural disasters. One study has examined posttraumatic growth in Sichuan, China, after the earthquake in 2008. This studentship is the first research to examine posttraumatic growth after an earthquake in a Western society.

**Aim:**

The current study aimed to examine posttraumatic growth in residents of Christchurch following the Canterbury earthquakes, and to explore the relation of posttraumatic growth to constructs such as positive social connections with others, the level of exposure to earthquake-related trauma, and measures of resilience.

**Method:**

39 residents of Christchurch who identified as ‘coping reasonably well’ after the earthquakes volunteered to be part of the study. Participants were recruited through flyers, websites, newspaper articles, and word of mouth. Participants were screened for psychiatric disorders using the Mini International Neuropsychiatric Interview. Those with psychological disorders developed in response to the earthquakes were excluded from the study, to keep the sample as a group who were coping reasonably well. Participants were interviewed and were asked to complete a questionnaire measuring posttraumatic growth. The Posttraumatic Growth Inventory is made up of five subscales: relating to others, personal strength, spiritual change, new possibilities, and appreciation of life. The questionnaire included statements with a rating scale to indicate the extent to which participants identified with each statement. Participants also completed measures of resilience, social functioning, subjective levels of distress experienced during the earthquakes, and objective exposure to traumatic events such as seeing buildings fall or people injured. Finally, demographic information was collected, including age, education, and ethnicity. Data were entered into the database Progeny, and analysed using the statistical package SPSS.

**Results:**

36 of 39 participants were found to exhibit posttraumatic growth. The most endorsed subscales were personal strength and appreciation of life; these included such statements as ‘I have discovered that I’m stronger than I thought I was’, and ‘I changed my priorities about what was important in life’. Second, exposure to a higher number of traumatic events was associated with higher levels of posttraumatic growth. Interestingly, participants who had spent a longer period of time in the education system, such as those with Bachelor degrees or Postgraduate degrees, were found to exhibit more posttraumatic growth. Finally, on the subscale “new possibilities”, older women showed higher levels of growth than younger women, while younger men showed higher levels of growth than older men. This scale included items such as ‘I developed new interests’. These results are tentative as the sample size is small; further data need to be collected to consolidate the results.

**Conclusion:**

A large proportion of Christchurch residents in this sample who self-identified as coping reasonably well showed signs of posttraumatic growth as a result of struggling with earthquake-related trauma or other significant traumas around the time of the earthquakes. In particular it appears that this group of Canterbury residents have been able to develop or identify new personal strengths, and identify new opportunities for themselves since the earthquakes. It seems that higher levels of distress experienced during and since the earthquakes has facilitated opportunities for more growth.
Leon Smyth
Cytochrome P450 CYP2C19 gene analysis and clopidogrel response in acute coronary syndromes

Supervisors: Professor Martin Kennedy, Associate Professor Peter Larson
Sponsor: Heart Foundation of New Zealand

Coronary heart disease is the leading single cause of death in New Zealand, accounting for nearly a quarter of fatalities. Clopidogrel (Plavix) is a drug which reduces blood clotting in arteries. This lowers the risk of heart attacks, strokes and other serious cardiac events in patients. Clopidogrel, in combination with aspirin, is the frontline treatment for people with acute coronary syndromes (ACS), that is, people who have had a coronary event. However, around one fifth of those treated do not respond to the drug, increasing patients' risk of further cardiovascular events. In addition to this, some patients are unusually sensitive to clopidogrel, and are at risk of bleeding.

One of the reasons such a large proportion of patients do not respond to clopidogrel is due to mutations in a gene for a liver enzyme (called CYP2C19) that normally makes the drug active once it has been taken into the body. Everyone has two copies of the gene, but several mutations are known which can damage the gene. The most prevalent are called *2 and *3. These mutations occur most frequently in Asians, Pacifica and Māori. Another mutation, called *17, is known to enhance drug activation, increasing the likelihood of bleeding.

The aim of this project was to determine the genetic make-up of 300 New Zealand ACS patients, using a novel genetic test to identify the CYP2C19 *2, *3 and *17 mutations. Frequencies of these gene variants were determined in the Māori and Caucasian populations, and the patients' drug responses were evaluated in the light of this genetic information.

The results showed that patients with mutations in both of their copies of CYP2C19 were significantly less responsive to clopidogrel than patients with one or no mutations. This was observed using two different measures of clotting. At both high and low doses response to the drug was significantly worse in patients with two mutations. This shows that CYP2C19 mutations which damage the gene are correlated with poor clopidogrel response.

Māori and Pacifica patients were shown to be three times more likely (14.6%) to have two damaged copies of the gene than Caucasian patients (4.2%). Similarly, there was a greater proportion of Māori and Pacifica patients with only one damaged gene (34.1%) compared to Caucasian patients (24.6%). All bar one of the mutations detected in the cohort were *2, and only one *3 mutation was found. The *17 test and further gene analyses are still being completed.

The novel gene test established here was also a clear and fast method for examining the gene. Therefore, this test could conceivably be used in a medical lab to determine patients' genes before they are treated with clopidogrel. The link between damaged CYP2C19 genes and poor response to clopidogrel was strengthened by this study. For people with two damaged CYP2C19 genes, the new antiplatelet drugs prasugrel and ticagrelor could be used, because they are unaffected by CYP2C19 status. This could lead the way for more effective treatment for people with ACS.
Nicole Sycamore
Assessment of the health utilisation of a group of high risk children to age 4 ½ years of age born to mothers on methadone and a comparative control group

Supervisors: Associate Professor Nicola Austin, Carole Spencer, Professor Lianne Woodward, Dr Stephanie Moor

Sponsor: Cure Kids

It is estimated that about 19,000 New Zealand adults have a drug use disorder. In Christchurch the illicit use of opiate drugs such as morphine, heroin and codeine is common and of concern. Those who are opiate dependent may be prescribed the drug methadone to help manage their drug dependency and minimize the harm associated with a lifestyle involving illegal drug use.

The Christchurch Methadone Programme was established in the 1970s, and women who are pregnant or who have young children are given priority in accessing methadone maintenance treatment services, with around 25-30 pregnant women each year on methadone maintenance.

Children born to mothers who use methadone while pregnant may experience withdrawal symptoms when they are born and require hospital care and drug treatment to manage this. These children are more likely to be born earlier and have lower birth weights and head size. Additionally, there is a higher chance of exposure to other environmental health risk factors. These include poverty, poor housing, parents with low educational achievement and poor physical and mental health, disrupted and violent relationships, crime, abuse and family dysfunction.

The health needs of these children and how mothers on methadone maintenance use health services for their children in New Zealand is not well known. Information gained about the use of health services for this high-risk group could greatly assist in the identification of local health pathways for these children in their early years of development.

The aim of this study was to get a better understanding of the physical health of preschool children up to the age of four born to substance dependent mothers, and compare this with a group of children born in Canterbury in the same time period. To do this we looked at how these children used hospital and GP services during these first four years. Ninety-five children born to mothers on methadone and 109 comparison children who are part of an on-going study of their development were asked to participate in this study.

Christchurch Hospital and Emergency Department records for all the children in the study were obtained from the Christchurch Hospital database. We obtained general practice records by requesting records from the GPs for those children for whom we had signed parental consent. We then entered the data on health utilization into a statistical programme.

We had a good response rate from the GPs, obtaining records up to age four of 72% of the methadone exposed and 83% of the comparison children. We found that both groups of children visited their GPs a similar number of times each year. However, children in the comparison group had a higher number of After Hours visits across all ages compared with the methadone exposed children. The methadone exposed children visited their GP more often for motor concerns, which included developmental delay, delayed walking and walking difficulties. However both groups visited their GP a similar number of times for all other early childhood illnesses. The records on immunisations were found to be incomplete as not all children were up to date with their four-year immunisations, and some were found to be using multiple sources for immunisations. Further investigation to account for these gaps is needed to identify any differences between the two groups for completion of immunisations to age four years.

Both groups of children were admitted to hospital, attended outpatient appointments and visited the Emergency Department a similar number of times. Methadone exposed children however had a higher number of hospital stays for trauma-related reasons during infancy (between the ages of 0 and 2). They were more likely to attend paediatric outpatient appointments across all ages, and between the ages of two and four to attend for developmental and behavioural concerns, compared with the comparison children. They also had a higher number of visits to audiology and ophthalmology outpatients.

Overall, children in the methadone exposed group, despite their high-risk status, were accessing health services at a similar level and for similar reasons when compared with the comparison group of children. The main differences...
identified between the groups were the higher use of After Hours care in the comparison group, and the higher number of visits to the GP and paediatric outpatients for development and behavioural concerns in methadone exposed children.
Harmony Thompson  
*Does early variation in sample separation time affect plasma glucose analysis? Implications for glucose meter evaluation*

**Supervisors:**  Dr Helen Lunt, Associate Professor Chris Florkowski  
**Sponsor:** Guardian Trust/ RG Bell Charitable Trust and the Diabetes Training & Research Trust

There are 200,000 people with diabetes in New Zealand. Many of them rely on their glucose meters for monitoring their glucose levels and making decisions about their diabetes medications such as how much insulin to inject. However, this year PHARMAC is withdrawing the funding for current glucose meters for most patients and changing over to a cheaper brand of meters and strips. This is expected to save the taxpayer about 10 million dollars a year.

This has caused concern in the diabetes community; they questioned the accuracy and usability of these new meters. A general comment was that the new meters were reading higher than the old ones, hence some people worried about overdosing on their diabetes medications, or not being able to manage their hypoglycemic (low blood sugar) episodes based on the readings from the new meter.

The study results from my studentship are divided into two parts, one of which compared results from the new glucose meters with results from the old ones. At the same time, we also managed to answer a second set of questions, which I will discuss later on.

For the first part of my study, I randomly recruited 60 people with diabetes from the outpatient waiting room of the Christchurch Diabetes Centre. The two types of glucose meters we compared were the Accu-Chek Performa (the old expensive meter) and the Caresens™ N POP (the new cheaper meter). After the participants had consented to the study, we did a finger prick test and measured this blood sample with the two different meters.

Our results showed that, as predicted by the patients, the Caresens is indeed reading higher than the Performa meter. The Caresens glucose results are on average 0.5mmol/L higher than the Performa values. However, on analysis, we found that despite the small variation in the readings, the results will not lead to the self-management errors that people feared.

The second part of my results is about quite a different topic. It is focused on blood sample preparation techniques, and the effect this has on blood glucose levels measured in the laboratory. When a patient’s blood is collected on the ward in the hospital for a blood test, the sample does not get to the laboratory immediately. If blood sits in a normal test tube without any processing, the red blood cells undergoes a process called glycolysis, decreasing the glucose over time, leading to a measured laboratory result that is lower than the patient’s initial glucose level.

In New Zealand, we are advised to collect blood for glucose measurement into grey top tubes that contain fluoride oxalate, which is believed to be a good glycolysis inhibitor. A study done in 1989 reported a 5-7% drop in the glucose when collected into fluoride tubes in the first hour. This study is very popular; it has been quoted 88 times in the literatures. However, we questioned the validity of that study because they had a small sample size of ten people. Our study is mimicking the 1989 study design but doing it with a much larger sample size of 60 participants with diabetes, also with more rigorous techniques.

For this second part of the study, we took nine tubes of venous blood from the participants’ arms immediately after their finger prick. The nine tubes consisted of four green tubes (lithium heparin), four grey top tubes (fluoride) and one purple top tube (EDTA). We processed each sample slightly differently. Two of the samples were prepared with a technique which we call the “gold standard”, which involves putting the test tube of blood into ice slurry immediately after the blood is collected, and separating the plasma using a refrigerated centrifuge. This sample was kept so cold that it did not have a chance to undergo any chemical reaction or glycolysis. For the other samples, we used a normal centrifuge to separate the plasma from the blood at different time intervals up to an hour.

Our results showed the glucose fell by an average of 2.9% in the first hour, which is lower than expected. We also compared the results of the lithium heparin samples (they contain a gel plug) which we centrifuged straight away, with the fluoride gold standard ones. We found the results are very similar, with a difference of only 0.07mmol/L.
In conclusion, our results show several things: Firstly, the new glucose meter is indeed reading higher than the old one, however, not enough to cause clinical problems. This will be very reassuring to those with diabetes who have been obliged to change over their meter.

Secondly, immediately centrifuging blood samples in lithium heparin tubes with a gel plug at room temperature gives a result as accurate as the gold standard of refrigerated centrifugation. This is very important for researchers as this is a more convenient type of sample preparation.

Thirdly, recent papers have criticized some of the historic papers that measured glucose in community settings. The glucose cut offs used to define a diagnosis of diabetes are based on some of these studies. There are concerns that delayed sample preparation may have resulted in a lower glucose by 5-7% in these studies and that they may therefore not be truly representative. If our findings of a smaller decline in glucose (around 2.9%) are applicable, then these historical studies may still be valid.

Finally I would like to thank my sponsors: Guardian Trust/RG Bell Charitable Trust for sponsoring me with this project. The Diabetes Society Christchurch Inc. also provided consumables for the meter study and will be helping with the dissemination of our results. In addition, a huge thanks to my supervisors Dr Helen Lunt and Associate Professor Chris Florkowski, the research nurses Flo and Helen, and the lovely people in the Diabetes Centre for helping me with this project.
Alice Turner  
*Christchurch Breast Cancer Register: Management of Breast Cancer*

**Supervisors:** Professor Bridget Robinson, Ms Val Davey, Dr Birgit Dijkstra, Dr Gavin Harris, Dr Logan Walker, Ms Helen Morrin

**Sponsor:** New Zealand Breast Cancer Foundation

**Introduction:**
The aim of this project was to review the current pattern of care in the Christchurch Hospital (CHP) Breast Cancer service.

The Christchurch Breast Cancer Register has recorded comprehensive data on all consented breast cancer patients diagnosed within the Christchurch region since June 2009. The register records data from both public and private patients and includes patient demographics, family history, pathology, treatment and outcomes. This review is limited to the 201 public hospital patients on the Register from June 2009- June 2010. It focuses on several specific objectives, namely referral times including delays in the management process, treatment offered in comparison to guidelines, and surgical complications, especially any effects on other cancer related treatment. The Register provided a large proportion of the numerical data while further data was retrieved from online patient management systems, including descriptive data found by reviewing clinical letters. The data was entered into an EXCEL spreadsheet for analysis.

**Audit of Referral Times:**
Of the 201 patients, 72 were referred from their GP directly to CPH General Surgery Department. Time from GP referral to first surgical appointment was on average 12 days (range 1-38 days). The other patients were referred to CPH via Breast Screen Aotearoa or Canterbury Breast Care. Twenty-six patients were excluded from the audit because they followed different management pathways, for example patients who received pre-operative chemotherapy and patients who had incidental findings as inpatients. For the 175 patients included, the time from the surgical first specialist appointment to theatre was 30 days on average, and longer than 30 days in 59 patients, compared with the guideline of 20 working days. The main reasons for these delays were the requirement for multiple workups, patient decision time or preference and referrals to other specialties required prior to surgery (all reasons described in the National guidelines as exceptions). The average time from theatre to oncology referral was 25 days, and was longer than 30 days for 33 patients. 20 of these patients required further theatre which is one cause of this delay. The Ministry of Health guidelines recommend that radiation therapy be commenced within 8 weeks of theatre and chemotherapy be commenced within 6. The average time from oncology referral to Oncology first specialist appointment was 13 days, range 0-37 days. The average time from oncology FSA to first oncology treatment was 24 days and this included hormone therapy, chemotherapy and radiotherapy. The main reasons for delays were patient decision time, patient personal holidays and surgery complications. Twenty patients who were diagnosed with pre-cancerous lesions (cancer ‘insitu’) rather than invasive cancer are included in this cohort because their referral times were all similar to those with invasive disease.

**Oncology Chemotherapy and Hormonal Therapy Guidelines**
Adjuvant! Online, an online tool designed to predict the benefit of systemic cancer treatment in an individual patient, who has had surgery for invasive cancer (162 patients), was used to calculate the % improvement in 10 year survival rate with chemotherapy and/or hormonal therapy. Data regarding chemotherapy and hormonal therapy administration was then extracted from the register. Overall the use of hormonal therapy was appropriate in accordance to the Adjuvant! Online predictions. All of the patients with a predicted improvement in survival rate of 6% or more received hormonal therapy with 2 patients undergoing surgical removal of their ovaries.

Overall chemotherapy was prescribed appropriately. The greater the survival benefit predicted, then the more likely the patient was to receive chemotherapy. In addition, in the lower survival benefit categories (<7%) younger patients were more likely to receive chemotherapy. Throughout all survival benefit categories the main reason for a patient not receiving chemotherapy was that the risks were deemed to outweigh the benefits of treatment. Examples of these reasons are work disruption, older patients with significant other health problems and preference for alternative therapies.

**Surgical complications**
In total 182 underwent surgery, 224 general breast operations. 41 patients experienced post-operative complications (22.5%), with an operation complication rate of 19%. In 7 patients, complications delayed further cancer-related treatment. The highest complication rate was for mastectomy (surgical removal of the breast) at 25%. Infections
accounted for 58% of all complications. Other complications were on-going pain, scar problems, surgical draining of blood clots or long-lasting fluid collections (seroma) delaying further therapy.

Twenty-five breast reconstructions were performed (10 immediate, 15 delayed), with 4 complications (16%), including asymmetry requiring further surgery, implant mal-rotation and scar revision. These were all late complications and had no significant impact on further breast cancer treatment.

Conclusion:
This review has provided an overview of the management of breast cancer in the Christchurch Hospital Breast Service. Half the women had surgery outside the 20 working day guideline from referral, and average time from surgery to oncology referral approached 20 working days. The results indicate the need for improving the efficiency of the management pathway from initial referral through to surgical and oncological treatments, such as automatic referral to the oncology service even before their operation date. Further review of complications may allow these to be minimised. Systemic oncology treatment was mainly consistent with guidelines. These data are invaluable in the future planning of the Breast Cancer Service to improve patient management and optimize outcomes including survival.
Familial Adenomatous Polyposis (FAP) is a genetic condition, meaning it can be passed from parent to child. Children of an affected parent each have a 50% chance of inheriting FAP themselves. The condition is characterized by the presence of 100 to thousands of polyps in the bowel, which generally appear in late childhood. Due to this abundance of polyps, without treatment, colorectal cancer will develop in almost all FAP individuals.

Early surgery to remove the bowel, as well as strict surveillance of any remaining at risk bowel tissue aim to prevent the development of colorectal cancer. Individuals with FAP also have a greater chance of developing upper gastrointestinal (GI) cancer, so they require screening of this area as well.

The NZ Familial Gastrointestinal Cancer Service has been established to help people manage conditions like FAP and coordinate their surveillance in accordance with the recommended guidelines. The Service generates each patient’s next due date for lower and upper GI surveillance procedures, sends a reminder letter in advance to the hospital that performs the patient’s procedures, after which the hospital department is responsible for booking and completing the procedure.

This project had 4 main aims:
- Define the population of FAP patients in NZ
- Investigate if surveillance of FAP patients is meeting international guidelines
- Investigate the current performance of the surveillance system
- Identify any discrepancies in FAP management between regions of New Zealand

These aims are significant as they identify how the FAP surveillance system in NZ is performing, and help to better understand the current management of FAP in NZ.

Data required for the study was obtained from Progeny (the Service database), and patient files. Data was exported from Progeny to Excel spreadsheets on 20/11/2012, and subsequently used to create a Microsoft Access database, where data analysis was performed. Statistical analysis was carried out in Excel.

There were 110 FAP patients registered to the NZ Familial Gastrointestinal Cancer Service as of 20/11/2012. The patients ranged in age from 2 to 74, with a median age of 36, and a gender ratio of 10 males to 7 females. Thirty-nine patients lived in the upper North Island (postcodes beginning 0, 1, 2), 35 in the lower North Island (postcodes beginning 3, 4, 5, 6), and 36 in the South Island (postcodes beginning 7, 8, 9). For the 53% of patients with age of diagnosis recorded, the range was 6 to 53, with a median age of 24.

Are FAP patients having surgery as recommended? Surgery to remove the bowel has been found to decrease cancer development in FAP patients, so is advised and ideally performed by the late teens. Of the FAP patients who were 18 years of age or older, 76% of records indicate the bowel had been removed. The median age at surgery was 25, and ranged between 11 and 60.

Are FAP patients having lower GI surveillance as recommended? According to international guidelines, generally FAP patients should have lower GI surveillance every 12 months from the early teen years until the age of 75. Of patients over the age of 14, 94% had lower GI surveillance recorded, beginning at a median age of 27.5. Results found the average frequency of lower GI surveillance to be every 27.9 months.

How about upper GI surveillance? Guidelines recommend upper GI surveillance to be performed on patients aged 25 to 75, the frequency of which depends on the individual and can range from 6 monthly to 5 yearly. Of patients 25 years or older who were eligible for upper GI surveillance, 76% had procedures recorded, surveillance beginning at a median age of 32.5. It was found that the interval between a patient’s last two procedures was on average 9.5 months shorter than...
their recommended screening interval, indicating that patients are having upper GI procedures more frequently than recommended.

How has the surveillance system been performing, and does the system benefit the patients? The Service provided procedure due dates for 90% of patients requiring lower GI surveillance. The next step in the system is for the Service to send a reminder letter in advance of the due date. Of the patients with due dates, 49% had a letter sent. When a reminder was sent prior to the lower GI procedure due date, on average procedures were performed 41 days after the due date, within 10 weeks of being due. When no letter was sent or the letter was sent late, this increased dramatically to 286 days. This clearly highlights the benefit of the surveillance system. The aim is for reminders to be sent about 2 months prior to the due date. On average, procedures were performed 114 days after the reminder was sent, so if letters were sent 2 months in advance, theoretically procedures would be performed 54 days after the due date. This indicates that adherence to the surveillance system can successfully result in facilitating procedures to be performed within 10 weeks of being due.

The Service employs the same system for coordinating upper GI surveillance, and results showed similar trends in performance to that of the lower GI system. Regional differences in aspects of the surveillance system’s performance were identified, which are reserved for internal use.

In summary, whilst most FAP patients are having their bowels removed, they are doing so later than internationally recommended. Whilst nearly all patients are having lower GI surveillance, they are starting surveillance later than recommended, and are having surveillance procedures less frequently than recommended. In contrast, patients are having upper GI surveillance procedures more frequently than recommended, however; again they are starting surveillance later than recommended.

The surveillance system, with the Service playing a major role, has been found to be very beneficial. When the system is performed as intended, and reminder letters are sent out to the hospitals before the procedures are due, patients have their procedures performed on time. However, there are 3 main areas in which the system is can improve:

- Generation of procedure due dates for each patient requiring surveillance can be more thorough
- Reminder letters can be sent for more patients, so that every individual with a due date has a reminder sent
- Reminder letters can be sent more promptly

In gaining an oversight of current FAP management, areas that require attention can be identified, which may help to further align the management of FAP in NZ to internationally suggested guidelines.
Model-based therapeutics in ICU: Mechanical ventilation and the modern computer

Supervisors: Dr Geoff Shaw, Professor Geoff Chase
Sponsor: The Govan Family Summer Studentship

A significant proportion of all ICU patients require mechanical ventilation (MV), the controlled delivery of gas directly into the patient’s windpipe by a machine. It takes control of breathing, giving injured lungs a chance to heal. MV is the primary treatment for people with Acute Respiratory Distress Syndrome (ARDS), a potentially fatal condition in which the patient is unable to adequately oxygenate their blood or expel carbon dioxide as a result of lung injury. There are many modes of MV, ranging from a supportive role for patients breathing on their own accord (spontaneous breathing) to strict control of breathing patterns.

Each ARDS patient is unique and therefore responds differently to various ventilator settings. It is important to choose optimal ventilator settings to achieve efficient oxygenation while preventing the lung from becoming overstretched. The major challenge of MV lies with choosing suitable ventilator settings and monitoring the effects on lung function. This remains a constant source of uncertainty, as the injured lung has proven deviously tricky to model due to the variable nature of lung physiology. Because of this, the ARDS lung has remained a proverbial ‘black box’ to clinicians.

Recently, bioengineers have become involved in modelling lung behaviour whilst on MV. The Lung Elastance model was developed in the Department of Mechanical Engineering of Canterbury University to measure degree of lung injury. Lung elastance is a measurement of lung stiffness; the higher the elastance, the stiffer the lung. Alveoli, the minute grape-like sacs that are the smallest units in the lung, are injured in ARDS. These normally open, gas-filled structures fill up with inflammatory cells and fluid that prevents them from carrying out their normal role of gas exchange. Essentially, a high lung elastance reflects tissue injury and inflammation of the alveolar units.

Over the summer, eight ARDS patients were recruited into an observational study in ICU at Christchurch Hospital. Data was prospectively collected from mechanical ventilators onto a laptop computer. The raw data, in the form of pressures and flow rates, was then computed using a program called Matlab. The software derived lung volumes from the raw data, as well as lung elastances and Positive End-Expiratory Pressures (PEEP), the pressure at the end of a breath.

Readings of heart rate, blood pressure, oxygen content and expired carbon dioxide were collected using hospital software (Bedmaster). These variables are widely used to monitor patient condition. Other variables such as patient turning by nurses and ventilator settings such as fraction of inspired oxygen (FiO2) were obtained from patient charts. All these parameters were then graphed and the final result was analysed qualitatively for correlations between traditional indicators of patient condition (heart rate, oxygen content, blood pressure) and lung elastance.

This project illustrates how the lung elastance model could be used to quantify and track lung injury. One patient showed particularly convincing improvement in lung function, illustrated by gradually decreasing lung elastance over an 18-hour period before starting to breathe spontaneously. Another patient’s worsening condition was tracked by a steeply increasing lung elastance. Unfortunately, the patient did not survive. However, lung elastance is highly variable and the model could not handle the extra variability of spontaneously breathing patients. Future research should focus on improving the ability of the model to adapt to this extra changeability. The challenge is now to implement and evaluate this patient-specific tool at the bedside to better inform clinical decision-making in real-time.
Uddaka Wijesinghe

Does 1st trimester HbA1c influence fetal birth weight?

Supervisors: Dr Ruth Hughes, Dr Jo Gullam

Sponsor: Canterbury Medical Research Foundation

Introduction and background

Hyperglycaemia (excess blood sugar levels) during pregnancy has many adverse effects on the fetus and on the pregnancy itself. Maternal diabetes is associated with many complications in pregnancy such as miscarriage, birth defects, pre eclampsia (high blood pressure in pregnancy) premature delivery, and macrosomia (large babies). Studies have also shown that the relationship between glycaemia and adverse pregnancy outcomes also exists at levels of blood glucose lower than that found in overt diabetes. Therefore it is paramount to ensure that a mother has good glycaemic control for the duration of her pregnancy.

The HbA1c (glycated haemoglobin) blood test is a useful indicator of the blood sugar control over the previous 4-6 weeks. This study focuses on how effectively 1st trimester (first 12 weeks of pregnancy) HbA1c levels in women without pre-existing diabetes can predict adverse pregnancy outcomes. The two adverse pregnancy outcomes that will be measured in this study are preterm delivery and large birth weight. The study builds on previous data collected in the department which demonstrated that both high and low levels of HbA1c in the first trimester were possibly associated with preterm delivery in women without diabetes. This relationship did not reach statistical significance, and more data is required to reach a firm conclusion. Previous large scale studies focusing on women without diabetes have demonstrated a relationship between late pregnancy HbA1c levels and preterm delivery and also macrosomia. This relationship was not as strong as the association between the oral glucose tolerance test (OGTT), which is a direct measure of blood glucose, and pregnancy outcomes. This weaker association of 3rd trimester HbA1c and pregnancy outcomes might be because the increased red cell turnover, and changes in iron status in late pregnancy may skew the HbA1c result, this lead to the question of whether 1st trimester HbA1c may show a stronger association. Ultimately this study will determine whether first trimester HbA1c is an effective alternative to OGTT in screening women at risk of pregnancy complications due to their levels of glycaemia.

Aims:

To determine whether 1st trimester HbA1c levels influence fetal birth weight or timing of delivery in women without diabetes.

Method

During 2008-2010 HbA1c, levels were measured in pregnant women upon booking at the maternity clinic at Christchurch Women’s hospital. This resulted in the formation of a database containing HbA1c levels, and the gestational age and birth weight of the baby at delivery. My study involved creating a new database that also included data on other possible predictors of fetal birth weight or preterm delivery. These factors are called confounders, and could be adjusted for in the statistical analysis, if necessary, to ensure that the relationship between HbA1c and the outcomes could be found. Data on the confounders (maternal height, weight, BMI, smoking status, ethnicity, mode of delivery), were from electronic and paper patient records. Birth weights were classified into large for gestational age, normal and small for gestational age. There were 2 classifications for preterm delivery, less than 32 weeks, and less than 37 weeks. The data was analysed by a biostatistician by separating predictors into categories (categorical analysis) and assessing the distribution of outcomes within the categories, a p value <0.05 was considered statistically significant. Logistic regression analysis was also carried out using HbA1c as a continuous predictor of preterm delivery.

Results

Data on 1184 mothers was collected. There was no significant relationship between 1st trimester HbA1c levels and preterm delivery or fetal birth weight. The logistic regression analysis carried out on timing of delivery also showed no significant association. Maternal height, weight, BMI, ethnicity and parity were all significant predictors of fetal birth weight. Smoking was associated with smaller babies, with 40% of smokers having children in the bottom 25% of birth weights. A significant proportion (18%) of Polynesian/Maori women had babies born in the bottom ten percent of birth weights.
Discussion and conclusion
The data from my research is different to the findings of the previous study carried out in the department. This study used more data and found virtually no association between 1st trimester HbA1c and birth weight in women without diabetes. The fact that we tested other proven predictors for birth weight such as smoking, parity, and BMI, and these were all significantly associated with birth weight adds validity to the study. 1st trimester HbA1c is clearly not an adequate predictor of birth weight or preterm delivery in women without diabetes. This is interesting because studies carried out on third trimester HbA1c levels and pregnancy outcomes in non-diabetic women do show an association with macrosomia and preterm delivery. Perhaps conditions in the uterus during the third trimester are much more relevant to the growth of the baby and the timing of delivery than the uterine conditions in early pregnancy. Also it may be that at HbA1c levels below those found in diabetes the effect of 1st trimester HbA1c is too small to determine pregnancy outcome. This study used a large sample size, and the fact that no significant relationship was found means that 1st trimester HbA1c is not an adequate predictor for women without diabetes who are at risk of macrosomia or preterm delivery. A future approach could focus on mothers who have HbA1c levels at the higher end of the normal spectrum, to see if they have different rates of preterm delivery or macrosomia. It would also be interesting to note how the OGTT test performs as a predictor during the 1st trimester. The significant proportion of Polynesian/Maori babies that were born underweight could also be investigated further to see whether this is a product of increased smoking rates among Polynesian/Maori women.
Max Wilkinson
Measuring plasma cytochrome c to assess mitochondrial damage

Supervisors: Dr Michael Lever, Professor Stephen Brennan, Dr Christopher McEntyre, Dr Sandy Slow, Professor Peter George

Sponsor: Canterbury Scientific Ltd

The mitochondria are structures within cells that are essential for providing the energy needs for all higher forms of life. Cytochrome c is an abundant protein in the mitochondria and is critical in this energy generating process. When released from the mitochondria into the cell cytochrome c has a second role as an important signal for programmed cell death, which is called “apoptosis”. Apoptosis is involved in development and controls the natural turnover of billions of cells in the body daily, but when dysfunctional it can lead to numerous diseases including cancer. By an unknown mechanism, following release from the mitochondria cytochrome c can also move out of cells into the blood. The amount of cytochrome c in the blood has been found in clinical studies to be associated with various diseases and organ injury due either to irregular apoptosis or mitochondrial damage. Measuring the amount of cytochrome c in the blood could therefore be useful for studying diseases (to determine if they are associated with apoptosis or mitochondrial damage), and could be used for prognosis and possibly diagnosis. However, current methods for measuring cytochrome c are unreliable at lower concentrations so are less useful for studying diseases where smaller scale mitochondrial damage is expected. The aim of my summer project was to develop and determine the feasibility of an alternative method to measure low concentrations of bovine cytochrome c in calf serum (a form of blood with red blood cells removed) that uses a technique called mass spectrometry. The method I developed has two parts.

The first part of the method is to purify cytochrome c from the large variety of proteins present in serum using a technique called high-performance liquid chromatography (HPLC). HPLC involves pumping the serum samples through a narrow column packed with a material that interacts with different proteins differently, so that the various proteins emerge from the column at different times. This separates cytochrome c from other proteins to allow it to be quantified with reduced interference. One of my jobs for the summer was to work out the conditions that gave the best separation of cytochrome c.

The second part of the method is to quantify the cytochrome c fraction of the serum by connecting the column to a mass spectrometer. Mass spectrometry is an analytical technique that takes charged forms of molecules and accelerates them through a series of magnets, which alters the motion of the molecules depending on how heavy they are and how much charge they can hold. The spectrometer can then detect how much the motion of the molecules changed and therefore calculate the mass to charge ratio of the molecules. The main advantage of mass spectrometry is that it can specifically select for a certain molecule (with a specific mass to charge ratio) and reliably give a signal even at very low concentrations, the strength of which corresponds directly to the amount of the molecule present. Over the summer my research has found that the best way of using mass spectrometry to measure cytochrome c is to use a form of mass spectrometry called MRM (Multiple Reaction Monitoring). In this form, the spectrometer has three chambers. The serum fraction from the HPLC is injected into the first chamber, which only allows molecules with the mass of cytochrome c to pass through to the second chamber. In the second chamber the molecules are blasted with nitrogen gas into fragments. The third chamber then selects and measures fragments of a certain mass corresponding to the fragmentation pattern of cytochrome c which I had determined in a separate experiment. This method has the advantage of greater selectivity as two criteria must be met before a signal is obtained (correct mass and then correct fragment mass), and better sensitivity (as smaller molecules are better at producing signals on a mass spectrometer). Using this method is a novel approach to quantify proteins that gives very promising results and to our knowledge has not been implemented before.

A second novel observation made over the course of this project was that mixing a solution of cytochrome c dissolved in water with the solvent trichloroethanol (a type of alcohol) results in cytochrome c moving completely into the trichloroethanol. This is a property of trichloroethanol that to our knowledge has never been observed before and is an unusual case of a water-soluble protein moving preferentially into another solvent. This potentially very useful observation will be investigated further after this project.

The end result from combining the optimised HPLC with the optimised mass spectrometry is a promising preliminary method that can measure bovine cytochrome c in calf serum down to a concentration of 10 picomolar, which is about a
100,000 -fold improvement over older methods. This method can be adapted for measuring human cytochrome c in human serum, is easy to automate and takes only 25 minutes per sample. It is therefore appropriate for large-scale studies, for example the research at Canterbury Health Laboratories which aims to determine whether mitochondrial damage is associated with the "metabolic syndrome", a combination of high blood pressure and obesity that is becoming more common in New Zealanders. However, before this method can be implemented some problems need to be resolved, using new mass spectrometers that have just been installed, and its reliability needs to be verified, which was beyond the scope of this ten week project and will be done in the coming months.
Cancer screening programmes are used throughout the world to reduce the number of people who die from cancer. A major national screening programme currently used in New Zealand aims to prevent cervical cancer, and is based on a pretty simple principle: when a woman develops cervical cancer it doesn’t happen suddenly. In fact it takes years to go from normal to cancer and during this time there are changes in the cervix that aren’t cancer, but aren’t normal either. These changes are collectively referred to as cervical intraepithelial neoplasia, or CIN, and are graded from 1-3. Cervical screening regularly tests women for these changes by smear testing and aims to stop them becoming cancer. CIN 1 is generally accepted to be mild and normally not treated, while CIN 3 is almost always treated.

However, when CIN 2 is detected in women younger than 25 it can become tricky to know what to do. This is because although CIN 2 might develop into cancer this is actually pretty rare. What most commonly happens is the CIN 2 goes away on its own. This is important because the treatment for CIN 2 (surgical removal of the abnormal area of the cervix) can cause problems with later pregnancies. So, if we treat every young woman with CIN 2, most of them may be worse off for it.

As a result, some practitioners have started to offer a new management strategy for these women: conservative management. Under this approach, young women with CIN 2 can choose to not be immediately treated and instead get closely watched over two years. If the CIN 2 is still present after two years or if it develops into something worse within the two years it will be treated. However, if the CIN 2 is going to go away on its own it is given a chance to do so, and women are spared unnecessary treatment.

To test the efficacy and safety of this approach a number of studies (including one from a previous studentship in Christchurch) have shown a marked reduction in the use of treatment amongst women managed this way, and found no evidence of any harm. However, no one has looked at what happens to conservatively managed women beyond two years. The issue here is that women who have had CIN 2 and not been treated for it might have a higher risk of it coming back later. This would raise questions about the efficacy of such an approach (if it’s just going to come back anyway there’s not much point in withholding treatment), and suggest a possible safety issue.

This is where my project comes in. My aim was to work out the long-term risk of potentially precancerous cervical changes in a group of women who had been diagnosed with CIN 2 but never received treatment for it (due to conservative management being used and the CIN 2 going away on its own). To put the risk in context, I also aimed to work out the risk of such changes among a group of women who had been diagnosed with CIN 1 but never received treatment for it. As mentioned above, CIN 1 is another cervical change that can be picked up by screening but is generally accepted to be low-risk – so conservative management of it is well-established and widely used.

I searched a number of databases to identify all women under the age of 25 who were diagnosed with CIN 1 or CIN 2 between January 2005 and August 2009 at Christchurch Women’s Hospital and Dunedin Public Hospital. I then looked through the full cervical screening records of these women to identify those who never received treatment due to the abnormality going away on its own within two years. This found 106 appropriate women with an initial diagnosis of CIN 2 and 278 women with an initial diagnosis of CIN 1. I then worked out what happened to those women since. On average there was about 4 years of follow-up available for each woman, and 20% had at least 5 years of follow-up data available. This meant I could determine long-term outcomes.

Reassuringly, although a few women in each group developed further pre-cancerous changes (9% of the women with CIN 2 and 12% of the women with CIN 1), there was no statistically significant difference between the groups. This means that the women who had had CIN 2 were at no higher risk than the women who had had the minor changes of CIN 1.
When following any group of women like this one it is to be expected that some will eventually develop cervical abnormalities (that’s why cervical screening lasts over decades of a woman’s life). The fact that some of the women developed such changes is therefore no cause for alarm. What is important is that my project found that the rate at which such changes was occurring was not high. There is therefore no need to be concerned that conservative management is only delaying treatment (rather than preventing it). My results also support the safety of this approach, although on-going trials (including one in New Zealand) will provide more conclusive data.

The option of conservative management can continue to be explored in New Zealand as a possible way for young women to choose to avoid unnecessary treatment.
Annie Yau  
Antipsychotics for older people in Canterbury: Understanding current prescribing practice

Supervisors: Dr Matthew Croucher, Dr Susan Gee  
Sponsor: The Canterbury Health Care of the Elderly Education Trust

Background  
There is increasing concern regarding the frequency of antipsychotic prescribing in the older population as these drugs are associated with increased toxicity, side effects, illness and even death, particularly for people with dementia. In addition they are one of the most expensive drug groups funded by PHARMAC – New Zealand’s Pharmaceutical Agency. There is also concern that some prescriptions may not be made in line with guidelines for best practice.

Little information exists about the use of antipsychotics for older people in New Zealand. A previous study conducted by the Psychiatry of Old Age Academic Unit in Christchurch used data from the National Pharmaceutical Collection to measure rates of antipsychotic prescriptions to older New Zealanders (1). This was followed up with prescriber interviews to explore details of use and compare prescribing decisions with best practice guidelines. Interesting findings included that a surprisingly high proportion of scripts were given as part of palliative care (defined here as end-of-life care) and that a small group of GPs accounted for a large proportion of prescriptions. However, prescription data collected in New Zealand does not record reasons for prescribing, residential status or prescriber characteristics. Our study was conducted to explore these questions, more specifically to measure the proportions of: prescribing due to palliative care, prescribing for people in aged residential care (ARC), and prescriptions made independently by GPs. A good understanding of prescribing behaviour is necessary to develop interventions to improve antipsychotic prescribing.

Method  
The sampling frame included individuals aged 65 years or older who took a new antipsychotic prescription to a community pharmacy in the Canterbury DHB region between July 2012 and mid-September 2012. Data were identified from the National Pharmaceutical Collection and new prescriptions were defined as those for people who had not presented an antipsychotic script in the preceding 4 months. Questionnaires for gathering background information about the prescriptions were sent to the prescribers. Individuals receiving the prescriptions were not contacted and all identifiable personal information was securely stored as approved by the University of Otago Ethics Committee. The form included questions about reasons for prescribing, residential status, prescribers’ clinical setting and how independently prescribers made their decisions.

Results  
A total of 213 people who received a new antipsychotic prescription were identified and questionnaires were returned for 74% of these individuals by their prescriber. This group of 157 people was made up of 56% women and the ages ranged from 65 – 98 years with a mean age of 80. There were no significant differences between the cases for whom completed forms were received and those for whom completed forms were not received in terms of age, sex, the antipsychotic agent used, whether the individual was living at home, or whether the prescriber was a GP. Most people were living at home (61%) rather than in aged residential care (ARC). GPs were the most common prescribers (70%) and the main drugs used were Haloperidol (58%) followed by Quetiapine (28%).

Prescriptions were categorised according to the main clinical context of their use and prioritised in the following order: palliative care (40%) > dementia (32%) > other (28%). Approximately a quarter of the palliative care patients also had a dementia. Within these categories, the more specific reasons for prescribing varied. In palliative care use, the main reasons for prescribing were nausea or vomiting (53%) and agitation, aggression or other challenging behaviours (28%). Amongst individuals with dementia, the main reason for use was to treat agitation, aggression or other challenging behaviours (70%). For other prescriptions the main reasons for prescribing were psychosis (23%) and sleep (21%). Haloperidol was the main drug prescribed in both palliative (86%) and dementia (56%) contexts. Quetiapine was the main drug used in the ‘other’ contexts (56%).

Specific reasons for prescribing also varied according to where a person lived. Agitation, aggression or other challenging behaviours (wandering, calling out etc.) were the main reasons for 59% of prescriptions in ARC but only for 22% of people living at home. Notably, the proportion of antipsychotic prescribing for people living in ARC with dementia for whom agitation, aggression or other challenging behaviours were the main reasons for prescribing was only 19% of
the sample as a whole. For those living at home, the main indication was nausea or vomiting (26%) followed by a range of smaller factors.

The individuals in the sample living in ARC were significantly more likely to have been prescribed to by a GP (89%) than were the individuals living at home (58%). Of the people living in ARC who received a prescription from a GP, 87% were prescribed to by a primary GP of that residential facility. In terms of prescribing decisions, 64% of GPs reported prescribing independently while 19% prescribed on the advice of another medical professional and 17% continued a prescription started by someone else. Overall, psychiatrists were the most likely health professionals to provide prescribers with advice (40%), followed by palliative care teams.

Discussion
These results highlight several potential limitations of previous research and guidelines relating to antipsychotic use for older people. For example, many publications have focused on antipsychotic use for older people with dementia living in ARC who present with challenging behaviours, but only 19% of our prescriptions were in this category and most of the prescriptions were given to individuals who were living at home. Therefore education and guidelines for antipsychotic use for older people need to include these broader groups.

In addition, these results emphasise the significant use of antipsychotics in the setting of palliative care. Therefore studies showing an association between antipsychotic use and death for older people may need to be interpreted cautiously, and antipsychotic guidelines need to account for palliative care use.

The key players in prescription decisions were confirmed to be GPs, including but not restricted to the primary GPs for ARC facilities. Much of this prescribing was reported to be independent of direct advice from other specialists. Providing support for best practice prescribing to GPs working in residential care could be one effective way of improving antipsychotic prescribing to the community.

This study has allowed us to gain deeper insights into antipsychotic prescribing for older people in New Zealand that we hope will allow the development of effective means of improving prescribing practice in the future.

Reference
5. Photographs from the Presentations

Judges of the presentations: Professor Lisa Stamp, Professor Martin Kennedy, Dr Gillian Abel and Professor Andrew Day

Dr Matthew Croucher, student Annie Yau and Dr Susan Gee

Wendy Fulton (CDHB) with student Katie Sleeman
Alison Benefield and Joy Powell, Lions Club of Selwyn representatives

Student Isabel Lee with Professor Peter Joyce, UOC Dean

Student Thomas Chima with his father and grandmother, Ann Haggard
Mr Ernie Poole with Liz Baxendine, Chair of Canterbury Age Concern Trust

Supervisor Mr Tim Eglinton with his student Tom Currie and sponsors Patsy and Warner Mauger, and Mr Ron Smith
Back row: Rex Harrison and John O'Brien, representatives from Diabetes Training & Research Trust, Emily Millar, Flo Logan, Helen Heenan and supervisor Dr Helen Lunt
Front row: Lyn Taylor and students Isabel Lee and Harmony Thompson

Edith Tripp with Professor Robin Fraser
Judy Brooks and Dr Deborah Errington, Canterbury representatives of NZ Federation of Graduate Women, with student Rachel McDonald and supervisor Dr Sue Bagshaw

Dr Gabi Dachs and student Delwyn Munn

Elizabeth Cunningham and Helen Morrin
Student Katie Sleeman with supervisor Dr Debbie Snell and representatives from the Rapaki Branch of Maori Women’s Welfare League

Student Leon Smyth with Dr Peter Gilberd, Deputy Manager of Royal Society of NZ Marsden Fund
Professor Gary Hooper with student Jonathan Bong

Student Lydia Dockrill with supervisor Dr Hilda Mulligan

Guy Johnson (Director of Canterbury Medical Research Foundation), Dr Gavin Clark, Dr Chris Kirk and Dr Helen Lunt
Student Georgie Allison (2nd from left) with her family

Joanne Sanders and student Imogen Nolan

Dr Geoff Shaw and student Nancy Wang
Paul Kelly and student Georgie Allison

Student Tom Loan and Dr Kit Doudney

Student Margaret He and Dr Joanne Young

Hannah Janssens and Dr Tracy Melzer
Awaiting the Judges’ results
Student Simon Hogg congratulated by Professor Margreet Vissers

Student Harmony Thompson congratulated by Professor Margreet Vissers

Student Angela Ballinger congratulated by Professor Margreet Vissers

Professor Richard Blaikie, Dr Dayle Matthews and Dr Chris Kirk