University of Otago, Christchurch

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2010 / 2011
Summer Studentship Programme
Lay Reports
COVER: Best Presentations Prize-winners: Helen Abbott (Laboratory Category); Tom Wilkinson (Clinical Category); Amanda Polkinghorne (Community Category and Overall Best Presentation); with Associate Professor Margreet Vissers, Associate Dean (Research)
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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. In this programme 52 students worked on a wide variety of projects, highlighting the breadth of health research in Canterbury. This booklet is a compilation of the reports submitted by the student participants in the 2010/2011 Summer Studentship Programme.

The main objective of the Summer Studentship Programme is to give undergraduate medical and health science students their first introduction to research. It is a regional programme that encourages participation from students and staff of the University of Otago, Christchurch campus; 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. We are grateful to the students, supervisors and host departments who have worked together to achieve a cross-institution synergy.

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 for providing the students with the seminar ‘Presentation Skills and Dealing with the Media’ and to Mark Brunton for his introductions to the students’ presentations.

We are grateful to the following members of the Research Committee: Dr Gillian Abel; Associate Professor Andrew Day; Dr Jenny Jordan; and Professor Martin Kennedy, who undertook the difficult tasks of assessing the project applications and judging the students’ presentations. Special thanks go to Joy Powell and Helen Patou from the Lions Club of Selwyn and to Judy Brooks and Shirley C’Allceta from the New Zealand Federation of Graduate Women, for their assistance with judging the final presentations.

Four prizes of $500 each for outstanding studentship presentations were awarded this year:

- Best oral presentation in the ‘Laboratory’ category – Helen Abbott, ‘Purification of Mycothiol from Mycobacteria and Investigating its Reaction with Bleach’. This prize was sponsored by Canterbury Scientific Ltd.
- Best oral presentation in the ‘Clinical’ category – Tom Wilkinson, ‘Urinary Cystatin C and Microalbuminuria as biomarkers of Sepsis and Acute Kidney Injury’. This prize was sponsored by the Christchurch Radiology Group.
- Best oral presentation in the ‘Community’ category – Amanda Polkinghorne, ‘Use of a hospital hydrotherapy pool by user groups from within the community: A mixed-method analysis?’ This prize was sponsored by the Lions Club of Selwyn Lioness.
- Amanda Polkinghorne was also awarded ‘Best Overall Presentation’ sponsored by the Canterbury Branch of the New Zealand Federation of Graduate Women (Inc.) Trust Board.

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 2011/2012 Programme.

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STOP THE PRESS!

40th Anniversary celebrations in 2012

In 1973, the first intake of fourth year medical students enrolled at the University of Otago Christchurch Campus (then the Christchurch School of Medicine). In February 2012, the school will celebrate 40 years of teaching and research.

As part of the 40th Anniversary celebrations, a trust fund has been established to finance future Fellowships and Scholarships at the Christchurch Campus.

Anniversary events will be held in Christchurch from 9th to 11th February 2012.

For further information contact the Research Office or view the web page at:

www.otago.ac.nz/christchurch/about/anniversary2012/index.html
2. Sponsors

- Anaesthetists’ Instrument Pool Ltd
- Arthritis New Zealand
- Asthma and Respiratory Foundation of New Zealand
- Cancer Society of NZ, Canterbury/ West Coast Division
- Cancer Society Ashburton Group
- Cancer Society Diamond Harbour Group
- Cancer Society Greymouth Group
- Cancer Society Hokitika
- Cancer Society Westport Group
- Canterbury District Health Board (CDHB)
- Canterbury Health Laboratories
- Canterbury Intensive Care Research & Education Trust
- Canterbury Medical Research Foundation
- Canterbury Scientific Ltd
- Christchurch Radiology Group Trust
- Christchurch Diabetes Society/ Diabetes Training and Research Trust
- Cure Kids
- Emergency Care Foundation
- Garth Streat Memorial Scholarship
- Health Research Council of New Zealand
- Health Sciences Divisional Summer Scholarships
- Helen Poole and Ian McDonald Memorial Summer Studentship
- Kidney Health New Zealand
- Lions Club of Selwyn
- Maurice & Phyllis Paykel Trust
- National Heart Foundation of New Zealand
- New Zealand Federation of Graduate Women (Inc.)
- Older Persons Health & Rehabilitation, CDHB
- Older Persons Health Specialist Services at The Princess Margaret Hospital
- Partnership Health Canterbury
- Pegasus Health
- Ruth Spearing Cancer Trust (initiated by Barry Mather)
- SYFT Technologies Ltd
- The Canterbury Health Care of the Elderly Education Trust
- The Govan Family Summer Studentship
3. Supervisors

Dr Gillian Abel
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Dr Vivienne Bickley
Candace Bobier
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Dr Anthony Butler
Dr David Carlyle
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Deborah Kendall
Professor Martin Kennedy
Associate Professor Ross Kennedy
Professor Tony Kettle
Dr Cameron Lacey
Dr Neil Lambie
Dr Helen Lunt
Associate Professor Sue Luty
Dr Virginia McIntosh
Associate Professor Dee Mangin
Virginia Maskill
Dr Pip Mason
Dr Barnaby May
Kelly Maw
Dr Daniel Milligan
Dr Peter Moore
Professor Roger Mulder
Dr Hilda Mulligan
Dr Peter Nagy
Dr Paul Pace
Dr Suetonia Palmer
Dr Colin Peebles
Dr John Pickering
Professor Richard Porter
Dr Timothy Prickett
Professor Bridget Robinson
Dr Karsten Schrobback
Dr Geoffrey Shaw
Dr Ian Sheerin
Professor Ted Shipton
Dr Ruth Savage
Dr Malina Storer
Kathryn Taylor
Dr Martin Than
Professor Les Toop
Dr Tony Walls
Dr Anja Werno
Dr Martin Whitehead
Dr Lisa Whitehead
Professor Christine Winterbourn
Dr Tim Woodfield
Professor Tim Yandle
4. Summer Studentship Reports

Helen Abbott

Purification of Mycothiol from Mycobacteria and Investigating Its Reaction with Bleach

Supervisors: Professor Tony Kettle
Sponsor: Asthma and Respiratory Foundation of New Zealand

Helen won the award for the ‘Best Presentation in the Laboratory Category’.

To many, tuberculosis (TB) seems a thing of the past. Certainly, the sanatoriums are, but the disease still poses a major threat to mankind. Worldwide, TB accounts for an estimated 9.4 million new cases and 1.8 million deaths annually. It is not isolated to the Third World, with an average of 350-400 cases presenting each year in New Zealand. To further complicate the matter, multidrug resistance is now widespread in many countries and strains have emerged that are resistant to all current therapies.

This deadly disease is caused by *Mycobacterium tuberculosis*, a resilient bacterium that usually attacks the lungs. The human body’s response is to recruit neutrophils and macrophages, two types of white blood cells. Recent studies of samples from people infected with TB have shown that neutrophils are more abundant than macrophages at sites of infection, and that mycobacteria appear to be rapidly replicating within the neutrophils. This suggests that neutrophils play the role of a “Trojan horse” for mycobacteria.

Factors that enable *M. tuberculosis* to survive and replicate within neutrophils are key targets to exploit in the battle against TB. One of these defensive mechanisms may be mycothiol, a molecule that is involved in protecting *M. tuberculosis* from toxic compounds. It is likely that this thiol, and others, react with chlorine bleach produced within neutrophils and protect mycobacteria from the oxidative killing mechanisms of neutrophils.

This project aimed to investigate the reactions of different thiols with chlorine bleach, and to assess the relationship between oxidation of thiols and killing of mycobacteria. A fast-growing non-pathogenic mycobacterium was used, as *M. tuberculosis* is extremely slow-growing and, quite obviously, pathogenic.

Firstly, it was important to establish how fast chlorine bleach reacts with different thiols. If the reactions are slow, then it is unlikely that the thiols play an important protective role for mycobacteria when engulfed by neutrophils. We studied two thiols present in mycobacteria that are available commercially, coenzyme A and cysteine. Both of these molecules reacted rapidly with chlorine bleach, and therefore are feasible targets.

Secondly, the products of the reaction of coenzyme A and chlorine bleach were studied to gain a better understanding of the reaction. Several products were identified, including a novel product unique to chlorine bleach. This product has the potential to form a diagnostic test, as high levels in fluid samples from the lungs would indicate an active TB infection.

Finally, the non-pathogenic mycobacteria were treated with increasing doses of chlorine bleach, and the number of mycobacteria that survived was determined by spreading them on a plate and waiting for them to grow. A reasonable dose was required to kill 99% of the mycobacteria. However, a change in thiol content was unable to be measured. To determine whether the amount of thiol in mycobacteria changes upon killing, a more sensitive method is required.

These results shed light on the reactions of thiols with chlorine bleach and their potential significance in TB infection. Further studies will confirm the identities of the reaction products and accurately measure changes in thiol levels in mycobacteria treated with chlorine bleach. Ideally, the same techniques will be used to examine the role of mycothiol, the most abundant thiol in *M. tuberculosis*. 
Maggie Anderson

Construction of a Spectral Micro-CT Phantom to Optimize the Geometry and Calibrate the Response of the MARS Scanner

Supervisors:  Dr Nicholas Cook, Dr Nigel Anderson
Sponsor:  Health Sciences Divisional Summer Scholarships

Abstract
This project was focused on developing and constructing a phantom for use with the MARS CT scanner, as part of a larger quality assurance project. CT is a very good structural imaging modality but has poor soft tissue discrimination. The development of the MARS scanner will provide a CT modality which is able to better determine soft tissues. The MARS scanner, currently in its third prototype, previously had no method for quality assurance. This report briefly covers the research and steps involved in producing the first quality assurance phantom for the MARS project.

Introduction
X-ray Computed Tomography (CT) is a non-invasive and very useful imaging modality. It provides excellent structural images and is cheaper than MRI. One particular limitation with the current CT technology is the poor discrimination of soft tissues, for example, distinguishing fat from healthy liver tissue.

Due to how x-rays are produced, x-ray beams cover a range, or spectrum, of energies. The energy of the x-ray affects its ability to penetrate materials, with higher energy x-rays being more penetrating. Traditional x-ray CT measures only the intensity of x-rays, not the different energies of the x-rays passing through the objects/patients, effectively seeing only black and white images as opposed to colour images. The aim of the Medipix All Resolution System (MARS) project is to resolve this through developing a CT scanner using a new type of detector, capable of detecting multiple energy ranges simultaneously. The MARS project is up to its third prototype stage as a micro CT scanner with a maximum sample size of approximately 100mm.

A need has recently been identified for a quality assurance plan for the MARS project. The chip detector used in the scanner is itself a prototype and the quality of images obtained from the chip has a temperature dependence, which encouraged an in depth analysis of the image quality. The MARS scanner is also starting to be sold to other research institutes with the aim of further development and a common procedure for determining image quality would make comparisons more meaningful.

Aims
The aim of this summer studentship was to construct a phantom to be used for quality assurance purposes with the MARS scanner, as well as a method of analysing the resulting images of the phantom. In imaging terminology, a phantom is simply an object which replaces a patient in the scan. This project falls within the larger, on-going quality assurance task for the MARS scanner.

Method and Results
There are many different factors used in determining image quality, such as the noise levels and resolution (both spatial and energy for a spectral CT). Building a phantom for all of them would be possible, but there were limits of the scanner to meet also. Size was the main restriction as the chip output is temperature dependant, but it did not yet have any cooling system. The chip produces a lot of heat so a small phantom was needed to keep the scan times short and the chip as cool as possible. The list of image quality factors was narrowed and spatial resolution was chosen as the key factor to measure. The spatial resolution is the minimum size of objects able to be seen clearly in the image.

With this in mind a review of the relevant literature was undertaken. This revealed a couple of commercially available micro-CT phantoms, however, these were deemed unsuitable. Also found in the review was a standard from ASTM International for determining the spatial resolution of CT scanners. With some alterations for both practicality and suitability, this standard formed the basis of phantom construction and image analysis.

The finished phantom is highly polished Perspex consisting of three sections, 5 mm, 10 mm and 15 mm in diameter. Perspex was chosen as it closely mimics average soft tissue in scans and a stepped cylinder design was chosen over a straight cylinder design as it was thought it would be of use longer than a single diameter cylinder. The surface of the phantom is highly polished as the spatial resolution is found through analysis of the sharpness of the boundary between the phantom and the surrounding air. If this boundary is blurred, then other objects within the image will also be blurred.
Also included in this standard was a definition of determining the spatial resolution from the images of the scanned phantom. A programme for image analysis was written following the steps given in the standard and this programme calculates an averaged spatial resolution of 13 cycles per mm. That is, if a cycle, or line pair, is made of one black line and one white line then 13 of these line pairs could be resolved in a millimetre before they become a grey smudge. This means the smallest resolvable object is 38.5 microns, or 0.0385 mm, in diameter.

**Discussion and Conclusion**

This result of 13 line pairs per millimetre is the averaged result from a number of images representing distinct positions along the length of the phantom, just in case one part was not as polished as another. This result requires further verification, through comparisons with results obtained from other phantoms and from other analysis methods, if available, to check our result is meaningful.

This result is a first step in the quantitative measuring of the quality of the images obtained with the MARS CT scanner with further analysis and more phantoms expected. Analysis of some of the other image quality factors is already underway.
Courtney Bennie

An Evaluation of the Content, Messages and Assumptions in New Zealand on Menopausal Hormone Therapy (MHT) Between 2002 - 2010.

Supervisors: Virginia Maskill, Beverley Burrell, Associate Professor Marie Crowe

Sponsor: Health Sciences Divisional Summer Scholarships

Introduction:
Menopausal hormone therapy (MHT) has a well-documented role in the treatment of menopausal symptoms and is commonly used for this purpose. Evidence for and against the use of MHT has changed drastically since the publication of several large studies in the early 2000s. Earlier evidence from observational studies supported the use of MHT for its favourable cardiovascular outcomes among other benefits. More recent findings provide contrasting results with risks outweighing any benefits found. There is now strong evidence from well-designed meta-analyses and randomised controlled trials demonstrating increased risk of breast cancer, heart disease, stroke and blood clots, and decreased risk of osteoporosis. In addition there is evidence from well-designed observational studies that show an increased risk of gallbladder disease and a decreased risk of colorectal cancer. Subsequently changes to medical organisations guidelines, including those in New Zealand, were made recommending that MHT not be used for the prevention of disease. Mass media provide a fundamental influence on public perception of issues related to health; however, often more extreme views are favoured by media coverage with risks and benefits not placed in perspective. Increasing media coverage emerged after the publication of these results leading to a decline in the use of MHT which was observed both internationally and in New Zealand. The decline in the global use of MHT has resulted in many women seeking safer alternatives. A notable increase in the promotion and interest around of natural or bioidentical hormone therapies (BHT) has been reported by several authors. Evidence for and against BHT remains limited and generally are of poor quality.

Aim:
This content analysis aims to analyse the content, messages and assumptions published in New Zealand media materials on MHT between 2002 and 2010.

Method:
Media material related to MHT published in New Zealand between January 2002 and November 2010 was retrieved from three electronic databases and from Television New Zealand archives. Full text transcripts of the retrieved materials were read by two authors and checked for relevance with duplicates being removed. A qualitative research design was used to conduct a content analysis of the media materials retrieved from the above sample. NVivo 8 computer software was used to organise the data.

Results:
185 media materials were deemed relevant for and included in this study. Five overall themes emerged from the data, i) Risks versus benefits of MHT, ii) MHT use in NZ, iii) Alternatives to MHT, iv) Indications for MHT and v) Quality of evidence.

Theme 1: Risks versus benefits of MHT
The focus of the majority of the retrieved media materials, particularly those published in the early 2000’s, is on the risks and benefits of MHT. The materials do however provide considerable variation in both the risks and benefits of taking this medication and on whether the risks outweigh the benefits. The vast majority conclude that the increased risk of chronic diseases is relatively small but most also indicated that health risks outweigh the potential benefits for anything other than short term use to relieve moderate to severe menopausal symptoms. Risks and benefits discussed in this theme included: dementia; blood clots; bowel cancer; breast cancer; cardiac events/heart disease; endometrial cancer; osteoporosis/fracture; ovarian cancer; quality of life; menopause symptoms; stroke; asthma; cervical cancer; gallbladder disease and gallstones; and lung cancer.

Theme 2: MHT use in NZ
The second theme describes the media coverage on the current and recommended use of MHT in New Zealand. MHT was reported in the media to be a widely and increasingly used medication for postmenopausal women in New Zealand prior to the 2000’s. The media reported a significant reduction in the use of MHT after this period. Current recommendations reiterated in the media are that if taken MHT should be used at the lowest dose for the shortest period of time. Some articles stated that MHT should not be used for longer than 3-4 years with many suggesting that MHT use should be reviewed every 6 months.
Theme 3: Alternatives to MHT
The third theme discusses the alternatives to MHT proposed by media materials. These alternatives included: bioidentical hormone therapy; contraceptives; phytoestrogens; black cohosh and other alternatives such as garlic. It was however mentioned that some women find no alternatives work. Additionally transdermal, sublingual and transvaginal methods of MHT delivery, including skin patches, creams, pessaries and sprays, are reported my many articles to have reduced risk than oral forms.

Theme 4: Indications for MHT
Signs and symptoms of estrogen deficiency were reported by several articles to be hot flushes, night sweats, vaginal dryness, and vaginal mucosal atrophy. It was proposed by some articles that the safest method is to prescribe MHT based upon correcting this hormone deficiency to restore normal physiological levels. The majority of articles propose that the hormone levels of postmenopausal women are tested to see if there is a hormone imbalance. It is recommended by several articles that if a hormone imbalance exists and treatment is necessary that the imbalance is corrected using bioidentical hormones in physiologic doses. One article goes on to suggest that initially testing is performed every three months and once a year after this balance is restored.

Theme 5: Quality of evidence
The majority of the retrieved media items were critical of the quality of evidence on MHT. The main criticism came from articles that were condemning of observational studies that have shown differing results from more recent randomised controlled trials. In addition studies on alternatives to MHT were also criticised by the media for being small, short term and uncontrolled.

Conclusion:
Considerable variations in views were presented in the media materials, particularly with regard to the risks versus benefits of MHT. Overall the opinions expressed and statements made in the media materials relate well to the conclusions drawn in current literature around MHT. This study will enable readers to obtain an appreciation of the understanding the New Zealand public could potentially form from accessing readily available media materials published in New Zealand.
In 2004 the 5 major centers in New Zealand (Christchurch, Auckland, Dunedin, Wellington and Hamilton) carried out 9000 colonoscopies (an endoscopic procedure involving viewing the colon via a scope passed through the anus) for screening and diagnostic purposes. In order to carry out a successful colonoscopy the faeces in the bowel must be removed. To do this patients are given a bowel preparation such as Picoprep®, a laxative, the day before the procedure. The active ingredients in Picoprep® are sodium picosulfate, a stimulant laxative that stimulates bowel movements and magnesium citrate, an osmotic laxative that increases osmotic pressure in the colon causing fluid to be retained in the bowel. A known adverse effect of Picoprep® is electrolyte disturbance. Previous studies have found a link between electrolyte imbalance and impaired cognitive function in elderly patients. For this study we hypothesised that Picoprep® would cause an electrolyte imbalance that would then cause cognitive impairment.

To see if there is any cognitive impairment we aimed to enroll 2 sets of patients, into the study. One group of patients were undergoing a colonoscopy, therefore having the bowel preparation, and the other arm of our study were patients undergoing a gastroscopy (an endoscopic procedure involving a scope being passed into the stomach via the esophagus). Both groups must abstain from eating for a given time period before the procedure, and both are sedated throughout the procedure, however only the colonoscopy patients are given the bowel preparation. The reason for including the gastroscopy patients is so we can compare the 2 groups and account for the learning phenomenon in our results. For this study we recruited 7 colonoscopy patients and 4 gastroscopy patients.

Patients completed 3 cognitive tests, with the first being 2-3 days before their procedure (this is used as a baseline), the second test being administered the day of their procedure (after the bowel preparation but before the sedation for colonoscopy patients) and the final test being taken the day after their procedure. The third test was to be used to determine if the change was short term if the first two tests showed a change in cognitive function.

Each cognitive test comprised of a series of tasks which tested a range of cognitive function domains such as motor speed and different types of memory. Sections of the tasks required the use of a touch screen computer while the rest were pen and paper exercises.

For the motor speed test we found that although all participants had the same baseline scores however the scores for the second test were different. The motor screening test timed how long it took subjects to respond to a cross on the screen. The experimental groups’ scores were 354 and 307 milliseconds for the baseline test and the second test respectively. The control groups’ scores were 349 and 199 milliseconds for the baseline and second tests respectively. Both scores dropped however the drop in the control group was over three times as much for the control which dropped by 154 milliseconds while the experimental group only dropped by 41 milliseconds. These results were not statistically significant. If this trend was statistically significant then one would assume that the difference was caused by something that was present in one of the groups and absent in the other in this case this would have been the bowel preparation.

For other parts of the test we found no difference in the first and second test scores indicating that bowel preparation did not significantly affect that cognitive domain. In the digit span the grand total for what the subjects could recall both forward and backwards showed no real difference with the control groups’ average score in the baseline and second tests being 14.29 and 14.71 while the experimental group had scores of 11.5 and 12.25.

Because of our small sample size we could not get any statistically significant results. We could see some trends in our data which, if we were to increase the sample size, which could potentially be statistically significant. The trends were only seen in a few cognitive domains and were relatively small which could indicate that if there is any effect the effect may not have any clinical significance.

To conclude, more participants would be needed to show more accurately if there was a change in cognitive function. If an effect is seen, research is needed to see if the change would have any major effects on the patients’ ability to carry out tasks such as driving or following pre-procedure instructions.
**Conal Boland-Bristow**

*Characterization of a Novel proCNP Peptide(s)*

**Supervisors:**  
Dr Timothy Prickett, Professor Tim Yandle

**Sponsor:**  
Health Sciences Divisional Summer Scholarships

C-Type natriuretic Peptide (CNP) is a hormone, or signaling molecule, found in many tissues in the body. Its main known action is to ‘tell’ bones to grow longer. This means when there is too much CNP in the bones it causes gigantism, while if there isn’t enough it causes short stature. CNP is however rapidly destroyed in the blood, so it is difficult to directly test for it. NT-proCNP is a peptide which is produced at the same time as CNP from a precursor molecule, and escapes destruction in the blood. This means that NT-proCNP can be tested for to determine CNP levels, and therefore growth velocity. Recent studies on NT-proCNP have found a new smaller fragment in pituitary tissue, known as novel proCNP peptide.

The main aim of this project was to identify the amino acid sequence which makes up this novel proCNP peptide. Amino acids are the building blocks of our bodies, which can be assembled in lots of different orders to make up different peptides and proteins. A secondary aim of the project was to find the levels of novel proCNP peptide in different tissues.

Initially, we knew that the novel proCNP molecule was a small fragment broken off the start of the whole, longer proCNP molecule. We also knew approximately how long it was, and its order of amino acids based on the initial prohormone. To find exactly what it was, a range of synthesized peptide fragments were obtained. These differed by one amino acid in length, and had the same amino acid order as proCNP (called proCNP(1-8), proCNP(1-9) etc., with proCNP(1-8) having amino acids 1-8). These were then separated out on basis of their size and polarity by a technique called high performance liquid chromatography (HPLC). This was also done to a sample of the novel proCNP peptide. The fragments were then compared to the novel proCNP peptide, to find out which peptide fragments were identical to it, and so could be assumed to be the novel proCNP peptide. After this, proCNP was extracted from many different tissues and analyzed to find its levels.

The synthesized fragments were so similar in size that they could not be separated by size-exclusion HPLC. Fortunately, they could be separated based on their polarity. The novel proCNP peptide was found to consist of four different peptides, of varying lengths. These peptides were proCNP(1-10), (1-11), (1-12) and (1-13). The most likely explanation for this is that the longer proCNP peptide is cut between amino acids 13 and 14, to give the peptide proCNP (1-13). Amino acids are then ‘nibbled’ off one end by enzymes, to give proCNP (1-12), (1-11) and (1-10). Different tissues had different levels of novel proCNP peptide in them. Some tissues, such as the kidney, had such low levels that it could not be measured. Most had levels between 115 and 415fmol/g, which are still very low. Pituitary tissue had by far the highest levels with 2.2pmol/g, five times more than the next highest tissue.

Now that this is completed, we have preliminary evidence as to the identity of the novel proCNP peptide, being a mix of proCNP (1-13), (1-12), (1-11) and (1-10). However, it is difficult to determine their exact levels using the assays I was using, as some peptides may have been missed. Mass spectrometry, a more accurate method, should now be used to obtain a more exact answer. The levels of novel proCNP peptide varied widely, with the highest levels being in pituitary tissue. However, these levels did not appear to correlate with the levels of CNP and NT-proCNP, possibly due to different rates of degradation.
Natural menopausal transition reflects a gradual decline in ovarian function before final cessation of menstruation at an average age of 51. The predominant symptoms experienced during this transition include vasomotor symptoms (including hot flashes), vaginal symptoms, insomnia and various psychological symptoms (such as mood swings or depression). Menopause can also be induced prematurely as a result of treatments for gynaecological disorders such as endometriosis, menorrhagia and gynaecological cancers. Surgically-induced menopause occurs as a result of procedures such as bilateral oophorectomy; where the removal of ovaries results in an immediate disruption of oestrogen production and a dramatic change in hormone levels, leading to sudden onset of menopausal symptoms. Cancer-related treatment can also induce premature menopause. Women with gynaecological cancers often receive pelvic radiotherapy which can disrupt ovarian function and subsequent estrogen production, while certain chemotherapies can curtail ovarian function within a few months of treatment leading to medically induced menopause.

Managing the transition following premature menopause can be difficult – particularly in the context of menopause induced by cancer treatment, where women must deal with heightened menopausal symptoms in addition to adjusting to a cancer diagnosis and dealing with other side effects of treatment. It is important that health care providers recognize the impact that sudden menopause can have on women, both physically and psychologically, in order to provide women with the necessary resources to successfully manage their health following treatment-induced menopause. Understanding the factors that women identify as impacting on their ability to self-care (these may be physical, emotional and/or social) is important to promote recovery and self-management of the long-term consequences of premature menopause.

The aim of this project was therefore to undertake a systematic literature review to identify and assess the factors that impact on a woman’s ability to self-care following treatment induced menopause. A systematic review is a rigorous process through which research pertinent to a specific question can be identified, critically appraised and synthesized in order to provide a reliable summary of the available research evidence. In this review, a comprehensive search of five health research databases was undertaken using search terms relating to premature menopause and concepts of self-care. Papers that were identified were those that focused on self-care outcomes in women following induced menopause (such as engaging in activities that promote health, interacting with health-care providers, adhering to recommended treatments and managing the effects of menopause on daily lifestyles). Three hundred and seventy-two papers were identified in the search, of which thirteen were directly relevant to the review question. Following assessment for methodological quality of these studies (this involved assessment of the congruency between the methods used and the study objectives, data analysis and interpretation of the results), eight studies were included for analysis in the review.

Four main themes were identified from the studies included in the review that impacted on the ability to self-care: understanding the condition, psychosocial factors, clinical factors and communication. The predominant theme identified across all the studies was the ability of women to understand their condition. Lack of or inadequacy of information from physicians or other health-care providers about the range of menopausal symptoms and what to expect was a difficulty reported by many women. In particular, it was reported that younger women, who were more frequently concerned about the impact that induced menopause could have on their lives, tended to receive more ambiguous information about menopause and its long-term implications. As a result of being unprepared and inadequately informed, women were often “blindsided” by unanticipated symptoms and were consequently ill-equipped to successfully manage the experience.

Various psychological or social factors that impacted on women’s ability to self-care were also frequently reported across the studies. Acceptance (or lack of acceptance) of menopausal status and its implications on lifestyles, attitudes held by women (such as fatalism, risk-management or cautiousness) and support from others were among the psychosocial factors identified by women as influencing their self-care ability.

Themes associated with clinical factors were related to the impact of symptoms or consequences of treatment. Women who experienced severe symptoms, or who perceived their symptoms as distressing,
reported difficulties in adjusting to being menopausal. Women who were menopausal as a result of cancer treatment, and who were close in time to diagnosis or treatment, tended to downplay the effects of menopause. These women chose to tolerate their often distressing menopausal symptoms rather than seek relief, and instead chose to focus their attention on the cancer diagnosis and treatment.

Communication between women and healthcare providers about aspects of the menopausal experience was another important theme identified in the studies. Some studies reported that women were uncomfortable talking about intimate and personal issues with their doctors, and other studies reported that some women perceived their doctors as being dismissive and insensitive about their menopausal concerns. Difficulties in communication sometimes impeded women’s ability to access information, as these women perceived their doctors as almost unapproachable.

The results of this review demonstrated that a variety of factors influence a woman’s ability to self-care following induced menopause. Successful management of premature menopause is reliant on a woman’s ability to manage the symptoms, treatment side-effects and the lifestyle changes and consequences of menopause. This requires adequate and timely information of the condition and its long-term implications from health professionals, and effective and supportive communication between women and their healthcare providers. Awareness of these factors, and of the underlying psychosocial and clinical constraints embedded within a woman’s menopausal experience, will help clinicians target effective support to improve health outcomes and enable these women to more effectively self-care.
Aindrea Brown

What Is The Clinical Value of SPECT Brain Scanning In Psychiatry Of Old Age?

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

Currently there are only rough guidelines available to clinicians judging which, out of multiple brain scans available, will provide the best diagnostic information for patients with suspected dementia. Structural neuroimaging such as CT or MR is suggested as routine practice in patients with suspected dementia, however functional imaging such as SPECT (single photon emission computed tomography) and PET (positron emission tomography) can estimate the functioning of particular brain lobes, and may detect significant brain-function alterations consistent with many neurodegenerative diseases, which may not produce structural abnormalities.

These functional brain scans use a radioactive agent to assess the relative perfusion of brain regions, with the agent used in SPECT scans having a longer half-life than that used in PET scans, so that SPECT has the ability to measure brain functioning over longer periods. Research has shown SPECT may have poorer resolution than PET; however the scan is cheaper and widely available in New Zealand, with existing evidence of its usefulness in the differential diagnosis of dementia particularly those in early stages or those with frontotemporal dementia.

The aim of this study was to ascertain the added value of SPECT scanning for clinical diagnosis and management and to identify the target population for whom there is greater or lesser value.

The information for this study was collected in the form of a questionnaire filled out by clinicians ordering brain scans dating back to 2004, accounting for 24 patients. In addition the SPECT patient database was reviewed to identify missing cases, of which a further 44 cases emerged. Data was unavailable for four cases. Missing information was then collected from patient case notes and by interviews with the referring clinicians to complete a data set totaling 64 patients.

The population referred for scans has been described in terms of age, gender, ethnicity, and duration of memory impairment and classified according to the preferred diagnosis dementia type before the scan; Alzheimer's dementia, Frontal type dementia, Dementia with Lewy Body or other (non-specified dementia or vascular dementia).

The main outcomes were analyzing which of these predicted dementia groups the SPECT scan was most useful to clinicians in diagnosis of their patient’s dementia, whether the scan resulted in changing the patient’s management and the rated usefulness of the scan in terms of the clinical management of the patient. A rating scale from 1 being ‘not useful’ up to 5 being ‘very useful’ was used for clinicians to judge the scans for their usefulness in diagnosis and in management for each case. In terms of management change clinicians were asked either ‘yes’ management was changed or ‘no’ it was not. In addition the clinicians were asked, if yes, in what way the SPECT scan had led to a change in management. The clinician was asked for their own interpretation of the scan along with their preferred diagnosis for each patient after having viewed the scan.

The sample analysed had a mean age of 70 years and 58% were female. The majority of patients were of New Zealand European/Pakeha ethnicity. Memory test (3MS) scores were available for most patients with most scoring toward having a higher level of functioning, having a mean score of 77.7% overall. Duration of memory impairment ranged from ≤12 months (17.5%), 12-24 months (20.6%), 24-48 months (14.3%) and ≥48 months (42.9%). Hence most of the sample were not recently experiencing memory problems at the time in which the SPECT scans are ordered.

Clinicians rated SPECT scans to have a greater rating for usefulness in diagnosis for patients with a preferred diagnosis of a frontal type dementia before having the scan requested, compared to patients without a preferred diagnosis of a frontal type dementia. We also found that of these patients with suspected frontal type dementia, the SPECT scan led to a management change in 64% of patients. This change in management was mainly concerned with the clinician’s level of support for prescribing cognitive enhancing drugs.

In contrast the study found that clinicians rated the SPECT scan as significantly less useful, both in terms of diagnosis and management, for those patients with a preferred diagnosis of Lewy Body dementia before the
scan, compared to patients without a preferred pre-scan diagnosis of Lewy Body dementia. Of these patients 31% had SPECT scans interpreted as non-specific, a significantly higher percent than all other patients.

These results show that SPECT scans are more difficult to interpret for patients likely to have Lewy Body Dementia, thus the scan offers less usefulness in terms of diagnosis and management. However the scan is clearer in confirming or in ruling out a frontal type dementia. These findings offer promise for the ability of the SPECT scan to aid in the management of patients suspected of having a frontal type dementia and hence provide a guide for clinicians as to the suitability of cognitive enhancing drugs for these patients.

This study has revealed trends providing a base on which to formulate hypotheses for future research in this area. The main trends in this study describe SPECT as being most useful for those patients suspected as having a dementia of frontal type both in diagnostic clarification and in a resultant change in management plan, primarily concerning the decision to use cognitive enhancers. The scan appears to be least useful in diagnosis and management for patients predicted to have dementia of Lewy Body type, seemingly due to non-specific scan findings in these patients. Further research involving larger samples is required in these areas to yield greater statistical power.
Nicole Coman-Wright

Cognition/Behavioural Function in Long Term SSRI Antidepressant Use: Control Group Study

Supervisor: Dr Claire Dowson
Sponsor: New Zealand Federation of Graduate Women (Inc.)

In general practices increasing numbers of people are prescribed Fluoxetine (an antidepressant) as a maintenance treatment to prevent recurrence once they have recovered from an episode of depression. Fluoxetine is a selective serotonin reuptake inhibitor or SSRI, which causes an increase in levels of serotonin in the brain. There are suggestions that SSRIs may impair cognitive function such as thinking, memory and concentration as well as affecting behavioural function. No studies to date have considered the effects of remaining on Fluoxetine once a person has recovered from an episode of depression. Prompting the development of the “Cognition and Behavioural Function in Long Term SSRI Antidepressant Use” study or Cognition & SSRI study which is currently underway in the Department of Public Health and General Practice. This report refers to the Control (comparison) Group part of this study.

The “Cognition & SSRI” study aims to determine the effect on cognitive and behavioural functioning from continued antidepressant use in previously depressed but currently well people. This will be done by way of a major 18 month Randomised Controlled Trial “The Antidepressant Cessation Trial”. The trial involves comparing cognitive and behavioural functioning, side effects and symptoms of depression in two groups of participants, with one group currently taking Fluoxetine while the other being tapered from their current Fluoxetine treatment to a placebo. Both participants and researchers are blinded as to who is taking placebos or Fluoxetine.

My role was to recruit and to conduct computerised assessments for the control (comparison) group. This involved recruiting people aged between 18 and 75 years, who have never taken antidepressants and do not currently consider themselves depressed, to participate in a control group. Their gender, education and ethnicity were recorded to be used as descriptive data to determine compatibility as a comparison group. The Montgomery Asberg Depression Rating Scale (MADRS) is a self-report measure of current depression and was used to screen participants before commencement of the computer test. The control group participants were instructed to use the CANTABeclipse program to complete a 45 minute computerized cognitive test panel comprising 6 tests. The tests examine participant’s ability to retain spatial information, manipulate remembered items in working memory, comprehension, visual memory, new learning and reversal. Of particular interest is frontal lobe dysfunction which has been associated with use of SSRIs in some studies. The tests involved are sensitive to changes to the fronto-striatal areas of the brain, measure frontal lobe, parietal lobe and ‘executive’ dysfunction, and are also a sensitive measure of general performance.

Demographic groups and MADRS scores were compared to determine any differences in CANTAB scores within the control group. The control group comprised 62 people with 66% being female. 85% participants identified with being New Zealand European and 1.6% Maori. The group’s average (mean) age was 42.81 and had an average of 15.24 education years and an average MADRS score of 4.56 (not indicating depression). In order for the control group’s CANTAB scores to be compared with the groups in the “Cognition and SSRI” study both the demographics and MADRS scores of participants must be comparable. At present the average age of the control group is lower than that of the main study group. Analysis within the control group showed an association between age and performance, meaning that with increased age there is a reduction in ability to perform cognitive tasks, with younger people having higher (better) scores. This was expected as the CANTAB tests rely on motor function which deteriorates with age and are not dependent on past learning or other aspects assessed in standard intelligence tests. No other factors (gender, occupation, education years, MADRS) appear to affect participants’ performance on the tests.

Overall interim analysis indicates that the control group is younger than the current main study group but comparable on gender, ethnicity and education, therefore we will need to recruit further older participants for controls. People are still being recruited for the “Cognition and Behavioural Function in Long Term SSRI Antidepressant Use” study. We will continue to recruit control group participants comparable in age and gender to the main study.
Abstract

Introduction: Mental health is an area of major concern in New Zealand with an estimated 5% of young people severely affected and likely to require treatment from specialist mental health services. These young people have specific needs and it is important that specialist mental health services for children and adolescents accommodate these.

The involvement of family, extended whanau, and close friends has been identified as being very important in the recovery journey of people with mental health issues. The Blueprint for Mental Health Services in New Zealand states that these people "whatever they think about the illness, cannot escape being affected by it" and "need, therefore, to be part of the healing or maintenance programme" (Mental Health Commission 1998). For young service users, their key supporters may include other young people like siblings, friends or classmates.

Up until now, research into family involvement with child and adolescent services, has mainly focused on the parents and caregivers. Little attention has been paid to the performance of specialist mental health services in involving young friends and family members in the treatment of youth service users.

Aim: To observe and describe the involvement of young supporters of youth service users engaged with child, adolescent and family mental health services. To suggest practical ways in which mental health services might better promote and support young people who are supporting youth in their services.

Method: Seventeen young people (15-25 years old) who supported a close friend or family member while they were involved with one of the Canterbury District Health Board’s mental health service catering for under 18’s were recruited for this study.

We advertised using flyers placed at throughout DHB sites as well as at the University of Canterbury and the Christchurch Polytechnic Institute of Technology. Participants attended one of six focus groups. The focus groups were guided by questions relating to eight key experience areas which included: what it was like for them prior to their young person being referred to a service; how they found the referral process; their first impressions of the unit their young person was referred to; their involvement in meetings; their experience of any privacy related issues; whether they themselves received any support in their involvement from the service; their experience of their young person’s discharge from the service; and what was their overall opinion of the service provided. Not all of the participants were able to talk about every key experience area as, for example, some were not involved in physically visiting units (e.g. in cases where their young person received outpatient care). Qualitative data was transcribed and analyzed by thematic analysis, which systematically identified common themes and trends from the focus group discussions.

Results: The seventeen participants consisted of 11 females and 6 males with an average age of 22 years old. Most of the participants identified themselves as close friends or partners, with a third identifying as family members, usually siblings.

Thematic analysis of the six transcripts revealed that participants on the whole felt the service provided to young people was beneficial. One participant said “they helped her get through a really hard time in her life” while others said they didn’t think their friend or family member “would still be here” without the help of the service. While the participants described a lot of positive experiences of the service, overall, they did not feel as personally involved in the treatment of their young person as they would have liked. A number of reasons for this were identified:

1. Participants didn’t feel they understood what was going on: Many participants felt that they were too young to understand what was going on with their young friend/family member. Most participants also expressed significant distress at their lack of understanding and feeling unable to ask questions.

2. Participants felt their relationship with their young friend/family member suffered while he/she was unwell: A lot of participants said they hadn’t recognised their young person’s behaviour as symptoms of a mental illness, but rather them “acting out” or “attention seeking”. Many of the participants who
discussed this said they still felt a lot of guilt at “not being supportive enough” or “losing patience” with their friend or family member.

3. **Participants had difficulty communicating with the parents or caregivers involved:** Many of the participants described having difficulty discussing their young person’s diagnosis with their caregivers. Siblings particularly expressed a feeling that they were being “protected” by their parents from what was going on. Friends mentioned feeling that their young person’s parents seemed to be “in denial” or too embarrassed to discuss the situation with them.

4. **Participants did not feel sufficiently informed or educated about their young person’s situation:** It was felt by many of the participants that there were not enough resources available written for young people about mental illness or the service. They also felt that they weren’t “kept in the loop” by other family members and staff.

5. **Participants didn’t feel like they were encouraged to be involved by staff:** Many of the participants who identified as “friends” experienced not feeling welcomed by staff. They discussed often feeling ignored or “deliberately excluded” when visiting units.

**Discussion and Conclusion:**

All of the participants felt that their young person’s involvement with a specialist mental health service had been beneficial. However, participants identified that they did not feel sufficiently involved in their young person’s care. A small number of participants didn’t feel it was “their place” to push for involvement, but the majority expressed regret that they were not more involved.
Borderline Personality Disorder (BPD) is characterized by an enduring pattern of difficulties that include emotional regulation, instability in personal relationships, self-image and impulsivity. The prevalence of BPD is estimated at 2% of the US population and is thought to occur at a similar rate in New Zealand. BPD occurs predominately in females (75%) and typically manifests in early adolescents and continues into adulthood (American Psychiatric Association [DSM-IV-TR], 2000). Thoughts of suicide, suicide attempts and self-mutilating behavior are particularly common with this disorder.

BPD is also characterized by its high co-morbidity with physical disabilities as well as other psychological disorders such as bipolar disorder, depression, anxiety disorders and substance misuse. This creates a problematic nature for BPD where individuals with the disorder are vulnerable to recurring crises, hospitalization, self-mutilations, suicide attempts, addictions and episodes of anxiety and aggression (Asselt 2007). Considering this, BPD is associated with substantial health service usage and tangible and intangible cost. For example Zanarini et. al 2001 estimated that individuals with BPD represent approximately 10% of patients seen in mental health outpatient clinics and approximately 20% of psychiatric inpatient admissions.

Despite the complexities that do arise with this illness, if a proper diagnosis is made BPD is increasingly seen as a treatable disorder. A number of studies have been carried out that demonstrate the efficacy of psychotherapeutic treatments (Bateman & Fonagy 2009). An example of this is the Mentalization Based Therapy (MBT). This therapy was introduced into Christchurch in 2009.

The degree of actual health service usage by this client group in urban New Zealand remains unclear. The aim of the current study was to conduct a cost analysis of secondary and tertiary health service usage from people with BPD. The study population consisted of 338 patients with a diagnosis of BPD. A second group of 157 patients was also included. This was called the possible group, where a clinician had suggested that the individual had borderline traits but a clear diagnosis of BPD had not been given.

Information in regards to mental health service usage was extracted from the mental health service database. Inpatient psychiatric hospital service usage was defined by the total length of stay in particular service. The average cost per night at Pipiri was calculated at $1045.12, Seager Clinic $493.97 and all other inpatient services at $724.30. The total inpatient length of stay for the diagnosed group was 5797 days with a total inpatient cost of $4,006,400. The average cost per patient was $11,853. The total length of stay for the possible group was 3526 days with a total cost of $1,324,550. The average cost per patient was $8,437.

Information for outpatient mental health service contacts was defined by the treatment category of the appointment and the clinician they saw. The average hourly costs for a nurse in 2008 was $39.67, Social Worker $36.08, Psychiatrist/Registrar $134.5, Clinical Psychologist $51.97, Occupational Therapist $38.17 and all other clinicians $36.08. The total number outpatient mental health service contact was 10,349 with a total cost of $466,209. The average cost per patient was $1,379. The total number of outpatient contacts for the possible group was 1910 at a total cost of $109,545. The average cost per patient was $698.

Respite bed usage for the year 2008 was also analyzed. This included crisis and planned bed day usage at Stepping Stones, Pathways, Newell House and Rivendell. The average cost per night for a crisis admission in 2008 was $156 and for a planned admission $118. The total length of stay for a crisis admission was 546 nights and 493 nights for planned admission, giving a total cost of $143,350. The average cost per patient was $424.11. The total length of stay for a crisis admission for the possible group was 148 nights and 138 nights for the planned admission, giving a total cost of $13,973. The average cost per patient was $89.

A cost analysis for emergency department contacts was also conducted. This data was extracted from the PMS database and costing was based on the triage category code. The cost of an immediately life threatening contact was $640, imminently life threatening; $400, potentially life threatening or potential adverse outcomes; $289, potentially serious or potential adverse outcomes; $240 and less urgent or dealing with administration issues only; $151. The total number of ED attendances for the diagnosed group in the year 2008 was 2270 at a total cost of $628,576. The average cost per patient was $1,860. The total number of
attendances for the possible group was 968 at a total cost of $266,963. The average cost per patient was $1,700.

Information for inpatient public health service contacts was provided by Decision Support. For the year 2008 there was 398 inpatient events at Public, Burwood and Christchurch Women's Hospital for the diagnosed group. The total cost was $952,672.05, with an average cost per patient of $2,818.5. The possible group had 103 inpatient events at a total cost of $199,062.08. The average cost per patient was $1,297.9.

The total secondary and tertiary health service cost for people with BPD in 2008 (average costs for specialist hospital outpatient services, medication and laboratory testing was unavailable within the time frame of this study) is $6,197,207 for the diagnosed group. The average cost per patient for 2008 was $18,335. The total yearly cost for the possible group was $1,914,093 with an average of $12,192.

This project has been the first attempt to comprehensively estimate the health service costs associated with BPD in New Zealand. The results of this study indicate that nearly 65% of total health service costs for BPD are due to psychiatric inpatient admittance. The remaining 35% is a combination of MHS outpatient, respite bed usage, ED attendance and admittance to hospital. This data can greatly help to contribute to service planning and comparisons with international cost analysis of BPD can now be made. Importantly this analysis was made in the year 2008 prior to the year of the introduction of MBT in Christchurch. It is hoped that this study will be repeated in the future. This will allow us to establish whether or not this psychotherapy has resulted in a decrease or increase in health service usage and cost by people who suffer from Borderline Personality Disorder in urban Christchurch.
Sarah George

Correlating Genotype and Phenotype in Familial Hypercholesterolaemia (FH)

Supervisor: Professor Peter George
Sponsor: Canterbury Health Laboratories

Diagnosis of patients with Familial Hypercholesterolemia (FH) is vital as they have a high risk of early Coronary Artery Disease (CAD) and accelerated atherosclerosis, but this can be prevented by timely treatment. FH has a high incidence rate (it is estimated at 1 heterozygote per 500 people), and affects not only the obvious candidates for high cholesterol, but also children and otherwise healthy patients. It is characterized by raised serum low density lipoprotein (LDL) cholesterol levels. If it is left untreated, patients develop fatty deposits in peripheral tissues known as tendon xanthomas, premature CAD and those affected are more likely to experience early death from a cardiovascular event. However despite these phenotypic similarities, there are a wide range of causative mutations, a number of which yet remain unidentified, and so mutation testing is an important tool for effective diagnosis.

As discussed, FH can seriously affect the lives of patients, particularly if left undiagnosed, and therefore effective detection is an important issue. Whilst mutation testing remains an important tool in effective diagnosis, it is also an expensive method of detection. This project aimed therefore to evaluate the ability of phenotypic traits to predict the presence or absence of mutation in a patient, in order to ultimately improve selection criteria of patients for mutation testing. As well as this it aimed to provide a basis to determine if patients with identified mutations have more severe clinical courses, and warrant a more extreme drug therapy than mutation negative patients.

A standardized data collection form was used to collect both clinical and genetic information from patients attending the Christchurch Hospital Lipid Clinic. We particularly focused on making correlations between potentially indicative clinical features of FH and whether patients were mutation positive or negative. Once collected, this information was entered into a new database focusing only on the phenotypic (physical manifestation) aspects of FH, and these results were compared to results gained from an initial analysis in 2008. The information gained from this project will be combined with FH studies based in Amsterdam and the United Kingdom in order to form a model of better treatment and will provide a basis from which we will be better able to select patients for mutation testing.

The results of the project showed that total cholesterol (TC) levels of patients who were mutation positive were not significantly higher than the TC levels of patients who were mutation negative. Mutation positive patients did however have significantly higher levels of LDL cholesterol than mutation negative patients. There was no significant difference between mutation positive and mutation negative patients in the majority of phenotypic indicators including: triglyceride, high-density lipoprotein, apolipoprotein AI, apolipoprotein B or lipoprotein(a) levels.

We also found that mutation positive patients were not more likely to have CAD than mutation negative patients, however when mutation positive patients did develop CAD, the average age was 46, six years younger for mutation negative patients experiencing CAD. Mutation positive patients were found to be significantly more likely to develop tendon xanthomas (21%) than mutation negative patients; however tendon xanthomas are still not a reliable indicator as 80% of mutation positive patients had not developed them.

Results also showed that mutation positive patients from this study overall had less severely raised cholesterol (TC and LDL) than patients initially analyzed in 2008. As well as this there was less separation between the scores of mutation positive and mutation negative patients than in the 2008 analysis. The most obvious reason for this is that in 2008 only more severely affected patients were selected for mutation testing, whereas the sphere for mutation testing has now widened to include less severely affected patients.

Overall, we have so far concluded that there are no clear clinical features that can distinguish mutation positive and mutation negative patients. Thus we cannot use the presence of any particular phenotypic trait as reliable selection criteria for mutation testing in patients. As such, to ensure best detection; all patients with significantly raised cholesterol levels of significant phenotypic indicators should be selected for mutation testing. As well as this, it would be beneficial to conduct further study with a wider test group of patients, as this will better highlight any significant differences that may not have shown in such a small test group. This will be carried out when the data from this project is pooled with data from the Amsterdam and United Kingdom test groups.
Andrew Gibb

Novel Behaviour of Polymorphic Alleles in an Imprinted Region of the Human Genome

Supervisors: Dr Kit Doudney, Professor Martin Kennedy

Sponsor: Health Research Council of New Zealand

Many DNA tests commonly used for diagnosis and analysis of genetic conditions rely on polymerase chain reaction (PCR) to increase the amount of DNA available to be analysed. PCR uses short pieces of DNA (primers) to initiate copying of the region of interest, which is then carried out by a DNA polymerase enzyme. It has previously been noted that certain structural features present in DNA can inhibit PCR by blocking the DNA polymerase and preventing it from carrying out successful amplification. Methylation, a modification of the chemical make-up of DNA, is thought to stabilise such structural features and therefore play a role in inhibition of PCR.

Recent work from our laboratory has led to an interesting discovery in a region of DNA near the human MEST gene. MEST is involved in mammalian development and maternal behaviour, and is controlled through being switched on or off by a process called genomic imprinting. DNA methylation is known to be involved in genomic imprinting. When examining the MEST gene in a sample of individuals, three single-nucleotide polymorphisms (SNPs, a type of DNA mutation) near the gene were found to behave in an unusual way. SNPs are a type of variation involving a single letter difference in DNA sequence between individuals. This difference creates two sequence forms, called alleles. Humans possess two sets of chromosomes, and therefore have two alleles for each variant. These two alleles can either be the same (homozygous) or different (heterozygous). For all three SNPs located near the MEST gene, people appear to only ever possess one allele or the other, and never both, which goes against genetic expectations. There is therefore a complete lack of heterozygous individuals in the populations examined. Our theory is that structural features are present in this region of DNA and are stabilised by the methylation which is known to occur there. These structures block DNA polymerase and prevent it from accurately copying both alleles, giving the impression that only one exists in an individual at any one time.

The aim of this project was to examine the presence of structural features in the region of DNA surrounding the MEST gene, and to investigate the role that methylation may play in stabilising such structures. Initially, DNA from 48 individuals was sequenced in order to find both the common and rarer homozygous forms for all three SNPs. Once both forms were identified, PCRs were optimised and carried out to increase the amount of DNA available for analysis. In order to examine whether methylation plays a role in preventing both alleles from being successfully amplified, half of the unmethylated PCR products obtained were methylated by enzymes. A further PCR was going to be performed on both methylated and unmethylated products, as well as mixtures of the two, to determine whether methylation is responsible for the unique behaviour of these SNPs. Unfortunately this has yet to be carried out, but several important findings have resulted from this studentship. Suitable DNA samples for further studies on MEST have been identified, and the PCR assay for amplification of these samples has been optimised. Additionally, doubts over whether restriction enzymes – used to cut DNA into smaller pieces – would work on the MEST fragment with the presence of structural features were dismissed after successful restriction enzyme digests. This work has provided solid grounding for future studies investigating why the three MEST SNPs behave in an unusual way, and the implications that this has for genetic testing.
Anxiety and insomnia (difficulty sleeping) are very common conditions that affect around 1 million New Zealanders nationwide. There are many different medications used to treat these conditions - one such medication is quetiapine. Until recently, quetiapine was a restricted medication used in high doses (over 300mg daily) to treat mental health conditions such as bipolar disorder, mania, and schizophrenia. Some self-reported evidence suggests quetiapine can improve anxiety and insomnia in some people if given in regular low doses (up to 50mg daily). High doses of this medication are known to cause side effects such as weight gain, and altered blood sugar and cholesterol levels. However, there has been little research into whether low dose quetiapine also causes these side effects.

Aim:
The aim of this pilot study is to find whether there has been any change in weight, blood sugar (glucose) and cholesterol levels while patients have been on a consistent low dose of quetiapine.

Method:

**Source population:** Patients of 16 Pegasus Health General Practitioners taking between 25-50mg of quetiapine daily.

**Sample population:** Patients from the source population who agree to take part in this pilot study. Database queries were run to find all patients fitting the study criteria. Any relevant information such as weight, body mass index (BMI), and blood glucose and cholesterol levels were noted.

Fifty six patients were found to fit the study criteria. These patients were sent a questionnaire asking if they had noticed any weight change since they started taking quetiapine. Their current height and weight, and other details related to weight change were entered into a database and simple statistic calculations were applied.

Results:
Thirteen of 56 patients responded to the questionnaire (a response rate of 23%). Eleven of these 13 patients reported a change in weight. Of these, 10 patients (76.9%) reported their weight had increased since starting quetiapine. If it is assumed patients who did not respond did not have a weight change, then of all patients sent a questionnaire 17.9% (10 out of 56) had gained weight.

The average current weight was 80.7kg, based on those who knew their current weight (12 out of 13). The average weight increase was 9.4 kg, based on the 9 out of 10 patients who knew their weight change. Out of the 10 patients who reported weight gain, 7 knew their current weight and by how much their weight had increased. Six of these 7 patients also knew their height. This allowed for calculations of body mass index (BMI) changes. BMI is a ratio of weight to height and is classified into ranges that are associated with health risk.

The range for each BMI (in kg/m²) category is:
- Underweight: less than 18.5
- Normal weight: 18.5-24.9
- Overweight: 25-29.9
- Obese: 30-30+

The average known BMI of patients before starting quetiapine was 26.43 kg/m². This means, on average 6 of the 13 patients who responded to the questionnaire were overweight before starting quetiapine. The average known BMI after starting quetiapine was 30.46kg/m². This means, on average 6 of the 13 patients became obese whilst taking quetiapine.

The weight increases seen in the study are significant. Some patients may put on enough weight to change them from being normal weight to being overweight, or from being overweight to obese. This change in BMI is important as being overweight or obese increases health risks such as heart disease and diabetes.
The most common reason patients gave for their weight gain was quetiapine use (80% of patients). The second most common reason given was change in eating habit (50% of patients). These results overlap as each patient could tick more than one answer.

Just over half of the patients (53%; 7 out of 13) who responded had a change in appetite. Of these, 4 patients reported increased appetite. Overall, 7% (4 out of 56) of all patients sent a questionnaire reported increased appetite (even assuming patients who did not respond did not have a change in appetite).

As this is a pilot study, the number of patients selected and the number of questionnaires returned are small. Therefore, this study can only detect a signal for further research rather than providing a definitive answer. This study relied on patients' memory and recall, and there were factors other than quetiapine that may have influenced weight gain.

**Conclusion:**
This pilot study showed that patients taking quetiapine who responded to the questionnaire had a clinically significant weight increase. Although this study was small and did not take confounding factors into account, an average weight increase of 9.4kg is large. Even if patients who did not respond had no weight change, this still shows at least 17.9% of the sample population gained weight. This is a strong signal that larger studies of people taking low dose quetiapine are needed to better see the adverse effects.
Emily Grant

Changes in the Nutritional Intake of Women with Bulimia Nervosa and Binge Eating Disorder with Cognitive Behaviour Therapy

Supervisors: Dr Virginia McIntosh, Dr Jennifer Jordan
Sponsor: Canterbury Medical Research Foundation

Binge eating is the consumption of a large amount of food in a short period of time (e.g. two hours) accompanied by a feeling of loss of control or not being able to stop eating. Cognitive behaviour therapy (CBT) is a form of psychotherapy commonly used to treat binge eating, which focuses on eliminating bingeing and resuming a normal daily food intake.

Women with bulimia nervosa (BN) and binge eating disorder (BED) engage in binge eating behaviour and these eating disorders have been linked to a range of health problems. Although CBT is an effective treatment for both disorders, relapse rates are high and CBT often does not result in weight loss for those high weight individuals with BED.

Little is known about changes in food and nutrient intake that occur over the course treatment for binge eating. A better understanding of this has the potential to improve the outcome of CBT or to help develop new treatments for binge eating. The objective of the current project is to examine changes in nutritional intake over the course of CBT for binge eating in women with BN and BED.

Fifteen women with BN and 15 with BED participated in the study; all were involved in a clinical trial of CBT for binge eating. Participants recorded their food and fluid intake for one week at three different time points: before beginning therapy, after six months of weekly therapy, and after a further six months of monthly therapy. Food records were entered into the Foodworks nutritional software programme, allowing intake of energy, water, macronutrients (fats, protein and carbohydrates) and micronutrients (vitamins, minerals and trace elements) to be computed. Statistical analyses were then conducted using the SPSS software programme.

First, changes in nutrient intake over the course of CBT were examined. Intake of energy and almost all macronutrients decreased during the six months of weekly therapy, but no further changes were observed after this. Intake of most micronutrients remained stable over the three assessments. Notable exceptions were vitamin A, sodium, potassium and selenium, which decreased from baseline to the end of weekly therapy, and then remained stable.

Nutrient intake over the course of CBT was compared for the two disorder groups: BN and BED. Nutrient intake did not vary between the two groups at any stage: the only differences observed were greater water intake and therefore higher weight of food consumed in participants with BN before therapy and after six months of weekly therapy.

These results show that the nutritional intake of women with binge eating disorders changes over the course of CBT, with the same pattern observed for both eating disorders. Reductions in energy and macronutrient intake but not micronutrient intake suggest that less binge-typical foods (such as bread and ice cream) are being consumed. This can be deduced because foods such as bread and ice cream are rich in macronutrients such as fats and carbohydrates, but low in most vitamins and minerals. However, the fact that energy intake remained higher than the recommended 8700kJ for an adult female may reflect some participants’ continued binge eating.

Future research on changes in nutrition over the course of treatment for eating disorders is needed to determine the impact of different forms of education and advice related to normalizing eating. Research on a larger sample size is also warranted.
Kirsten Gray  
*The Effectiveness of a Metabolic Screening Programme in a Specialised Mental Health Service*  

**Supervisor:** Associate Professor Sue Luty  
**Sponsor:** National Heart Foundation of New Zealand  

**Introduction**  
Cardiovascular Disease contributes significantly towards the excess mortality rates in individuals with chronic mental illness when compared to the general population. Risk factors for this include type II diabetes, hypertension, obesity and metabolic syndrome, all of which are more prevalent in severe mental illness even before treatment. The newer atypical antipsychotics and mood stabilizers (both common psychiatric medications) are being recognised as further increasing cardiovascular risk as they are often associated with weight gain, dyslipidaemia, insulin resistance and diabetes. Accordingly in mental health services where these are prescribed, it is important for clinicians to be aware of the increased cardiovascular risk of patients, and whether they are accentuating pre-existing risk.

A project was undertaken last summer which evaluated the assessment of cardiovascular risk and metabolic syndrome in patients enrolled in the Mothers and Babies perinatal Mental Health service at Princess Margaret Hospital. Patient notes were accessed and data was gathered regarding at risk medications and documentation of risk factors. Results showed that monitoring of risk factors was lower than desired and that there was a lack of identifiable screening protocols. Due to these findings, a basic cardiovascular and metabolic screening sheet was added to all patient files in August in an effort to improve patient care.

**Aims**  
1. To evaluate the effectiveness of the new screening tool at Mothers and Babies  
2. To update patient files ensuring all current patients are included in the programme including those who entered the service before August  
3. To further improve the metabolic monitoring programme at Mothers and Babies

**Method**  
First the notes of all patients entered since August were accessed and the use of the screening sheet was assessed. Although staff had committed to the programme with efforts to include the sheet in all notes, it was clear the metabolic monitoring programme was not yet fully established in the service as no monitoring had been started yet. The main issue seemed to be a lack of structure to the programme, for example no defined inclusion criteria and a lack of a step-wise procedure to follow. Initial feedback also revealed that a lack of confidence in metabolic testing was a barrier for some staff.

From this initial investigation I developed and implemented strategies to alleviate these concerns and enable the programme to work to its full potential. Some of the strategies included:

1. A literature search of other metabolic monitoring programmes. Conclusions drawn from this allowed me to develop inclusion criteria and reference ranges for our programme. The search also uncovered an example of a more sophisticated screening tool with which to base the Mothers and Babies programme around.
2. A strong effort to further educate staff about aspects of the programme – written information sheets about reasons for/parameters of metabolic monitoring and demonstrations of how to use monitoring equipment
3. Utilizing weekly staff meetings by allocating a time slot to discuss metabolic monitoring concerns
4. Prompting staff to initiate screening - giving a list of patients on at risk medications to each case manager and adding the new screening sheet to all patient notes myself (this time including patients entered before August)

At the end of the 10 week summer studentship I once again accessed patient notes to assess the use of the enhanced screening programme. I also developed a brief questionnaire to be completed by staff to assess attitudes towards the programme and to gain further feedback on how the programme is working in practice after these recent changes.

**Results**
Despite the original screening tool being added in August, no patients had been started on metabolic monitoring by the time I began the project in November. The strategies listed above were successfully implemented between November and January, and by the end of January 15% of at risk patients had baseline measurements recorded. The metabolic monitoring programme has been included in the Mothers and Babies Service Provision Framework (SPF) and will be continued in 2011.

Conclusion/Discussion
This result is a positive start to the Mothers and Babies metabolic monitoring programme. In the context of the holiday season, with many staff away and outpatients not attending appointments, to have 15% of patients underway is quite significant. Staff have commented they have already discovered patients with dangerous metabolic profiles and, regardless of the figures, any increase in awareness of cardiovascular and metabolic risk by staff and patients is beneficial. The programme has even brought up the idea of a ‘lifestyle balance’ group to be started within the service as a way to educate and assist patients in improving their physical health.

The work done this summer has provided a solid base of a system to build on through the year. The issues holding back the original screening tool have been resolved and every effort has been made to make the programme as easy and accessible as possible. The inclusion of metabolic monitoring in the SPF recognizes its importance within the Mothers and Babies service, and in time I expect it to be even more successful and part of standard practice for all patients.
James Hadfield

Preliminary Genetic Analysis in the Antidepressant Cessation Trial (ACT)

Supervisors: Professor Martin Kennedy, Associate Professor Dee Mangin
Sponsor: Canterbury Health Laboratories

Antidepressant use in westernized societies is widespread with around one in seven people in Christchurch currently prescribed long-term antidepressants. Cessation of medication may produce withdrawal symptoms mimicking recurrence of depression. The Antidepressant Cessation Trial (ACT) is designed to investigate the gradual cessation of fluoxetine (Prozac) in a group of around 300 patients in New Zealand.

Fluoxetine is classed as a selective serotonin reuptake inhibitor (SSRI) along with other common antidepressants such as citalopram and sertraline. Serotonin is a neurotransmitter often associated with feelings of well-being and happiness. Fluoxetine is believed to target the serotonin transporter, which shuttles serotonin from the synaptic space (between neurons) back to the pre-synaptic neuron. Thus, inhibition of this transporter theoretically results in higher serotonin concentrations and increased feelings of well-being. Genetic variability in a number of serotonin-related genes has been associated with both depressive symptoms and antidepressant response. Hundreds of studies have been undertaken but the results have been less than clear with many reporting no-association results and conflicting genetic effects.

Genetic variability of two genes was explored to see if these were linked to patient characteristics collected from the ACT study. The serotonin transporter (SLC6A4) has a number of identified genetic variants that affect function of the gene; one of these well studied variants is called 5-HTTLPR. A second gene, encoding for a serotonin receptor (HTR2A), has two forms which may influence the outcome of antidepressant treatment. DNA testing of the subjects via blood samples allows us to see whether the genetic variability affects their antidepressant response during the ACT study.

This research looked for a correlation between selected phenotypes (observable symptoms and behaviours) and the genotypes (DNA variants) for the two genes studied. In particular we were interested in overall depressive feelings collected via an internationally recognized clinical scale (Montgomery-Asberg Depression Rating Scale - MADRS), as well as other phenotypes related to some of the known side-effects of SSRIs such as nausea, insomnia and weight change.

The genotypes of patients were found to be similar to those expected in the wider population, and were in accordance with another study on the general Christchurch population. Given that this was a preliminary analysis on quite a small sample it should not be surprising that we found no significant correlation between sample genotypes and most phenotypic data. In particular MADRS scores were not significantly associated with the serotonin genotypes we looked at, although the average scores were seen to increase as the study progressed, irrespective of genotype.

Serotonin is also a regulatory agent in the digestive system which could explain the common SSRI side effect of weight change. We found a significant association between 5-HTTLPR genotype and patient weight when looking only at females (probability of less than 1% that this is due to chance). Despite small study numbers (DNA available for 97 females) the average weight difference was well in excess of 10kg, providing tentative evidence for the serotonin transporter as a body weight regulator.

Data collected by the ACT study is well suited for genetic analysis into depressive phenotypes. Here we have successfully examined two genes relevant to the action of SSRIs and shown that there is neither allelic imbalance with the wider population nor genotypic effect on clinically relevant depression scores. Notably we have detected a relevant association between serotonin transporter genotype and weight of female, depressed patients, although this preliminary finding will need to be further tested. At the conclusion of the ACT study the genetic data will be compared with the main outcome of the ACT study. This analysis should detect if genetic differences affect the symptoms commonly felt when withdrawing from fluoxetine.
Min-Hi Han

Identifying cell targets for hydrogen peroxide

Supervisors: Dr Paul Pace, Professor Christine Winterbourn
Sponsor: Health Research Council of New Zealand

As we begin to understand the fundamentals of complex diseases within our ageing population, there is now even more incentive to fully understand the precise mechanisms of the billions of cells that make up our body. Cells contain proteins that regulate and facilitate the numerous reactions that exist to keep us alive. When our body is under stress or attacked by infections, white blood cells produce oxidants that help to fight and protect us. Oxidants are generally toxic, but they are also found to be important at low levels for communication within the cell, and to signal various functions in response to stress as an early warning system. However, we also have a safety mechanism to protect our own cells from the reactive oxidants and free radicals by having proteins called antioxidants. Commonly known antioxidants are vitamin C and E contained in many fruits and vegetables. How cells respond to oxidative stress is significant to the pathology of many diseases.

Antioxidants, such as peroxiredoxins (Prx), react with and eradicate oxidants such as hydrogen peroxide ($H_2O_2$), a very common oxidant produced in our body. Research in my supervisors’ laboratory is focused on how one of these peroxiredoxins present in the cytoplasm of our cells, Prx2, is involved in the cell in response to $H_2O_2$, and the signaling role this protein could have. It has been found that Prx2 interacts with a protein called ERp46 that is present in the endoplasmic reticulum, although the exact mechanism of interaction is unknown. ERp46 is important in protein production by the cell and helps proteins fold correctly to their active structures. Characterising the interaction between Prx2 and ERp46 could prove to be important for understanding the mechanism of signaling within the cell in response to $H_2O_2$ stress and exposure.

To investigate this, we made our own Prx2 proteins that are identical to the ones in our cells so that we are not limited in quantity. We also placed a tag on the protein so it can be easily purified and separated from endogenous proteins. Adaptations to the putative interaction domains (cysteine residues) within the Prx2 protein were also made to identify which parts of the protein are important for interaction. We added these proteins under different conditions to cell lysates that had or had not been treated with $H_2O_2$. Binding or non-binding of our Prx2 proteins with the ERp46 present in cell lysates will tell us whether an interaction occurs and by what mechanism.

Through this project, I was able to modify the Prx2 proteins by oxidation so they mimic how they behave in the cell. I used a specialized column to purify the tagged proteins and their interactions. However, we detected non-specific interaction between our proteins and the columns. Further work is required to address this problem but it is highly likely that one of these cysteine residues is important for the interaction between Prx2 and ERp46, and that ERp46 has to be oxidized by $H_2O_2$ for this to occur. By using mass spectrometry we were able to confirm the presence of oxidised Prx2 proteins in their modified state. A novel finding was found in that one Prx2 cysteine mutant, which was previously thought not to exist in a dimer configuration, was detected with a molecular size that is equal to a dimer, and its implications warrant further investigation.

In conclusion, various parameters that are crucial in optimizing the protocol for determining the interaction between Prx2 and ERp46 were established, further paving the way for this fundamental process to be fully understood.
Endometrial cancer is cancer that arises from the lining of the uterus. It is the leading gynecological malignancy in New Zealand. The disease has a tendency to become progressively worse and cause death. Recurrent and metastatic endometrial cancer can become resistant to conventional chemotherapy and radiotherapy. Radiotherapy is the medical use of radiation as a part of cancer treatment. Radiation is usually applied directly to the tumour where it kills the malignant cells. It is the current mainstay in treatment regimens. Resistance to radiotherapy is frequently observed in patients and this hampers the efficiency of treatment regimens currently available. Therefore, there is a need for a novel therapeutic agent.

My research looked at the compounds in green tea as a therapeutic agent. Epidemiological data suggests green tea inhibits the development of some cancers. In fact green tea has been shown to contain active compounds with anti-tumour activity, including epigallocatechin gallate (EGCG) which has anti-tumour activity in vitro and in animal models. Therefore, I studied the effect of both pure EGCG and of a green tea extract, which contained EGCG and other active compounds. It is understood that the active compounds in green tea affect the tumour cells by interrupting signaling pathways. Within cells, signaling pathways are important events involving protein-protein interactions which are stimulated by environmental factors. Numerous studies have shown that radiotherapy alters signaling pathways in cancer cells. Thus, it was a plausible idea that using EGCG or a green tea extract together with radiation would produce a more pronounced anti-tumour effect. Hence, the additive or synergistic effects of combining these treatments were investigated.

A sample of endometrial cancer must be cultured to investigate the effects of an experimental treatment in vitro. This is known as the cancer cell model. Microtumours were the cancer cell model I used in my research. A microtumour is a 3-D multi-cellular structure, essentially a small mass of aggregated cancer cells. Traditionally, a 2-D (monolayer) culture has been used as the cancer cell model; however this does not mimic the in vivo tumour observed in patients. Microtumours show several aspects that resemble real tumour tissue.

Microtumours were generated from an endometrial cancer cell line. Normally, if endometrial cancer cells are placed in a culture disc with some medium, they will grow on the surface of the disc in a single layer- i.e. a 2-D monolayer. To prevent the cells adhering to the surface of the culture disc and encourage microtumour formation the culture discs were first coated with poly-HEMA, a polymer which renders the culture discs non-adhesive to the cells. The microtumours were then cultured for at least 4 days before being subjected to experimental treatments. To allow rigorous analysis of the effect the treatments had, a total of 8 culture discs were used; a control, three individual treatments of EGCG, green tea and UV radiation, the two separate treatments of EGCG and green tea extract administered before UV radiation, and the two separate treatments of EGCG and green tea extract administered after UV radiation. The microtumours were then incubated for a further 24 hours before being analyzed.

The first analysis investigated microtumour proliferation. Proliferation represents the growth and development of cells. Cells of the endometrium normally proliferate rapidly as a part of the menstrual cycle, furthermore cancer cells are characterized by uncontrolled proliferation. Before a cell divides it replicates its DNA so that both daughter cells have a copy. The proliferation assay uses a fluorescent nucleotide analogue called bromodeoxyuracil (BrdU). BrdU is incorporated into newly synthesized DNA, where it can then be detected by flow cytometry. Flow cytometry is a technique used to detect fluorescence and count cells. The results showed that the proliferation of microtumours was significantly reduced when EGCG or green tea extract were administered after UV radiation. Additionally, there was also a significant reduction of cell proliferation if green tea extract was administered before UV radiation. In contrast, green tea extract and UV radiation alone did not exert anti-proliferation effects. This suggests additive effects occurring between active compounds in green tea and UV radiation. More importantly, the order of administration is a crucial factor to produce the desired anti-tumour activity from combinations of green tea and UV radiation.

My research also investigated apoptotic activity of EGCG, green tea extract and UV radiation. Apoptosis is programmed cell death. It is a complex biochemical process resulting in change of cell morphology and leads to cell death. An assay using a fluorescent protein marker called ‘Annexin-V’ and flow cytometry
investigated apoptosis following the treatments. Results showed that no treatments had a statistically significant impact upon apoptosis.

An Enzyme-Linked Immunosorbent Assay (ELISA) was used to investigate vascular endothelial growth factor (VEGF) secretion. VEGF is a protein secreted by cancer cells to initiate angiogenesis, the growth of new blood vessels from pre-existing ones, a process which is crucial to tumour growth. Results from the ELISA showed, with the exception of UV radiation, that all treatments significantly decreased the secretion of VEGF relative to the control. There were no additive effects observed, which suggests EGCG/green tea extract alone suppress VEGF secretion.

The research also examined glucose metabolism of microtumours after treatments. Glucose metabolism represents the ability of the cancer cells to generate energy to sustain cell growth and survival. Cancer cells are normally characterized by high glucose metabolism, representing the high energy demands for rapid proliferation. An assay incubated microtumours with the fluorescent glucose analogue called ‘2-NBDG’, the subsequent fluorescent staining could be detected through flow cytometry. Results showed UV radiation caused a significant reduction in glucose metabolism relative to the control. The combinations of EGCG/green tea extract and UV radiation also significantly reduced glucose metabolism, however this can be attributed to the reduction caused by UV radiation alone.

In conclusion, my results suggest that combinations of EGCG/green tea extract and radiation produce measureable and additive effects in microtumours, especially the effect on reduction of microtumour proliferation. Thus, using EGCG/green tea extract as a novel therapeutic agent in conjunction with current treatment regimes, such as radiotherapy, may improve the effectiveness of endometrial cancer treatment. The results here will contribute to a growing body of knowledge that aims to increase the efficiency of treatment regimens and ultimately increase the overall survival of patients.
Breast cancer is a major cancer affecting New Zealand women, with an excess of 2,500 new diagnoses and 600 deaths each year. Aging is the most common cause with more than 70% of new diagnoses occurring in post-menopausal women. However, obesity has also been shown to increase the risk of breast cancer and is an increasing health problem in the population.

Chemotherapy, particularly in women is associated with loss of lean tissue and increase in body fat. Macrophages (a type of white blood cell that are involved in our response to infection) are thought to be more abundant in the body fat of people who are obese than from those of normal body weight. Excess fat/oil that escapes into the blood stream can provoke inflammation of the blood vessels. The human body responds to this by releasing various proteins into the blood stream. Plasminogen activator inhibitor-1 (PAI-1) is one of these proteins.

It is thought that PAI-1 assists in cancer development by increasing the number of tumour cells, supporting the tissue network on which they grow, and aiding new blood vessel growth. Several studies have shown that high tissue levels of PAI-1 are associated with a poor prognosis in breast cancer. PAI-1 is also involved in blood clotting, which lead to strokes and heart attacks and pose a significant risk to cancer patients.

The aims of this summer project were to; (1) determine whether PAI-1 directly affect breast cancer cells growth and migration and (2) observe whether there is an association between moderate differences in body weight/composition of people with breast cancer, the number of macrophages in their tumour and PAI-1 levels in their blood.

This study involved various laboratory techniques including:

Migration Assay
To assess cell migration the breast cell line MCF-7 was cultured in the presence of PAI-1 protein and cell mobility was assessed using a scratch test. Breast cancer cells were allowed to adhere to a plastic well. A scratch was made through the cell layer and photographs were taken at different time intervals to observe the movement of the cells.

Cell Division
To assess if cells were dividing more rapidly in the presence of PAI-1, a 5-bromo-2'-deoxyuridine (BrdU) incorporation assay was carried out. In this assay a fluorescently labeled antibody that recognises BrDu is incorporated into newly dividing cells. The intensity of the fluorescence can then be measured to give an indication of the number of cells in which the fluorescent label has been incorporated. Three different dilutions of the MCF-7 cells were grown in plastic wells in the presence of three different concentrations of PAI-1. The cells were then assayed to measure the incorporation of BrdU.

Assessment of macrophage numbers
Blood and tissue samples from patients with breast cancer (n=19) were obtained from the Cancer Society Tissue Bank (CSTB). Breast cancer tissues were immunostained to look for the presence of macrophages in the vicinity of the tumour. This technique uses an immunological marker called an antibody, which attaches to and colours a specific target protein. When the staining was complete all breast tissue specimens were examined under a microscope. Ten areas were selected in each breast tissue sample, and the macrophages within this area were counted. An average of the cell counts was calculated and used to correlate with patient information.

Assessment of PAI-1 activity in blood samples
The PAI-1 activity in each of the plasma samples was determined using a PAI-1 activity ELISA assay. This assay used a pair of antibodies that were raised to recognize PAI-1. The first (capture antibody) was adhered to a plastic well. The plasma was then added and PAI-1 in the plasma was captured. The second (detection) antibody was added. The capture antibody incorporated a fluorescent label and the fluorescence could be measured to give an indication of the amount of PAI-1 present in the sample. The results were correlated with patient information.
In these assays; the scratch test clearly indicated that migration was increased in the presence of PAI-1 and that it increased with increasing PAI-1 dose. Statistically the PAI-1 treatment accounted for 29.35% of the total difference between the different concentrations (p-value 0.0173) therefore, the effect is considered significant. The BrdU incorporation ELISA assay indicated that PAI-1 does not increase cell proliferation at the different cell concentration or PAI-1 concentrations that we tried. Immunostaining for macrophages in the breast tumours suggested that the number of macrophages decreased within the tumour, however observation suggested that they may be increased numbers within the fat outside of the tumour, but these were not counted. PAI-1 intensity in the plasma increased as breast weight increased. Breast weight was grouped into a low (287g – 484g) and a high (703g – 2040g) category. The PAI-1 intensity in the plasma illustrated a strong correlation between PAI-1 activity and cancer grade. Some of the absorbance readings for the plasma samples fell below the detection of the kit. Therefore, having a kit that is more specific in this lower range would help to validate the results obtained.

This experiment concludes that PAI-1 increases cell motility but does not increase cell proliferation. Breast weight does appear to have an effect on the PAI-1 intensity in the blood and the number macrophages within the tumour, as PAI-1 activity increases and the number macrophages within the tumour decreases as the breast weight increases.

This study has provided valuable biological pilot data to suggest that larger and more extensive studies are warranted to look at the benefits of achieving healthy body weight for women recovering from breast cancer treatment.
Katie Jefferson  
Exploring and Understanding the Learning Needs of General Practice Administrative Support Staff  
Supervisors: Professor Les Toop, Kelly Maw  
Sponsor: Partnership Health Canterbury

Over the past 10 years we have seen an increase in the delivery of services and a shifting of roles and responsibilities within general practice. This in turn impacts on the complexities of roles within the practice teams, and greater efficiencies required for the ongoing management of the businesses and delivery of health services. As front line staff for general practice, Practice Managers and administration support staff (this includes receptionists, administrators and secretaries) make up a large percentage of our primary health care workforce. They are the staff who receive the initial phone calls, meet and greet the patients, give that first impression of the general practice team to the general public. Their job is varied and requires skills in a number of different areas such as customer service, computer programmes, finances and more. Although their positions require the use of many skills, there are currently very few training programmes in place to support this group and no structured professional development to help them increase their skills and keep informed of the ever-changing health system. Although results from a practice audit by Pegasus Health in 2010 indicated that administration support staff are identified in their workplaces by varying role titles and undertake many differing tasks daily, we recognized a gap in our knowledge and understanding of their professional development needs. There also appears to be no previous research into the backgrounds and learning needs of this group.

The purpose of this study was to explore the various titles, qualifications and position descriptions of general practice support staff. The study also aimed to establish the learning needs and levels of training required to support this group.

An initial literature review into current training and professional development programmes revealed that the only available course specific to practice managers in general practice is run by NZIM (New Zealand Institute of Management) and there are limited opportunities available specifically for receptionists in general practice. There are a few customer relations courses available through Kiwi Host as well as some general management courses available through various other institutions but nothing specific to general practice. The only professional development currently available is either organised by the practice, through PMAANZ (the Practice Managers Association of NZ) or occasional information sessions facilitated by Pegasus Health. From this review a questionnaire was designed and sent out to 349 administration support staff from Partnership Health Canterbury PHO, whose details were listed on the Pegasus database of practice staff. The responses from these questionnaires were analysed and volunteers participated in a focus group where issues that were raised in the questionnaire were explored in more depth. The focus group discussion was audio taped and transcribed so that themes could be drawn from it.

We had a 43% response rate from the questionnaire with 46% of respondents identifying themselves as receptionists, 26% as practice managers, 21% as administrators, 3% as secretaries and 5% as other. Although the survey supported our previous findings regarding various roles and titles, the research project did not explore how these roles differ. Almost all of the respondents were female and a number (23%) reported that they did not have position descriptions for their current role. The majority (66%) of respondents had some sort of formal qualification with a tertiary qualification being the most common (21%) followed by attendance at a receptionist course. 64% of respondents reported they did not have a structured orientation programme for their current position. The survey requested participants suggest fundamental content for a standardised orientation resource; the top four were a written job description including expectations from their employer, an introduction to the practice including the staff and patients, a run-through of all policies and procedures for the practice and a trial period including one on one tuition in the role with a current staff member. Surprisingly the majority of people said that they were well informed of professional development opportunities and most said that they were able to participate in professional development opportunities when and if they arose, even though lack of time was the most common barrier to participation in professional development. The second aim of this project focused on the learning needs and training required to support this group. Although only 25% responded to this question the focus group discussion centred on this area and mirrored responses from the survey. Findings from the survey identified the most common learning need was in the area of business skills, closely followed by computer programmes.

The lack of structured education opportunities was discussed at length within the focus group and the need for the development and formalization of a standardised orientation resource was highlighted. This need
was also mirrored by a large number of participants from the survey who reported that they did not have a structured orientation programme in their most recent position. The formation of a standardised orientation resource would ensure that staff in all practices had opportunities to develop the same skill-set to confidently perform the tasks required. Another suggestion was to have a modular course or information sessions on a variety of “hot topics” – areas that people struggle with or have undergone recent change and require a refresher. Some suggested topics included confidentiality, the health system, finances, legislation and customer relations. It was also suggested that there could be different sessions for practice managers to receptionists and administrators as the roles require different knowledge and skills. Another suggestion that would provide this group with more support was the formation of peer group meetings where staff from different practices could meet and discuss problem-areas and through their combined knowledge come up with a solution. It was noted that this would be especially beneficial for reception and administration staff as they currently do not get the opportunity for this sort of discussion, whereas practice managers do. A theme that was consistent throughout the discussion was that some standardisation across practices would be beneficial. Of course every practice is individual and caters to its own specific needs, but it was agreed that standardisation of some policies and procedures would be a good thing and would help to support the practice managers. Along with this it was suggested that resources be available online so that practices have an easier way of communicating and sharing with each other. This would also provide a repository for framework templates and guidelines for writing policies and procedures and so help to standardise important management aspects of the general practices.

Administration staff in general practices play a very important role in the provision of care to patients, so it is important that they are equipped with the necessary skills and knowledge required to perform their roles effectively. This group is identified by varying role titles; the majority of them hold a qualification for their role and most have a position description. The survey identified that this group would benefit from the formation of a structured professional development programme including an orientation resource, modular sessions, peer group forums and improved availability of resources.
Approximately 50% of acute admissions to medical wards in Christchurch Hospital (CH) are over 75 years old and about 20% of these are referred for rehabilitation prior to discharge home. As the New Zealand population ages and medical admissions continue to increase [10% per year] so will the demand for rehabilitation.

Furthermore, elderly patients are predisposed to de-conditioning and delirium during hospital stay. This could trigger a downward spiral that leads to loss of independence and further health problems. In order to prevent this scenario, elderly patients need timely intervention during the recovery phase of their acute illness. In CH this is usually initiated by nurses, physiotherapists and occupational therapists. However staffing levels are variable and acute wards are not specifically equipped for rehabilitation. Princess Margaret Hospital (PMH) has 5 specialised rehabilitation wards which continually receive patients from CH, the majority from general Medicine. When a referral is made, a fax is sent to PMH and the patient is allotted to a geriatrician who will assess the patient and decide whether transfer to PMH is appropriate.

The aim of this project was to prospectively analyse the waiting times from referral to PMH to transfer for elderly patients admitted to General Medicine at CH over a one-month period from 6/11/10-3/12/10.

My method involved identifying all patients from the 5 general medicine wards in CH who were referred to PMH (whether for transfer and rehab, for HLC sign off, for PSE input or just for advice on clinical care) over the aforementioned 4 week period. These patients were identified each working day through the return faxes that were sent from the coordinating secretary at PMH every time they received a referral. The occasional outlier was picked up through examining the waiting list and the list of patients who were admitted to PMH each day. Patient demographics, medical conditions, and waiting times between referral, assessment and transfer to PMH were recorded from the patient notes.

Results:
During this 4 week period I recorded a total of 118 patients who were referred to PMH, either through a Psych Services for the Elderly (PSE) referral or an Older Persons Health Specialist Services (OPHSS) referral. Of these 118 patients 11 had referrals to both services while 12 patients had referrals purely for PSE. This left 95 patients referred just through OPHSS. 1 patient was lost to follow up as I could not locate...
their file, while 4 patients died during the data collection. Where available any information I had on these patients was included in analysis.

The average age was 82.4 years, with the oldest patient being 98 and the youngest being 62. There were 62 female patients and 56 males. In regards to ethnicity, there were 94 of European descent, 9 other European, 2 NZ Maori, 4 other ethnicity and 9 were not stated. 39 of these patients lived home alone, 40 lived at home with another person, 3 lived in independent units, 27 lived in rest homes, 4 lived in hospital-level care while for 5 patients this information was unavailable.

The mean waiting time from referral to transfer was 4.7 days [range1-16]. Broken down - the mean waiting time to be assessed by a geriatrician was 1.4 days [range 0.5-11]. The mean waiting time for transfer after assessment was 3.3 days [range 0.5-15]. The mean length of stay in CH was 9.1 days, [range 2-33] but half of this time [4.6 days, range 1-25 days] was prior to referral.

Problems:
- General Medicine is the acute geriatric admitting service for Christchurch and despite a decreasing average length of stay [4.5 days over-all] there is still severe pressure on bed occupancy. Therefore 4.7 days is too long for elderly patients to be waiting for rehabilitation. Currently half the patient’s stay in CH is spent waiting for assessment and transfer. The wait between assessment and transfer is the main problem.
- There is some evidence for patients de-conditioning while they wait.
- CH wards are not specifically equipped for rehabilitation, particularly after the patient is accepted for PMH transfer.

Potential Solutions:
- Permanent Geriatrician in CH to patrol all general medicine wards, with admitting rights to PMH
- Community geriatric services that can assess patients and refer to PMH without admitting to CH
- Better rehabilitation facilities at CH e.g. implement a rehabilitation ward
- Education for general medicine doctors about timely rehabilitation during acute admission
Hannah Kennedy

Mitochondrial Targets of Isothiocyanates

Supervisor: Associate Professor Mark Hampton
Sponsor: Garth Streat Memorial Scholarship

Isothiocyanates are a group of naturally occurring chemical compounds found in cruciferous vegetables such as watercress and wasabi. It is these compounds that produce the bitter taste and pungent smell, and may act as an insecticide for such vegetables. Previous research into isothiocyanates has shown that they may have both anti-cancer and anti-inflammatory effects. In cancerous cells the normal regulation of natural cell death is disrupted causing unchecked growth. Isothiocyanates have been shown to trigger natural cell death in these cancerous cells making them an interesting group of compounds to study for cancer researchers.

If it possible that by identifying exactly how isothiocyanates kill cancerous cells, then new targets for novel chemotherapy drugs may be uncovered. These novel drugs would be important in the case of cancerous cells that are resistant to conventional chemotherapy options. Previous research on the mechanism of isothiocyanates on cells has been carried out to look at what proteins interact with isothiocyanates in the cell (as these will be important in reestablishing natural cell death). One protein in particular was identified as a target of isothiocyanates; Migration Inhibitory Factor (MIF).

The current project aimed to identify targets of isothiocyanate action in cells by physically isolating interacting proteins from cells that have been broken open. In order to isolate these proteins a synthetic form of an isothiocyanate was produced that would chemically bind to tiny beads. These beads can then be incubated with the broken cell mixture and any proteins that normally interact with isothiocyanates will bind. The non-interacting proteins can be washed off the beads, leaving only proteins of interest. These proteins can then be removed from the beads and separated for identification on a gel matrix.

It was expected that the previously identified protein MIF would be one of the proteins that the beads would separate, but we were also interested in other proteins that may interact but were being overshadowed in the first study by the large amount of MIF present. The cells used in this study were Mouse Embryonic Fibroblast cells (MEF’s). Two strains were cultured; one normal strain, and one that was missing the MIF protein. In this second strain we would not expect to find any MIF protein so other targets may be more obvious.

Two initial experiments were required before the bead experiment could be performed;

i) Firstly, the effectiveness of the synthetic isothiocyanate needed to be compared to the natural form. In order to do this, cultured MEF cells were treated with both natural isothiocyanate and the synthetic form over six dosages. The effectiveness was determined by measuring the percentage of cells that had died after 24 hours of treatment and graphing these values against the treatment dosage. The viability curves produced from the synthetic form matched the natural form well indicating it is similarly effective in producing cell death.

ii) Secondly, a blocking step in the bead experiment procedure was investigated. The beads attach to the isothiocyanate via a chemical linker that may also bind unwanted proteins (not true targets). To avoid this, a blocking agent is normally added to the beads after the isothiocyanate is joined to use up any of these remaining linkers. We investigated three different concentrations of blocking agent and discovered that this produced no difference between the amount of background proteins that were attached to the beads. This indicates that the background binding of proteins to the linkers on the beads is low and blocking the linkers does not have a great effect. Interestingly by looking at the proteins binding to the beads with and without the isothiocyanate attached, and with or without blocking agent if was found that a lot of the extra proteins that were binding were doing so non-specifically, in other words onto the bead itself and not through the linkers.

Since non-specific binding was occurring it was important to include a control of beads without isothiocyanate attached that were completely blocked with blocking agent before being exposed to the cell mixture. Proteins recovered from these blocked beads as well as the isothiocyanate conjugated beads can be visualized by separating the proteins on the gel matrix. The two patterns of proteins can then be compared and any proteins visible on the isothiocyanate beads but not on the blocked beads would be of interest to follow up.
Both the normal MEF cells and MEF cells missing the MIF protein were tested with both blocked beads and isothiocyanate conjugated beads and the bound proteins separated on a gel matrix. Although proteins were successfully pulled out of these cells onto the beads there were no visible proteins of interest. The previously identified MIF protein was also not seen in the normal MEF cells as was expected.

Although these results differ from the previously reported interaction of MIF and isothiocyanate they were drawn from a different cell type. The previous work involved the use of Jurkets cells not MEF cells. There is the possibility that the levels of MIF protein in MEF cells is much lower than the Jurkets and the method of isolating proteins is not adequately sensitive. The next step would be to repeat this experiment in the Jurket cells originally used, to confirm that MIF can be isolated using the current isothiocyanate and the same methodology used in this experiment.
Most patients in intensive care units (ICU) are mechanically ventilated. Sedation is required to keep these patients asleep and to ensure they do not respond to noxious events. A common regime used in Christchurch for sedation includes the use of the two drugs propofol and fentanyl. Propofol is a hypnotic anaesthetic with amnesic effects, and fentanyl is a rapid onset synthetic opioid used to treat pain. Maintaining the correct level of sedation is complex. Patients need to receive enough to allow for ventilation but higher drug levels take longer to wear off, are costly, and side effects are increased. Staff in the Christchurch ICU have a special interest in sedation and have developed drug dosing regimens and computerised delivery systems. These systems record dosage and the data can then be easily used in spreadsheets. Using tools developed in anaesthesia, drug levels can be calculated from these dosage histories.

The aims of this project were to derive the propofol and fentanyl levels using models at the time of interventions, and explore the relationship of these to patient responses and to look at the propofol and fentanyl levels used over time in the clinical setting, and relate the blood levels to established sedation scores.

Data were collected from automatic recordings and patient charts. Patients were observed and their responses scored on a sedation scale. Models were used to calculate drug levels and combined to produce a likelihood of response score.

Our results showed it is feasible to calculate blood levels over time using the available data. Most patients spent most of their time sedated in a certain zone of combinations of propofol and fentanyl. It was not possible to relate the sedation score to blood levels across all patients because of patient differences. Eight patients whose sedation levels were scored more than nine times were looked at closely. The combined drug levels scores produced by the anaesthetic tool appeared to correlate with the observed sedation level for six of these patients. In the other two the results diverged over time. This may have implications for clinical management because the divergence may represent a change in drug needs or clinical state.

This study has shown that it is possible to calculate drug blood levels in ICU. There appears to be an association between the modeled combined drug scores and observed sedation scores. These models are currently used in anaesthesia and this study suggests it may be feasible to use similar models in ICU. An issue with the current models is they are based on results from healthy people over shorter time periods than an average ICU stay. ICU patients also have a diverse range in physiological disturbances so the accuracy of the models used can be questioned.

Further research is needed to establish the accuracy of the models. Actual blood levels of different groups of ICU patients need to be compared to the modeled data over time. Further investigation needs to look in more detail at how the combined scores relate to clinical measures. Finally, a system that allows real time display of predicted sedation level needs to be developed and evaluated to aid in the complex clinical management of sedation.
Jeremy Keown

Use of Radio-Opaque Nanoparticles for Micro-CT Scanning Using the MARS-CT System

Supervisors: Dr Bruce Dobbs, Associate Professor Randall Allardyce, Dr Anthony Butler

Sponsor: Christchurch Radiology Group Trust

The goal of the Medipix All resolution System (MARS-CT) project is to develop a spectral CT to replace current CT technology. The role of the nano-particle team, as part of the wider MARS-CT development group, is to demonstrate the ability of MARS-CT to visualise biological processes. My role in the nano-particle team was to produce, size and test the effectiveness of different contrast agents in demonstrating tissue and organ function and microanatomy using MARS-CT.

X-rays are produced at a range of wavelengths, this spectrum, when measured by standard CT, gives a greyscale image based on the attenuation, of the transmitted x-rays (Usually x-ray images are shown as negatives, black = little absorption, white = large absorption.). The degree to which the x-rays are attenuated, reduced in total intensity, is determined by the relative densities of the materials the x-rays pass through before they reach the detector. Standard x-ray based computed tomography (CT) shows bone (calcium) as white but will also show contrast agents such as iodine or gold as white, even though the absorption spectra are different.

The unique Medipix detector, utilised in the MARS-CT, is able measure the energy of individual x-ray photons, enabling high resolution of x-ray energy and tissue spatial relationships. By comparing images above and below the k-edge (the point at which the photons have more energy than the K-shell electrons) it is possible to discriminate regions of different atomic composition.

To improve the ability of the MARS-CT scanner to visualize biological processes I created nano-particles filled with iodine to improve contrast within the scan. Nano-particles are microscopic particles that can be synthesized to hold many contrast agents; in essence they are a small ball of fat that has a layer of surfactant that allows the fat to be soluble in water. The interior of the ball contains iodine, which due to its distinct atomic structure allows MARS-CT to readily distinguish it within organs and tissues.

We had previously shown that the emulsion particles were of a consistent size but were unsure as to whether they degraded over time. To test the stability of the particles I travelled to Dunedin where I measured the size distribution of the particles, I found that the particles were of a very stable nature.

From here we chose to try a different contrast agent in colloidal gold, this is micro gold dissolved in aqueous media. Gold is much denser than iodine and hence gives a better signal when imaged. We started by directly injecting this into the foot pad of a mouse, where it travelled through the lymph system, however the MARS-CT configuration that we were using at the time did not possess a sufficiently high powered x-ray source so we were unable to differentiate the gold.

Our most recent experiment involved injecting small volumes of Omnipaque, an aqueous form of iodine, into the tail vein of a mouse with the hopes of visualising parts of the renal system. In this we succeeded by distinguish both Kidneys from surrounding tissue.

In conclusion we have shown the stability of our nano-particles over time, have validated our injection protocols with regards to intravenous tail injections and the usefulness of this method to give good images using MARS-CT. It has also shown a gap in our method with the incorrect configuration of one MARS-CT scanner, since this was discovered a new higher energy x-ray source has been acquired allowing us to discriminate gold.
“Free Radicals” are reactive chemicals which are produced in the body. They are known to be toxic and contribute to aging. The most abundant free radical in vivo is superoxide, which forms as a by-product from the oxygen we breathe. The average adult is thought to produce approximately 10 kg of superoxide per year. Superoxide has been shown to be toxic as animals genetically modified to have no superoxide dismutase, an enzyme that removes superoxide, cannot survive. However the mechanisms of superoxide toxicity are not well understood. Superoxide has been shown to react with another free radical, nitric oxide, in vivo to form a highly toxic molecule called peroxynitrite. The formation of peroxynitrite contributes to superoxide toxicity but does not explain it fully.

Proteins are made up of amino acids, including one called tyrosine. Another potential mechanism suggested to contribute to superoxide toxicity is the modification of this amino acid on proteins. Tyrosine can be converted to a free radical form called a tyrosyl radical. Tyrosyl radicals can be produced by a certain type of enzyme called peroxidases. Some other enzymes form tyrosyl radicals in their active site as part of their functional processes. Also, radicals on proteins generated during oxidative stress (for example at sites of inflammation), tend to localize on tyrosines to form tyrosyl radicals. It is known that superoxide reacts rapidly with tyrosyl radicals to form a modified tyrosine. However these reactions are yet to be demonstrated in vivo.

My previous work has shown that the superoxide-modified tyrosine, in a range of short amino acid sequences, reacts with a molecule called reduced glutathione (GSH) to form a “superoxide-modified tyrosine–glutathione adduct” (TGA). We also determined that TGA can form on a specific protein (sperm whale myoglobin) in a test tube. GSH is very abundant in the cellular environment; therefore my aim was to characterize the chemistry of the formation of TGA to indicate if it is likely to form in cells, and how it may be detected as a potential biomarker for superoxide modification of proteins.

My investigations over this summer indicate that the formation of TGA is likely to be favorable and rapid in cellular conditions. However the reaction is reversible, such that in high concentrations of GSH (such as is present in cells), a high proportion of superoxide-modified tyrosine will form TGA, but when the concentration of GSH is low, the TGA will disassociate.

This reversibility has significant impact on the detection of TGA on proteins, because processing of samples to detect the TGA may lead to the dissociation of TGA. However collaborations within the group have demonstrated a chemical method that can stabilize the TGA, and remove GSH attached to proteins by other mechanisms. This chemical stabilization has been shown to prevent dissociation of the TGA during analysis of our model protein sperm whale myoglobin, significantly increasing the amount of TGA detected.

This method provides a lot of promise for our ultimate goal of being able to identify this modification on proteins from inside cells using an antibody that specifically recognizes and binds to glutathione. When successful this method should lead to identification of proteins that are modified by superoxide in vivo, thereby contributing significantly to our understanding of superoxide toxicity in disease and aging.
Maori in New Zealand experience significant health disparities and inequalities compared to non-Maori. Maori are dying on average 15 years younger than non-Maori, and the rate and death toll of many diseases are significantly higher than non-Maori. There are many factors that contribute to these disparities, but even after statistics are adjusted for factors such as socioeconomic status, the gap between Maori and non-Maori is still very significant.

It has been acknowledged by previous studies and by the public, that culturally competent health professionals are needed to bridge this gap. Failure to acknowledge and understand the cultural variations in health beliefs can hinder the relationship between clinicians and patients. A good relationship between patients and health professionals is essential to have trust, good communication, understanding and patient satisfaction. Patients that are comfortable with their clinicians are more likely to share vital information that they might not have otherwise done so. Ultimately, it leads to better health care and outcomes for Maori.

At the University of Otago, Christchurch School of Medicine, Hauora Maori is an important part of the curriculum from 2nd to 6th year. One of the pivotal parts of the Hauora Maori curriculum is the Hui Process. The Hui Process applies traditional Maori principles of greeting, introducing, starting a relationship and closure to the contemporary setting of a medical consultation. This framework is a very important part of the medical school curriculum and is taught to be integrated and used with any Maori patient contact.

The aim of this study is to evaluate what Maori think of the Hui Process, and to see if it improves the cultural competency of the health professionals who uses it. This was carried out via the Hauora Maori day, which was a student led clinic offering healthcare and wellbeing services to the Maori community. This was provided by 25 clinical supervisors and 98 fifth year medical students, held at Rehua marae on the 16th March 2010. Participants, students and clinical supervisors were then asked to fill out a questionnaire to rate perceived appropriateness of utilizing the Hui Process within a clinical setting. The questionnaire consisted of questions asking how the students did in the different components of the Hui process, as well as their overall impression of it; details of demographics and socioeconomic status was also collected.

Approximately 200 members of the community attended the Hauora Maori day. 110 Maori community members (whom completed the survey and met the inclusion criteria), 98 students and 25 clinical supervisors completed the questionnaire. Overall, Maori community members gave very positive feedback about the Hui Process that was undertaken by the medical students. Most of the Maori community members in this study rated the Hui Process highly. 80% of them agree/strongly agree that the Hui Process enhanced the relationship between student doctors and themselves. 77% of them agree/strongly agree that all health services should adopt the Hui Process, and 83% agree/strongly agree that they would be more likely to attend if this was the case. This was significantly different to the fact that only around half (55%) of Maori community members in this study agree/strongly agree that their current health provider is using the Hui Process when interacting with them. Students and supervisors scored very similarly to the Maori community members in the questionnaire, agreeing that the Hui Process enhanced the relationship between student doctors and the Maori community members; and that it should be used by all health practitioners. However, students and supervisors rated the ability of their current health provider to use the Hui Process, significantly lower than the Maori community members. Students and supervisors agreed more than the Maori community members that they would prefer all health practitioners to use the Hui Process, and believe patients would be more likely to attend health services if this was the case.

In conclusion, Maori community members, students and supervisors in this study believe the Hui Process enhances the relationship between patients and clinicians. They would like all health professionals to use the Hui Process when interacting with them, and would be more likely to attend health services if this was the case. This study is one of the first to evaluate how Maori received cultural competency intervention. The Hui Process has proven to be an effective tool to increase the cultural competency of health professionals; and adoption of the Hui Process could improve Maori experiences within the health system, potentially decreasing the Maori health disparities.
Participants included five women with binge purge type anorexia nervosa (ANBP), five women with restricting type anorexia nervosa (ANR), twenty women who are constitutionally thin (CT) and eighteen healthy weight women as a control group (HC). All participants were from the Christchurch area and were aged 16-50 years at the start of the study. Participants kept a three day food diary, in which they recorded all foods and beverages they consumed each day. Each participant had an interview after completing the food record to ensure all recording was clearly understood. The food diary information was entered into the Foodworks computer programme to calculate average daily nutrient intakes and composition of the energy intake (% of daily energy from each macronutrient) for each group. This information was input into the SPSS statistical package where some differences between the four groups were identified.

There were no differences in the age of women in the four groups. All women in the underweight groups had a BMI of between 16 and 19 whereas the healthy control group had BMIs ranging between 20 and 27. We found that women in the HC group had higher energy intakes than women in either the ANR or CT groups which is consistent with the BMI of these groups, i.e. the group with higher body weight had higher energy intakes. However, this pattern did not hold for the ANBP group whose intakes were much higher than all other groups including the HC group despite being lower in weight. The ANR group consumed less total fat than all other groups, and less saturated fat then the CT and HC groups. These women also consumed less cholesterol than the HC and ANBP groups. This suggests that women in the ANR group chose foods lower in fat than all the other groups. There were no differences in the intakes of carbohydrate between groups. Women in the ANR group consumed less protein than women in the HC group. Women who are constitutionally thin had a lower fibre intake than those women in the HC group. Women with ANR obtained a lower proportion of energy from fat than other groups, and a higher proportion of energy from carbohydrate than CT and HC. There was no between group difference for energy obtained from protein.

Our results are similar to some previous studies that have also found that healthy controls consume more energy than women with anorexia nervosa. No other research has looked at dietary intake of CT women versus women with ANR so it is surprising to find that their energy intake is the same. Participants with ANBP on average had a much higher energy intake than all other groups, probably due to episodes of binge eating. This suggests that the ANBP subjects in this study may not be comparable to those within anorexia nervosa groups in other studies. Some other studies have grouped both anorexia subtypes together into one category and our results show that this is not a true reflection of eating patterns in these women.

In our study, women with ANR consumed less protein than those women of healthy weight. There is conflicting evidence as to whether anorexia nervosa patients generally consume different amounts of protein than those without anorexia nervosa and therefore there are no reported trends. Constitutionally thin women had lower fibre intake than HC, but there were no patterns observed for those with anorexia nervosa. Few studies have reported that women with anorexia nervosa consume more fibre control subjects; however other studies have reported no difference. Other studies have noted that due to lower energy intake in anorexia nervosa, there is generally a lower intake of carbohydrate, however no differences were observed in this study. Women with anorexia nervosa may choose to eat high sugar foods such as lollies to provide...
energy without consuming a lot of calories at one time. If this was the case, it would increase the amount carbohydrate intake in these women. There is agreement in the research that those with anorexia nervosa tend to consume less fat than those without anorexia nervosa; therefore it is not surprising that this was also the case in our study.

Looking at the percentage of energy from different sources (i.e. fat, carbohydrate and protein) informs the macronutrient composition of the diet. There were no differences in the percentage of energy obtained from protein amongst the groups; however women in the ANR group obtained more energy from carbohydrate than women without an eating disorder (CT and HC groups). Other research is unclear as to whether there is either increased intake or no difference for both of these macronutrients suggesting more research is needed to confirm any trends. Women with ANR tended to obtain less energy from fats than other groups. This is consistent with other research indicating that the most noted trend in restricting type anorexia nervosa is to primarily restrict fat intake. There were no differences in the macronutrient composition of the diet between women in the HC, CT and ANBP groups. This means that regardless of how much energy they consume, they consume around the same proportions of fat, carbohydrate and protein.

Limitations of this study include small sample sizes in the anorexia nervosa categories, and inclusion of subjects with differing binge/purge habits, and psychological profiles. Differences in the days and seasons each participant kept their food diary, as well as being unable to account for energy lost in purging in the ANBP group meant that results may be less accurate. Strengths of this study include use of three day food recording instead of methods that rely on memory such as 24 hour recall, and training participants in food recording.

Further research should focus on comparing food intake in larger samples of women with ANBP, ANR with CT women. This will allow patterns in food choice of underweight women to be identified and may help to inform why women with different anorexia subtypes choose the foods they do, and how this compares to women of the same weight who do not have anorexia. Therapies for different subtypes may be informed by identifying differences in food choice between groups and tailoring focus to problem areas. Comparing women with anorexia to constitutionally thin women who have similar energy intakes and body weight may aid further understanding of psychological issues faced during food choice in anorexia nervosa and hence further inform therapy.

In conclusion anorexia nervosa subtypes have differing diets from each other, and each subtype tends to show differences in the amounts and proportions of macronutrients consumed compared to similar weight constitutionally thin women and normal weight controls. This information will add to the current knowledge surrounding diets of women with anorexia nervosa, and will introduce some interesting new knowledge about the diets of women who are constitutionally thin.
Cholesterol is an essential type of fat which made in the liver and transported in the blood. It is utilised by tissues all over the body and is crucial for the creation of cell membranes and some hormones. However when cholesterol levels are continuously high in the blood it can accumulate in unwanted places including arterial walls, creating a major risk factor for cardiac events such as, heart attack and angina. Usually elevated blood cholesterol is caused by dietary factors, particularly the excess consumption of saturated fats and cholesterol from animal products. However, some people are genetically predisposed to high blood cholesterol levels because they are unable to efficiently clear it from the blood, even when they do eat a healthy diet. When carried in the blood, cholesterol is contained in protein covered particles called lipoproteins. The carriers known as Low density lipoproteins (LDL) are responsible for heart disease because they are able to deposit cholesterol in these unwanted places.

Inherited high cholesterol or high cholesterol due to your genetic makeup is known clinically as Familial Hypercholesterolemia (FH). Changes or mutations in genes can affect the function of the protein they encode. For example the most common cause of FH are mutations in the LDL receptor gene. The LDL receptor protein is located on outer cell membranes and is responsible for removing the LDL carriers from the blood, where the cholesterol is taken up by the liver or other cells and used or excreted from the body. Genetic defects cause the receptor to no longer recognise the LDL in the blood. Therefore, the LDL accumulates in the blood. Mutations in another gene known to be associated with FH, PCSK9, act in a slightly different manner. One of the jobs of the PCSK9 protein is to regulate the amount of LDL receptors on the cell surface. PCSK9 does this by causing the degradation of the LDL receptor protein. Genetic mutations usually reduce the functionality of the corresponding proteins but in rare situations, mutations can change, or increase protein function. These are known as gain of function mutations, some of which have been found in the PCSK9 gene. Gain of function variation in the PCSK9 protein would cause increased degradation of the LDL receptor, reducing its levels on the cell surface. Therefore less LDL can be recognised and removed from the blood, ultimately leading to dangerously high cholesterol levels.

During this study we focused on extending the analysis of local people with FH who had been previously identified as having no mutations in the LDLR and APOB genes. Variations in these two genes are most commonly found to be causative of FH. In these patients we had two goals. Firstly, we wanted to screen these patients for mutations in the PCSK9 gene. For this screen we gathered stored DNA samples from 135 people with FH who met the study criteria. Secondly we wanted to look into regions of the LDLR gene which had not been examined previously. Specific mutations in these regions known as splicing mutations can cause the protein to be put together wrongly and become dysfunctional.

To look for PCSK9 variations we attempted to use an inexpensive and high through put method known as high resolution melting (HRM). This method identifies variations by looking at different DNA melting patterns. When a variation is present, the DNA will melt faster. Then only the DNA samples whose melting profile indicates the presence of a variation are analysed further by DNA sequencing.

The identified Splicing mutations were investigated using RNA, a copy of the DNA recipe which can be read by the machinery that produces the protein. By looking at the size of the RNA we can determine whether parts have been included or excluded from the message. If the message is incorrect, a normal protein will not be made. Abnormal sized RNA products indicate an error in gene splicing has occurred and this is likely to effect the functioning of the protein. The splicing error occurs due to underlying gene mutations, which are then identified by DNA sequencing.

This summer project validated the HRM technique for use in screening regions of the PCSK9 gene for variations in the DNA. Samples which displayed a different melting profile did indeed contain one or more variations in their DNA sequence. During the 10 week period I was able to screen around half the regions of interest in PCSK9 in 135 FH patients using the HRM method. This reduced the amount of expensive and time restraining sequencing necessary to screen these patients. The other regions of PCSK9 were not suitable for HRM analysis at this stage however I have worked on the optimization of this process which may allow for more HRM screening of these regions in future.
A previously unidentified mutation was found in Exon 2 of the PCSK9 gene which changes the 129\textsuperscript{th} amino acid in PCSK9 from an Aspartic acid to Asparagine. This simple G to an A base change in the DNA has not been observed before in the literature but interestingly a different change to the same amino acid is has been linked with FH. Typically to establish if this mutation is causative of FH in this patient, family screening will be undertaken. By testing family members you can determine if the mutation is present in family members with FH and absent in those without FH, giving a good indication that the mutation is linked to the high cholesterol.

This project has set the stage for faster and less expensive screening for mutations in PCSK9. It has also set up a robust and more efficient system for detecting errors in splicing. This extension of current genetic analysis for FH will hopefully in future give us a better understanding of the often illusive genetic causes behind this condition.
Several research studies of high dose Erythropoietin (EPO) have been conducted around the world for treatment of conditions such as stroke and heart attack. The Christchurch Kidney Research Group recently completed a trial (the EARLYARF trial) using high dose EPO in individuals with Acute Kidney Injury (AKI). Administration of low dose EPO has been associated with increased blood pressure in haemodialysis patients when the haemoglobin has been increased rapidly by treatment, suggesting that high dose EPO may also increase blood pressure. How an increase in blood pressure is caused by EPO in these individuals is uncertain and controversial. The aim of this study was to assess whether high doses of EPO causes increases in blood pressure in participants in the EARLYARF trial.

The large number of participants (162) in the EARLYARF trial, as well as the availability of hourly blood pressure recordings provided us with a unique opportunity to analyse the immediate blood pressure effects of high dose EPO (within 1-4 hours). Our results also potentially shed light on the mechanisms by which hypertension is induced by EPO, since a rapid increase might suggest that EPO has a direct effect on blood vessel reactivity, which has not previously been demonstrated.

Method
Our study was conducted in both Dunedin and Christchurch Hospitals and involved a retrospective review of records to obtain information about blood pressure and medication use. The data were collected 8 hours before EPO or placebo (study drug) was given and for up to 72 hours afterwards from 158 out of the 162 patients. The 8 hour interval before drug administration provided the baseline to assess the extent of change in blood pressure over the following 24 hours. We compared the changes in blood pressure in the patient group who received EPO with those who did not receive EPO (the placebo group).

Patients in the ICU often receive blood pressure increasing drugs (vasopressors), such as adrenaline, noradrenaline and vasopressin. In order to identify whether changes in blood pressure we observed might have been due to these vasopressors or EPO, we corrected for their use. This was achieved by converting the individual vasopressor medication into units that were based on the effectiveness of the different vasopressors so they could be compared directly. These equivalent doses were then used in our statistical analysis.

Results
There were no differences in blood pressure responses between individuals who received EPO compared with placebo at any time point in the first 24 hours after treatment. To double check our results we divided the 158 patients into three subgroups: those who received no vasopressors (59 patients), those who received noradrenaline only (42 patients) and those who received other or multiple vasopressors (57 patients). We found no differences in blood pressure responses between the EPO and placebo group regardless of the blood pressure support given.

Conclusion
We can conclude that high dose of EPO probably has no direct blood pressure effects in ICU patients. This is important as it potentially removes a safety concern regarding the use of high dose EPO in clinical trials.
Samantha Moody

Implementing Next-Generation Glycaemia Control in the ICU - The STAR TGC Protocol

Supervisors: Dr Geoffrey Shaw, Professor Geoffrey Chase

Sponsors: The Govan Family Summer Studentship and Canterbury Medical Research Foundation

Critically ill patients are frequently at risk from hyperglycaemia (high blood sugars) due to the stress of their condition and/or increased resistance to insulin, the hormone the body produces to control blood glucose. Hyperglycaemia can lead to substantially higher rates of infection, cardiac events (such as heart attacks) and mortality. Tight glycaemic control (tight control of blood glucose) can simultaneously reduce morbidity and mortality and costs for critical care patients, as has been shown in numerous international studies. However, achieving a balance of blood sugars at a healthy level in critical care is a complex task, both in terms of physiology (bodily function) and the nursing time and effort involved. Most control protocols require extra staff for implementation are not user-friendly and cannot adapt to the highly variable and dynamic critically ill patient which can lead to significant hypoglycaemia (low blood sugars). Development of a novel, successful and user-friendly protocol involves accounting for both physiology and functionality to ensure widespread clinical usage.

The Intensive Care Unit (ICU) in Christchurch Hospital currently uses a paper-based glycaemic protocol called SPRINT, which was developed and actively researched by Mechanical Engineering at Canterbury University and Intensive Care at Christchurch Hospital. SPRINT has the most effective glycaemic control worldwide, but is unable to adapt to all patient variability and dynamics. Continuing research and development over the past 5 years has led to an innovative, advanced computer-based protocol: STAR (Stochastic TARgeted controller), a computer model that tracks patient response to insulin in real-time, and uses a predictive formula that allows greater flexibility and adaption to individual patients. STAR also optimizes nursing effort through reduced need for measurements and/or interventions. In addition, STAR decreases the risk of hypoglycaemia, thus increasing safety, as has been assessed in simulation studies and clinical research trials overseas. It is desired to upgrade the SPRINT system with this new development, both in Christchurch and in other hospitals worldwide, including the Centre Hospitalier Universitaire de Leige in Belgium.

Although virtual patient simulation results show that STAR has been developed into a highly promising protocol, it has not yet been trialled in a clinical environment. This project focussed mainly on the human factors involved with the implementation of the new protocol. This was to ensure that nursing staff became comfortable with the use of STAR, to encourage compliance with recommended treatments. Support of the nursing staff is fundamental for success both in initial clinical trials and in the planned full practice change.

Close collaboration with nursing and clinical staff is vital to merge STAR with current ICU practice. STAR was presented to the nursing and other clinical ICU staff and they were trained in its use. STAR was also further developed for adherence to nurse preferences. Implementation issues in the highly complex program were resolved, thus this project employed the process of translational research.

Nurse training involved group presentation sessions, where nurses were familiarised with the program and in turn were given the opportunity to express opinions, preferences and concerns which were then considered in the updates of STAR. Nurses were also provided one-on-one support when first using the computer and a detailed User Guide was created.

Ongoing clinical trials to test the use of STAR commenced, and have provided an opportunity to resolve implementation issues with nursing staff prior to any clinical practice change.

STAR has been successfully developed from a research tool to a system suitable for everyday clinical use. This project has produced the final development of a computer-based glycaemic control protocol that achieves effective and reliable control, is able to adapt to individual patient characteristics and that optimizes conditions and resources in the ICU and adheres to the preferences of clinical staff. STAR trials results have improved upon SPRINT's world-leading performance, with 4% mild hypoglycaemia (Blood glucose <4.0mmol/L) and zero severe hypoglycaemia values (Blood glucose <2.0mmol/L) and 94% of blood glucose values between 4-8mmol/L. When the data was run on SPRINT in simulation, STAR had lower blood glucose mean and median than SPRINT would have produced.
STAR delivers accurate glycaemic control, while guaranteeing safety from hypoglycaemia in simulation studies and research trials. This project provided the nurses and other clinical staff in the ICU with an effective medical tool. Clinical effort is reduced and the program is operated in a user-friendly and intuitive manner. The experience gained in piloting STAR into Christchurch ICU practice will be valuable when implementing this technology internationally.
Zea Munro

Determination of an Acceptable Rate of Major Adverse Cardiac Event Following Discharge from Hospital after Attendance with Chest Pain

Supervisor: Dr Martin Than
Sponsor: The Emergency Care Foundation

Introduction: Chest pain is the second most common reason a person will present to the emergency department in their adult life. This equates to in excess of 8 million visits in the United States of America (US) and 6,000 presentations to the emergency department of Christchurch Public Hospital each year. The majority of these presentations will not be serious, however a small proportion will be. An Acute Coronary Syndrome, or ACS, is one of the serious conditions that can cause chest pain. An Acute Coronary Syndrome is a medical term that is used to describe decreased blood flow to the heart muscle. As chest pain is such a common presentation it becomes an important skill to be able to distinguish patients that are at high risk of having a serious underlying condition, such as an ACS, from those who may be discharged home safely. A thorough history, examination and preliminary testing, such as a blood test, can aid in the distinction as to whether a patient requires further investigation. However, the further investigations are not perfect and in a small number of patients may in fact cause harm. This could be direct harm from the investigation, but may also include harm from unnecessary invasive procedures a patient may undergo if the initial investigation gives a false positive result. A patient that initially appears at low risk of having an ACS may be subjected to harm by undergoing further investigation. Therefore there is a threshold of risk, albeit low, when it becomes acceptable to send a patient home with no further investigations.

Aim: To determine the threshold of risk, when it becomes acceptable to send a patient home with no further testing, which we have described as an acceptable rate of a patient coming to serious harm due to a problem with their heart within 30 days of their attendance to the emergency department.

Method: This project consisted of two phases. The first was to calculate the point of diagnostic equipoise, or the point at which harm from investigation is matched by the harm of a missed diagnosis. This was carried out by utilising a mathematical equation published by Pauker and Kassirer. This entailed gaining all of the relevant information regarding the accuracy and possible complications associated with each investigation along with the harms and benefits of treatment.

The second phase was to survey Medical Professionals to gain a subjective impression of what they would consider an acceptable threshold. The questionnaire asked participants to select what level of risk they would consider acceptable, that a problem with the heart is missed and the patient comes to serious harm as a result. The questionnaire was distributed to audiences at two international conferences on Emergency Medicine in the US and Australia.

Results:

Mathematical Calculation: The calculation used determines the point of diagnostic equipoise, or the point at which harm from further investigation equals the harm of a missed diagnosis. This was calculated separately for populations in New Zealand and the US as the number of patients undergoing each investigation or receiving each method of treatment differs and it was therefore important to assess what effect this differing distribution may have. The figure calculated for the New Zealand population was 1.78%, this equates to a probability of 1 in 56. This figure suggests that if the risk of a patient having an ACS is below 1.78%, they would in fact be subjected to a greater risk of harm from undergoing further investigation. The figure calculated for the US was 2.37%, or 1 in 42. The slight difference between these figures is due to the more invasive approach taken in the management of chest pain in the US.

Survey of medical professional: A total of 829 Medical Professionals were surveyed. The majority were Emergency Medicine physicians, 81.5%, with an average of 14.6 years since graduation. Of those surveyed 61.2% were practicing in the US, 21.5% in Canada, 10.4% in Australia and 4.7% in New Zealand. The data from Australia and New Zealand was analysed together as Australasia. Overall there were two peaks in the distribution of an acceptable threshold. The first peak was 1 in 1,000 which 20% selected. This means 20% of Medical Professional surveyed would accept a risk of 1 in 1000, of a patient coming to serious harm from a missed problem with their heart as an acceptable threshold to send a patient home with no further investigation. The second peak was 1 in 100 which 27% selected. When the data was analysed cumulatively 70% of medical professional were comfortable with a level of 1 in 400, and 83% selected a level of 1 in 100 or above. When analysed by country of practice, medical professionals in the US and Canada accepted a higher rate of missed problems than in Australia and New Zealand.
Discussion:
As discussed previously chest pain is a very common reason an adult will present to the emergency department. Currently we do not have an investigation that is completely able to rule out an ACS that does not itself entail a risk of causing harm to the patient. Therefore the assessment of chest pain is a risk based assessment with the aim to expose the patient to the least amount of risk, whether this may be from further investigation or a missed diagnosis. According to scientific literature approximately 2-4% of patients with an ACS are incorrectly sent home. The majority of Medical Professionals surveyed selected a level of risk below the calculated point of diagnostic equipoise. This suggests they feel more comfortable giving patients that are at low risk of having an ACS further investigation, rather than sending them home. One reason for this may be assumed to be legal liability of a missed diagnosis. A patient coming to harm from a missed problem with their heart is the most common cause of medical litigation in the US. However in contrast to this Medical Professionals in the US accepted a higher rate of missed diagnosis than here in New Zealand and in Australia. The difference in risk acceptability between countries may be explained by the approach taken in the management of chest pain. The risk assessment of chest pain is currently a popular area of research, with the aim to help guide clinicians in their assessment of chest pain and researchers in the development of new diagnostic tools. This project complements such research by giving a mathematical and subjective approximation of an acceptable rate of a patient coming to serious harm from a missed problem with their heart within 30 days following discharge from hospital after attendance with chest pain.
The elderly population in New Zealand is expected to increase dramatically in the coming years. Elderly patients are more likely to develop and die from cancer, yet are significantly underrepresented in most trials. Chemotherapy, when given in conjunction with other treatments such as surgery or radiotherapy, has been shown to improve survival in several common cancers such as breast, colorectal and lung cancers. Oncologists need to better assess the use of treatment options in these patients and plan for the predicted rise in elderly patient numbers with as much information as possible.

Clinically there has been a noticeable shift in the Christchurch Hospital Oncology department, with an apparent increase in referrals for elderly patients with a wider range of malignancies. We aimed to document this change in oncology referral patterns over the preceding 20 years for patients over the age of 75 years, and ascertain their outcomes. We chose this age group as it reflects in our assessment a more challenging age group than the previously defined over 65 years old retirement driven cutoff. We hoped to document the escalating numbers of patients of this age being seen and identify the key drivers of change so that improvement in patient selection and management could be investigated and initiated.

We identified patients aged 75 years and older from 300 consecutive referrals to the Christchurch Hospital Oncology Service, starting from 1 February, in the years 1990 and 2000. We then reviewed these patients’ Oncology notes and collected data on cancer type, extent, and related co-morbidities – acting as a “snapshot in time for each decade” of patient characteristics and management. This information was then compared and analyzed for patterns of change. The project was designed to run in conjunction with another studentship, which looked at similar data from 2010*.

In 1990 we identified 51 patients aged 75 or over (17%), and this compared with 62 patients in 2000 (21%). An increase of 4% in referrals was seen. Data from 2010* documents that this had risen dramatically to 40% in the next 10 years. This confirms that there has been an increasing number of elderly referred to the service over the past two decades with a trend toward rapid recent change. It is notable that the mean age remains similar throughout the two decades (80 years).

To attempt to identify the key drivers of this change we assessed for any shift in cancer diagnosis between the two decades. From this data we were able to see several key differences. Skin cancers represented 34% of referrals in 1990, but fell to only 10% in 2000. Prostate cancer referrals also fell from 16% of referrals in 1990 to 8% in 2000, essentially halving. Colorectal cancer however rose significantly, representing 4% of referrals in 1990 and climbing to 15% in 2000. We also identified that a small number of patients were referred for conditions other than cancer, and were usually managed with radiation.

We obtained dates of death from the Ministry of Health, and calculated survival from date of referral. Patients referred in 1990 survived an average of 38.9 months (std dev 50 months) while patients referred in 2000 survived an average of 28.9 months (std dev 35 months). This was an interesting finding. The longer survival time seen in 1990 may reflect a referral bias with only those patients whose cancers could be managed with radiotherapy alone and with good long term outcome (such as skin cancers). We plan to investigate this relationship by analysing with respect to treatment intent, as we believe the majority of treatment in 1990 was with curative intent. Median survival time however showed a shift in the opposite direction measuring 8.4 months in 1990, while for patients referred in 2000 it was 14.1 months. This maybe a more accurate result as the median would allow for the assessment of a small number of outliers who did well, and may suggest improved allocation of treatment, or newer, more effective therapies emerging in this decade. The survival information in this elderly cohort also needs to be assessed with respect to the underlying co-morbidities. We have collected this data and are in the process of reviewing it.

The primary treatment modality in both decades was radiotherapy, with 64.7% receiving radiotherapy in 1990, and 45.2% in 2000. We note that 4 patients in 1990 (7.84%), and 3 in 2000 (4.84%) received either chemotherapy alone, or in conjunction with radiotherapy. Chemotherapy is associated with greater toxicities than other treatments, and these toxicities may be exacerbated by co-morbidities. We believe that these are low percentage uptake figures given proven treatment options at the time, and may represent underlying concerns in the elderly cohort. This pattern shows dramatic change however when we add data from 2010*.
in which 13.5% received chemotherapy. This suggests that there has been a sizable shift toward the use of chemotherapy in treating the elderly in the department in recent years.

The number of patients whom did not receive oncology specific (chemotherapy, radiotherapy or hormone) treatment for their cancer, or where no treatment was stated in their medical records, was also assessed. In 1990, 2 (3.9%) patients did not receive any active treatment, whereas in 2000, 12 (19.4%) patients did not receive active treatment. Reasons underlying this may represent either the clinicians’, or patients’ choice and we are attempting to elucidate this. Of patients who were referred in 2010*, 34% did not receive any active treatment. This may represent a later stage of disease or new disease types being referred to the service from the community.

Our data confirm our suspicion that there is an increasing number of people aged 75 years and over being referred to the Christchurch Hospital oncology department over the past 20 years, and that management of their cancer has changed. The predominant treatment modality continues to be radiotherapy; however there has been a dramatic increase in the number of patients receiving chemotherapy. The number of patients not receiving active treatment has also increased. We also note that mean survival has decreased, but median survival has increased. Research will be conducted in the near future to further investigate this.

* Current Oncology Service Management of More Senior Patients by Nadia Schwass (Prof. Bridget Robinson and Dr Dean Harris)
Breast cancer is the most common cancer among New Zealand women, with approximately 2500 women being diagnosed each year. More than 600 women die from breast cancer in New Zealand each year, making it the second leading cause of cancer death among women.

Early breast cancer is breast cancer that is still confined to the breast tissue and has not spread to other parts of the body either right next to the breast (such as the muscles and other tissues making up the chest, or to the surface of the skin) or areas farther away in the body like the brain, bones, or the liver.

The mainstay of treatment for early breast cancer is surgery, followed up sometimes by chemotherapy (using special drugs designed to kill cancer cells) and/or radiation therapy. Radiation therapy for breast cancer involves using specialized equipment to deliver X-rays at the area of the chest from which the cancer has been removed. This helps to kill any remaining cancer cells which may remain after the surgery, as they are particularly vulnerable to radiation (in comparison to the surrounding healthy body tissue).

Only some patients with breast cancer are offered radiation after their mastectomies. These are patients who by virtue of the characteristics of their cancer (such as the size of the tumour removed, the number of lymph nodes/glands involved, and how the tumour appears under a microscope) are thought to be at high risk (where “high risk” might be a 1 in 5 chance after 5 years) of having their cancer re-grow where their breast was removed.

Since 2004, in response to international research, the Christchurch Oncology Service changed the way in which radiation is delivered to breast cancer patients who have had mastectomies. The total amount of radiation delivered is 40 grays (a measure of the amount of radiation for a given amount of tissue), which is split up into 16 doses (or “fractions”) delivered to the patient on separate consecutive weekdays. Total radiation dose and fractionation programmes vary somewhat internationally, so it is therefore important to check on the progress of patients treated with this radiation regimen by the Christchurch Oncology Service to ensure that they are getting results comparable to other patients overseas. If results are comparable, then the doctors who are treating patients with radiation therapy can be completely confident that what they are prescribing is an appropriate regimen.

The aims of this project were:
1. To create a list of all patients of the Christchurch Oncology Service treated with radiation after a mastectomy since 2004.
2. To collect information about their breast cancers.
3. To find out how many of them had their tumours return.

The Christchurch Oncology Service keeps both hard copy and computerized records of patients treated. A computer search for the relevant breast cancer patients who had mastectomies followed by radiation treatment since 2004 was made to find relevant patients. Their medical records were then used to collect information on their tumour at diagnosis and to see if they had had their cancer return at any point.

133 patients were found. Analysis of the information about their breast cancers showed that the majority of the patients treated fitted the department guidelines on which patients should get treated with radiation after a mastectomy. Patients that did not strictly fit the guidelines typically had some other risk of having their cancer return, for example, doubt as to whether the whole cancer had been completely removed during surgery.

Among the 103 patients for which there was up-to-date follow-up data available, 4 (4%) had their cancer return at their mastectomy site. This is comparable to what is seen in patients overseas, but more detailed statistical analysis needs to be completed to ensure high confidence in the results.
Borderline personality disorder (BPD) is a serious psychological disorder characterized by a pervasive pattern of instability in affect regulation, impulse control, interpersonal relationships, and self-image. People with BPD often engage in self-harm and suicidal behaviours in order to regulate their emotions and gain a sense of well-being and control. Up to 10% commit suicide, which is a rate significantly higher than in the general population. BPD is highly co-morbid with other psychiatric illnesses such as depression, PTSD, other anxiety disorders and eating disorders. It affects about 1-2% of the population in other countries and it is estimated to be the same here, however very little is known about this group in the context of New Zealand.

Research has been conducted into the utilization of health care resources by those with BPD and those displaying features of BPD. More specifically, it has been suggested there is a link between BPD and treatment utilization. One study found the prevalence of BPD in a primary care sample was four times higher than the median value found in most community samples, while another study found participants with symptoms of BPD showed higher utilization of primary care resources than those without symptoms.

The aim of this study is to estimate the utilization of primary health care resources by those with a diagnosis of BPD and those displaying symptoms of the disorder in urban Christchurch in 2008. From this, cost of central government health provision and cost to the patient will be calculated.

**Method**

Using the CDHB database, 338 patients were identified as having a diagnosis of BPD (diagnosed group), while 157 patients were identified as having a diagnosis of bipolar disorder, post-traumatic stress disorder, depression, or anxiety whilst having a suggestion of BPD traits (possible group). These patients were selected to test the hypothesis that they may have had BPD but were never diagnosed. The patient Health Care User (HCU) numbers were provided to Pegasus Health who returned information on the visits to general practices supported by Pegasus Health and the 24-hour surgery (24HS) on Bealey Ave in 2008. Dates of each visit, practice attended, and doctor (GP) seen were supplied. Each HCU number, practice, and GP was coded to protect the confidentiality of those involved. Information regarding costs was supplied by Pegasus Health.

**Results**

**Visits of the diagnosed group**

The total number of visits to a GP by this group was 2003. The average number of visits was 5.93. However, only 242 patients of the 338 in this group had at least one visit to a GP during 2008. The average for the 242 visiting patients was 8.28. The total number of visits to the 24HS was 179 with an average of less than one visit per patient. However, only 67 of the 338 patients had at least one visit to this surgery leading to an average of 2.67 visits for this subgroup.

**Costs of the diagnosed group**

Costs in primary care can be complicated. The government pays each practice $31 per year for each enrolled patient based on an average of two visits per year. Using this figure, and assuming that all of the 338 patients in this group were enrolled at a practice, the government cost in 2008 was $10,478. For patient fees, the amount of $42.50 was selected as an estimated average as there is a range of consultation fees across the practices. There are also subsidies that patients may be entitled to, however, these are individual patient specific and difficult to determine with the information we have. Thus, using $42.50 as an average patient fee, the total cost for all visits to GPs in 2008 was $85,127.50. As an average across the 338 patients this is $251.86, and across the 242 that visited the average is $351.77. Visits to the 24HS are not subsidised by the government, thus the average charge of $70 per visit is borne completely by the patient. The total cost of all visits to the 24HS was $12,530. Averaging across all patients the cost is $37.07, but averaging across the 67 visiting patients only the cost is $187.01. Total cost for visits to GPs and the 24HS was $97,657.50, which is an average of $288.93 across all patients and an average of $382.97 across the visiting patients.

**Visits of the possible group**
The total number of visits to a GP by this group was 655. The average number of visits was 4.17. However, only 104 patients of the 157 in this group had at least one visit to a GP during 2008. The average for the 104 visiting patients was 6.30 visits. The total number of visits to the 24HS was 49 and the average number of visits was less than one. However, only 22 of the 157 patients had at least one visit to this surgery so the average for these 22 patients was 2.23.

Costs of the possible group
Using the costs outlined above, the total cost of visits to GPs was $27,837.50 for this group. This averages out to be $177.31 across all patients and $267.67 for those that visited. The cost to the government was $4,867. The total cost for visits to the 24HS was $3,430, which is an average of $21.85 across all patients and an average of $155.91 across those that visited. In total, the cost for this group for visits to GPs and the 24HS was $31,267.50. The average across all patients was $199.16 and across the visiting patients was $286.86.

Discussion
These results clearly show the level of treatment utilization and costs for these two groups for the year 2008. For comparison, Pegasus Health provided us with the average number of visits to GPs per visiting NHI across the whole PHO for the year to 30/06/2010. This figure was approximately three. When this is compared to the average of 8.28 visits for the diagnosed group and 6.30 visits for the possible group it suggests that these patients used GP services more often than the general population, and thus incur greater costs.

There is a complementary summer studentship project looking at secondary and tertiary health service utilization, and the results of both projects will be combined to determine the overall healthcare utilization and cost. Both studies will be replicated in the future and the results of these projects, for the year 2008, will be compared with the results of another year, possibly 2012. These two summer projects are part of a larger study investigating a treatment programme for BPD which started here in Christchurch in 2009. This is a replication of a study done in the UK which showed decreases in health service utilization following treatment, hence the need to measure health service utilization.

Overall, this project has investigated an area that has been overlooked here in New Zealand and has provided us with valuable information regarding these groups of people. Further research is needed, however, to fully understand BPD in the context of New Zealand. Future studies, which would provide us with a greater understanding of this disorder, could have implications for the treatment of those with BPD and influence provision of health care resources and funding for these people. Identification and treatment are key in helping those with BPD recover and lead successful lives.
Mariam Parwaiz

Capillary Glucose Meter Performance in Pregnancy Complicated By Diabetes

Supervisors: Dr Helen Lunt, Lindsay Irons, Deborah Kendall, Dr Peter Moore, Associate Professor Chris Florkowski

Sponsor: Diabetes Training and Research Trust

Introduction

Diabetes mellitus is a chronic metabolic disorder that leads to high blood glucose levels. If left untreated, there are many long-term complications, including heart and kidney disease. There are three main types of diabetes – type 1, type 2 and gestational – and they are treated using a mixture of diet, exercise, insulin and medications.

If a woman has diabetes while pregnant, the disorder can cause further problems for the mother and the child, such as birth defects, early labour or very large babies (macrosomia). Therefore, it is vital for pregnant women with diabetes to have a tight control on their diabetes, to ensure a positive outcome. This means that the women need to keep their blood glucose levels within a narrow healthy range. This is achieved by extensive self-monitoring of blood glucose using capillary ‘finger stick’ glucose meters and adjusting the treatments accordingly.

Since blood glucose meters are heavily relied upon for diabetes care and management, it is important that the meters are an accurate reflection of the ‘true’ glucose value. Meter performance studies have been undertaken in non-pregnant patients, and these show that all locally funded meters are within 20% of the venous blood glucose value, which is considered to be an acceptable range. However, there are very few published studies on meter performance during pregnancy. This is particularly significant as there are changes in the characteristics of blood in pregnancy that could, in theory, lead to changes in meter performance.

The aim of this summer studentship is to pilot the capillary glucose meter performance study in a real world setting; that is, to see how accurate and precise meters are at reporting blood glucose results in pregnancy. This will be achieved by undertaking a direct comparison of capillary glucose results with a simultaneous venous glucose result.

Data collection

All women with diabetes that went through the Antenatal Clinic at Christchurch Women’s Hospital were eligible to take part in the study. The supervisors had previously developed a specific data collection approach for meter studies, and the same approach was adapted for this studentship. Those patients requiring blood tests for routine care were invited to take part in the study. Consent was obtained, and demographic information was collected. As well as routine tests, extra blood was taken from the arm for a venous blood glucose reading, as was haematocrit, which is the proportion of red blood cells in overall blood volume, as this is known to affect capillary glucose results. Directly afterwards, capillary blood glucose was measured by the two meters most commonly used by the clinic – the Accu-Check Performa and the Abbott FreeStyle Lite. This meter reading was later compared with the venous blood glucose reading taken earlier. Finally, participants were asked about their last meal and whether they took any insulin with the meal. This was noted to see if the timing of the last meal has an effect on the capillary blood glucose results.

Results and conclusions

At the time of writing, data collection is still underway. So far, 20 patients have been recruited. The average age of participants is 31 years, with 70% being New Zealand European, 20% being Maori, and 10% being Asian. 45% have gestational diabetes, 40% have type 1 or other forms of diabetes, and 15% have type 2 diabetes. Their average period of gestation is 30 weeks. Most of them (80%) are on insulin. Other commonly taken medications include metformin, iron, aspirin, iodine, and vitamin supplements. Preliminary results show that capillary blood readings generally fall within 20% of the venous blood glucose value, and so are within the acceptable range.

Meter performance remains an important issue for clinicians and patients, as meter results play a vital role in determining treatment plans for diabetes management. This pilot shows that it is feasible to undertake a study of capillary glucose meter accuracy to a high standard in the antenatal clinic. Preliminary analysis of results available to date would suggest that meters are sufficiently robust not to be affected by physiological changes seen in pregnancy.
However, further statistical analysis is required to confirm the preliminary results, and reach further conclusions. This will be undertaken, with the help of a biostatistician, to look at the effect of haematocrit and the last meal on the capillary meter readings. Blant Altman plots and Clarke error grid analysis will be used to assess bias and error.

**Significance for the future**
This pilot study has shown promising results for meter performance in pregnancy complicated by diabetes. The study will now be expanded and more patients will be recruited from the Antenatal Clinic, with the aim of reaching at least 100 participants. In addition, two other arms will be set up as control groups to allow for further comparisons. These will look at non-pregnant patients with diabetes, and healthy volunteers.

I would like to thank all my supervisors for their help and support during the summer studentship. I would also like to thank Flo Logan (diabetes research nurse), Yvonne Sheenan (phlebotomist) and Mei Gu (hospital aide) for assisting me with the study.

Finally, my many thanks go to my sponsor the Diabetes Training and Research Trust for their generous support.
**Amanda Polkinghorne**  
*Use of a Hospital Hydrotherapy Pool by User Groups from Within the Community: A Mixed-Method Analysis*

**Supervisor:** Dr Hilda Mulligan  
**Sponsor:** Older Persons Health and Rehabilitation, Canterbury District Health Board

Amanda won the awards for the ‘Best Presentation in the Community Category’ and the ‘Best Overall Presentation’.

Water based physical activity is renowned for its physical, mental and social benefits to individuals of all ages and abilities. It is the second most preferred form of being recreationally active after walking for individuals with disabilities. Despite public promotion of physical activity for health and well-being to all of the population, individuals with physical and/or intellectual impairment are one of the most physically inactive groups within our modern society.

The hydrotherapy pool, located at the Burwood Hospital in Christchurch, provides weekly access to 20 unique community user groups. The aim of this study was to discover why these community user groups choose to undertake their water based physical activity at this hospital pool and to determine their understanding of and compliance with the hospital’s health and safety regulations for the pool.

This study was conducted in two parts. The first part consisted of focus groups or individual discussion with 38 participants belonging to 17 of the community user groups. Discussion determined reasons for choosing water based activity, reasons for choosing the Burwood pool, and what access to the Burwood pool provides for them as individuals. Discussions were audio taped and then typed out word for word. After analysing all of the discussions, we were able to categorize the information into two themes: (1): Prized and life enhancing participation; (2) Rightful access to life enhancing participation … or not?

Theme one captured how the Burwood pool provides both the scope and the opportunity for individuals with disability to partake in physical activity. This was not perceived by them to be accessible elsewhere. For individuals with disability the buoyancy and the warmth of the water allows ease of movement, longer duration of exercise and the ability to exercise without pain. They had experienced that this prevented the occurrence of secondary physical and/or mental health issues that would then require expensive health care resources to remediate.

*given me my life back (Focus Group 2, Participant 6)*

*if we didn’t have these facilities we would be patients (Focus Group 7, Participant 13)*

*it’s the only place I can ever in this world be pain free for my three quarters of an hour that I’m in there and I just cherish that (Focus Group 4, Participant 2)*

Participants with disability regarded access to the Burwood pool so highly that they were prepared to travel long distances (e.g. up to 50kms), and to prioritise their discretionary income to receiving the benefits of this type of physical activity.

The pool also provides scope to individuals whose cultural preferences require access to an easily accessible private pool and it allows for the promotion of health and well-being to employees of Canterbury District Health Board who work on the Burwood Hospital site. Participants identified feelings of well-being and a sense of comradeship and social support from participating in aquatic activity with other pool users with similar interests or needs. This was seen by all participants as life enhancing and resulted in hesitancy to ‘advertise’ the resource to others as this would potentially limit their own access due to current capacity being fully allocated.

Theme two identifies the concept that despite New Zealand’s focus on equal opportunity and access for all, there are significant barriers that prevent individuals with disability from making use of public aquatic facilities. Disabled participants strongly identified that public pools present with no “more than a token gesture towards anyone with a disability” (Focus Group 7, Participant 11), that physical access was difficult or feels unsafe and that the social environment feels unwelcoming and unhelpful. However, even though Burwood pool is seen as a suitable resource, it nevertheless provides access to only a limited number of potential users within the Canterbury region.
The second part of the study gathered data on attendance numbers and the size of each user group to provide information about current use of this resource. Twenty unique community user groups currently have regular (weekly or bi-weekly) allocated time slots ranging from one hour to three hours. The majority of the user groups utilize the pool to its maximum capacity at any one time (with up to 30 individual users). However, three of the user groups have a maximum current attendance of less than ten individual users. Two user groups have a current attendance rate which is over the allowed capacity (up to 90 members). These user groups therefore choose to either spread their members over a three hour slot and/or give members in the group a six week on, six week off roster.

Part two involved analysis of audit data from 16 user groups. The audit examined their understanding of and compliance with the Burwood pool's health and safety regulations. Thirteen items of this audit that were considered to be vital to safe use of the pool were scored as a pass or fail.

Results showed high compliance with documentation of attendance records, the presence of an identifiable supervisor and presence of a land based observer as required. However, the audit uncovered a lack of effective and appropriate strategies to successfully manage specific pool emergency situations. Five of the 16 community user groups failed to articulate appropriate management strategies for at least four of the five emergency situations highlighted in the health and safety audit, for example use of the emergency bell and evacuation procedures. This was despite high compliance of attendance at the previous annual health and safety hospital pool update.

In conclusion, this study has shown an underlying need for public water based recreational facilities to become more easily accessible to individuals with both physical and intellectual impairment. The hospital pool is providing a necessary and highly appreciated service, but only small proportions of those who could benefit are receiving these benefits due to the limits inherent in having only one suitable resource within the Canterbury area. The safety of the community user groups when using the hospital pool facility, particularly for those with medically vulnerable members, is questionable under the current arrangements.

Implications of this study are: (1) clarification is required as to whose responsibility it is to provide accessible resources for the disabled Canterbury community, (i.e. is it Canterbury District Health Board or Christchurch City and Regional Councils?); and (2) safety of the current users needs to be addressed.
Ronald Puni

Pacific People and Non-Financial Factors Influencing Access to Mainstream General Practice Services

Supervisor: Dr Lynley Cook, Dr Gillian Abel
Sponsor: Partnership Health Canterbury

There is evidence that Pacific people, along with other populations in New Zealand, have a reduced accessibility to primary care services. This is concerning as Pacific people have a greater burden of disease in comparison with the total population, and poor access could compound inequalities in health.

Access can be defined as the degree to which individual and groups are able to obtain needed primary care services. There are many factors that influence access, with cost being the most frequently cited barrier to access for minority populations including Pacific people. However it is clear that factors other than financial barriers must be operating to explain reduced utilisation of services.

Aim
- Identify non-financial factors (social, environmental and organisational) in general practice that act as barriers to accessing these services for Pacific people
- Identify non-financial strategies (social, environmental and organisational) that mainstream general practice could adopt to make their practices welcoming and more accessible for Pacific people

Method
Three focus groups were conducted with Pacific people in English. One group was Youth orientated aged 17-25; the second group was community based with individuals 25+ and a third group was held with Pacific Health Workers (PHW). All three groups were mixed male and female. Ethnicities that were present were Samoan, Tongan, Niuean, Fijian, and Cook Island.

The discussions were facilitated by a Pacific researcher who is experienced in conducting focus groups, and was supported by a Pacific tertiary student undertaking a Summer Studentship.

Participants were sampled purposively. Initial participants were approached and snowball sampling was used to invite additional participants into the study. All three focus groups were audio taped then transcribed. The transcriptions were then thematically analysed to identify any themes concerning non-financial barriers to mainstream GP services and any non-financial strategies to improving access.

Results
A total of 20 participants were recruited for the three focus groups, there were 8 PHWs, 6 Community participants and 6 Youth participants. There was one male in each of the PHW and Community groups and three males in the Youth group; the remaining participants were female.

Barriers identified were communication, personal barriers and structural barriers.

Communication barriers included language, which was identified by all three focus groups as a barrier to GP services. Limited vocabulary in English often meant it was difficult to describe their concerns to the GP. Participants also expressed difficulty in understanding medical terms, which was not restricted to those born overseas, with one participant feeling “dumb” in the fact that she was New Zealand born but could not understand what was being said.

Proper explanation of treatment was also identified as a barrier. Failure to properly inform the patient of realistic outcomes of the treatment lead to high expectations in terms of recovery, and posed a barrier to access. When those expectations were not met it deterred some patients from going to the GP and some would instead resort to alternative medicines which were often publicised by influential members of the community. These were seen as ineffective and detrimental to their health as they were no longer taking proper treatment. Those who faced language barriers were identified by one participant as being more susceptible to such “scams” as they were unable to understand the ingredients on the packaging of the alternative medicines.

Personal barriers refer to one’s beliefs, experiences and values which prevent one from accessing mainstream GP services. Participants expressed certain emotions which acted as personal barriers towards
The participants mentioned several emotions. Embarrassment arose within the participants over debt or over exposure of the body; fear of the unknown or fear due to the exposure of immigration status or fears over privacy and confidentiality. Confidentiality was regarded as being a relevant issue for pacific people, as pacific communities were relatively small, which lead some participants to request workers outside the family and sometimes outside their own communities.

Differences in priorities were also seen as a personal barrier: different family obligations, employment or just “putting it off” until the condition worsened, were some reasons identified. In the case of employment one participant questioned whether they could afford to take the time off before making an appointment.

Some participants reported that past experiences also dictated access. For example, some participants did not go to the GP when first falling sick because in the past they had been given paracetamol, something which they could have done themselves without incurring a fee. Traditional medicines were also sought due to past experiences, where modern medicines were found to be ineffective. One example was of a participant flying to the Cook Islands to give her child a traditional bath to cure her of her skin ailments which was found to be successful.

The participants also identified several structural barriers. The receptionist was recognised as being important as they were the “first point of contact.” Some receptionists were reported to have abrupt manners which some believed acted as a barrier. However, it was unable to be identified if their manners were racially motivated.

Availability was also identified as a structural barrier. Several participants said that when they had gone to see their registered GP, they had been unable to see them and were either transferred to another GP or incurred a long waiting time ranging from a few days to two weeks. One participant had a “back-up doctor” where she was registered as a casual, and went there when her usual GP was unavailable.

**Conclusion**

Several non-financial factors have been shown to influence access to mainstream GP services including barriers to communication, personal and structural barriers. If health inequalities are to be reduced by increasing access to GP services, then these barriers must be addressed, and training in cultural competency must be undertaken to ensure better access for Pacific people.
Nadia Schwass

Current Oncology Service Management of More Senior Patients

Supervisors: Professor Bridget Robinson, Dr Dean Harris

Sponsors: Cancer Society of NZ Canterbury-West Coast Division and Cancer Society Diamond Harbour Group

Requests to the Oncology Service for care of new patients with cancer continue to increase significantly every year. The proportion of older aged patients is predicted to increase most rapidly. Management of these patients is complicated by a number of factors such as wide variability in individual’s health status and functional reserve, difficulty efficiently assessing this and also a general lack of specific treatment guidelines. There is a strong clinical need for assessment tools that determine fitness for treatments to enable clinicians to appropriately target treatments within this age group. To begin the process of implementing such a tool the current provision of Oncology care must be investigated.

The aim of this project was to define current Oncology Service management of patients aged 75 years and older to ascertain how comorbidities (concurrent medical conditions) and functional status are assessed, and to what extent treatment options are modified because of age or functional status.

A retrospective review was completed for 200 consecutive referrals to Oncology Service of patients aged 75 years and older, from 1 February 2010 onwards to allow 6 months follow-up of all patients reviewed. Patients were all referred for a new episode of care and were found using the Oncology database and Patient Management System. Records were viewed through an electronic record database (Concerto) and patient charts. Information was collected on reasons for referral and their source, cancer diagnoses and extent of spread (stage), medication, comorbidities, living situation and supports, functional status, treatment offered and planned, reasons for differing from standard treatment regardless of age, dose adjustments and outcomes.

Comorbidities were collected using a risk index (a modified Charlson Risk Index) which contains a number of medical conditions that may impact on life expectancy and treatment tolerance. Information on patient level of functioning was collected using ECOG Performance Status and modified Activities of Daily Living (ADLs) and Instrumental ADLs (IADLs). ECOG Performance Status is a standardised measure of wellbeing. Dependence in ADLs or IADLs means that assistance is required for some specific activities.

The average age of patients was 81 (range 75-92). Most referrals (78.5%) were requesting systemic therapy (drug treatment) or radiation treatment (RT). Comorbidities were recorded in almost all cases. Patients were assigned a weighted comorbidity risk score of low, 31%; medium, 45.5%; high, 17%, or very high 4% (unknown, 2.5%). A large number of patients had been diagnosed with a different cancer previously (32.5%). 29% of patients lived alone and 16.5% lived in a rest home or hospital level care. 45 cases had some type of formal help at home recorded (e.g. home help, personal cares assistance, meals delivered, District Nurse input). The mean number of medications being taken by patients was 6 (range 0-19). Recording of functional status was inconsistent however 43% of cases had an ECOG Performance Status recorded.

49.5% of patients were offered standard treatment (according to clinic notes and the ‘Oncology Handbook, 2011’). RT was received the most (94 cases) and was generally well tolerated. Observation and supportive care (no active treatment) was decided on in 68 cases. 27 patients received chemotherapy (anticancer drugs) and 18 of these had reduced doses recorded. Physician preference (91), competing causes of morbidity and mortality (75), concerns about side effects (63) and patient preference (e.g. desire to remain fit) (51) were common reasons for not receiving standard treatment. Overall 94 patients completed their planned treatment, the majority were those who received RT. The outcomes at 6 months were alive, 53% (including 16% with worsening of cancer); death due to cancer, 32%; unknown or N/A, 15%. Both standard treatment being offered and chemotherapy planned decreased with both increasing age and decreasing function. Completion of planned treatment declined with decreasing function.

In this observational study age and functional status influenced receipt of standard treatment. Although many patients did not receive standard treatment because they were deemed ‘unfit’ several others did not receive it in order to remain ‘fit’. Comorbidities and function were recorded in most cases however there was no consistent method used. The data gathered in this review will form a baseline for future trial of a tool to facilitate assessment of functional status and accurately classify older patients across the spectrum between frail and fit.
Articular cartilage tissue has a very limited regeneration capacity. Damage to cartilage can lead to the onset of very common chronic diseases such as osteoarthritis, in which the cartilage covering bones decays. This causes reduced motion and pain. *In-vivo* evaluation of cartilage would be very useful for studying the treatment of such degenerative diseases as well as for quantifying tissue quality of engineered samples.

Cartilage is a soft tissue. It consists of specialized cells which are called chondrocytes. Its extracellular matrix consists for the largest part of type II collagen. Cartilage is a connective tissue; however, it does not contain any blood vessels which contribute to its poor regeneration capability. Normal healthy cartilage is also rich in glycosaminoglycans (GAG).

Soft tissues are usually very difficult to image. This is due to the fact that µCTs use x-rays to produce cross-sections of 3D objects. Photons are ‘shot’ at the object and absorbed by it. A projection of this is detected and processed on a slide. Cartilage is usually so soft, that photons shoot right through the tissue without being detected and projected on the slide. Yet, there is a way to cope with this problem. An ionic contrast agent that binds to specific molecules within the tissue can be injected.

We injected the ionic contrast agent ‘Hexabrix 320’ and exploited the highly negative charge of GAGs within the tissue. GAGs are abundant in the middle and deep layers of healthy cartilage tissue. They form proteoglycans and also attract cations, as well as binding water molecules. This property leads to high elasticity and high pressure resistance of the tissue.

A negatively charged contrast agent will have an inverse relationship with negatively charged GAGs. The higher the GAG content in the tissue, the less the contrast agent will be visible.

Furthermore, since normal µCT scanners only have one energy source, they can only measure the overall attenuation of the x-ray. The x-ray attenuation is equal to the contrast agent distribution in the tissue. The scanner we used for our experiments (Medipix All Resolution System, MARS) however has more than one energy source. It can ‘shoot’ high and low energy photons which differentiate between atomic density of and variation within tissue. That means that the MARS scanner determines the characteristics of attenuation, rather than the overall attenuation. This enables the correct measurement of location and quantity of GAGs within cartilage tissue.

Our first goal was to use MARS-µCT to determine the GAG distribution in native articular cartilage. A bovine knee was acquired from the local slaughterhouse. It was cut into sections of ± 3mm x 5mm using a hacksaw. The sections were fixed in formalin. Fixed sections were incubated in different concentrations of Hexabrix; solutions ranged from 20% Hexabrix/80% PBS to 50%Hexabrix/50% PBS. The sections were all incubated for 24 hours at 37°C on a rocking device to assure complete hydration of the samples. For every condition 2 sections were incubated at the same time to allow for histological staining and biochemical assay after scanning.

Four sections at a time were scanned at high and low energies (13.32 keV and 30.84 keV). The samples were wrapped in parafilm and positioned on a holding device in the scanner to keep the samples from drying out or moving during scanning.

The images were pre-processed using the technical computing programme ‘matlab’. Afterwards they were reconstructed using the virtual experimentation programme ‘octopus’. Reconstructed images were combined with colour maps and different enhancement techniques by a fellow student from the HitLab NZ.

Histological staining with Safranin-O (stains GAG content red), Haematoxylin (stains cell nuclei blue) and Fast Green (stains alkaline proteins green) was performed on one sample from each condition. Red staining was expected to occur in the middle and lower layer, whereas blue and green staining was expected to be found predominantly in the superficial layer.
Reconstructed colour coded 3D images of cartilage samples following MARS scanning showed high x-ray attenuation in the superficial cartilage layer and low x-ray attenuation in the middle and lower layers as expected. Furthermore, the 50%Hexabrix/50PBS solution showed the clearest and least blurry images with the MARS scanner.

The histological stains correlated well with the MARS images. The low x-ray attenuation areas were stained red, whereas the high x-ray attenuation areas were stained blue/green.

Therefore, it can be concluded that the MARS scanner is an appropriate method to non-invasively image cartilage tissue in a clinical setting. Further research should aim towards making MARS an affordable technique in clinical settings to image pathogenic, healthy and engineered cartilage in patients.
New Zealand has one of the highest rates of colorectal cancer (commonly known as bowel cancer) in the world. Colorectal cancer is the second most common cause of cancer death in New Zealand, sitting behind lung cancer in terms of fatalities. The most effective method of diagnosis is via colonoscopy, where a camera is inserted through the anus and into the colon to view the wall of the digestive tract and take samples of abnormal growths. Unfortunately, demand for the procedure far exceeds the services hospitals are able to provide, and this gap is set to widen when colorectal cancer screening is introduced.

To ensure that those at high risk of bowel cancer (or precancerous growths, called polyps or adenomas) have a better chance of undergoing a colonoscopy, the Canterbury District Health Board (CDHB) developed a scoring pathway based on symptoms known to be related to bowel disease. The symptoms in the scoring pathway include bleeding from the anus, a change in bowel habit (e.g. development of diarrhoea or constipation), weight loss, and anaemia; personal and family history of abnormal growths was also included. Each symptom was allocated a point value depending on how well it predicted bowel disease. If the total number of points for a particular patient was equal to or greater than 20, the patient was deemed as being at high risk for significant bowel disease; they were consequently given higher priority for receiving a colonoscopy or a computed tomography colonography (CTC, better known as a “cat-scan” – a type of x-ray scan also used to diagnose colorectal cancer).

The aim of our project was to look at how many referrals were made using the scoring pathway (as opposed to simply writing out symptoms on a referral letter); the number of cancerous growths diagnosed in patients referred via the pathway versus referral by letter; the value of each symptom listed in terms of predicting whether a patient had cancer; and whether the current score threshold of 20 should be revised (in case too many cancers were being missed, or too many unnecessary colonoscopies were being carried out).

We identified 703 patients who had recently (July to December 2010) been referred for a colonoscopy or CTC because they presented with bowel symptoms (bleeding, diarrhoea) or had abnormal blood counts associated with bowel disease. We collected their referral letters and retrieved their results from hospital databases. Patient demographic information, symptoms, risk factors, and the results of their procedure were entered into our custom-made computer database. From there we could use statistics to analyse the data.

We found that approximately 20% of referrals were made using the scoring pathway. 35% of the referrals from general practitioners (GPs) used it, compared with less than 1% of specialist referrals; this was expected because the pathway was developed to be used by GPs via their computer systems (although the pathway has not yet been implemented in this way). Of the 703 patients, 49 had cancerous growths in their bowel. A higher percentage of cancers was detected amongst patients referred via the pathway than those referred by letter, and the score for cancers tended to be higher than the score for non-cancerous diseases (such as bowel inflammation or diverticulosis, a weakening of digestive muscles). These results suggest that the scoring pathway is working, because it provides more information than the referral letters (many of which neglected to mention important symptoms).

Some symptoms on the pathway appeared to be better predictors of colorectal cancer than others. These symptoms included sinister rectal bleeding (bleeding from higher up in the digestive tract, which appears dark or black because the blood has coagulated as it moves through the digestive system), anaemia due to iron deficiency (due to overt or unnoticeable bleeding), outlet rectal bleeding (bleeding close to the anus, which appears bright red because it has not coagulated) and loose bowels. These symptoms were the ones we expected based on past research.

Of the 49 patients with cancerous growths, almost a third (14) scored below the threshold of 20 points. If the 20 point threshold had been strictly enforced, these patients would not have had colonoscopies/CTCs and their cancer would not have been diagnosed until a later, difficult to treat stage. However, of the patients with cancer referred on the scoring pathway, only 1 out of 16 had a score lower than 20; this suggests that using the pathway guides referrers towards considering more symptoms that may point to bowel cancer.
In conclusion, the scoring pathway had a reasonably good level of use by GPs, which was pleasing because it was developed for them to use. The pathway appears to be effective; referrals made using the pathway had a higher percentage of bowel cancer diagnoses than referral letters and provided a higher level of relevant information. With the threshold score set at 20, nearly a third of patients found to have cancer would not have received a colonoscopy or CTC – it may be beneficial to lower the threshold so we do not overlook patients in need of diagnosis and treatment.
Lynch Syndrome is a hereditary condition which results in an increased risk of some cancers and is the cause of 2-5% of colorectal cancer. A key feature of this condition is a predisposition to early onset colorectal cancer—average age 45 years old, compared with 63 years old in the general population. It occurs as a result of a mutation in the mismatch repair genes MLH1, MSH2, MSH6 or PMS2. These genes code for proteins which repair errors that occur in our DNA during cell replication. A person with a mutation in a mismatch repair gene may not produce a functional protein, thus as the cells in the body replicate, errors in the DNA accumulate and may ultimately lead to cancer.

Immunohistochemistry staining (IHC) for mismatch repair genes is a process where tumour samples are stained to identify functioning mismatch repair proteins. If the tumour cells do not stain, it indicates a defective protein, which may be due to Lynch Syndrome. Therefore all individuals who show a loss of expression should be referred for genetic testing to check for a mismatch repair mutation. The use of IHC is important because it allows us to identify the patients most likely to have Lynch Syndrome, thus avoiding expensive genetic tests for each and every colorectal cancer patient.

In 2006, in line with international recommendations, Christchurch Hospital implemented new guidelines stating that all patients diagnosed with colorectal cancer aged 50 or under should routinely have IHC for mismatch repair proteins performed on their tumour specimens. Previously patients would only have IHC performed if specifically requested by a clinician or pathologist. Individuals demonstrated to have loss of expression of a mismatch repair gene should then be referred to the NZ Familial Gastrointestinal Cancer Registry (NZFGICR) and offered genetic testing.

The aim of this research was to assess whether IHC for mismatch repair proteins has become routine practice in the management of colorectal cancer patients diagnosed aged 50 and under and what impact this has had upon IHC rates in this age group. In addition we investigated whether patients have been appropriately referred for genetic testing if loss of staining was observed.

We reviewed Christchurch Hospital records for patients 50 and under diagnosed with colorectal cancer between January 1 2004 and June 30 2010 and divided these into two groups, before and after January 1, 2006.

We found that after the guidelines were introduced in 2006, IHC rates amongst the 50 and under age bracket increased from 43% to 84%. If the results only included removed bowel segments and the smaller biopsy specimens were excluded, the IHC rate was 92%. Furthermore almost 90% of these results were available within one month of the samples being taken. Of the thirteen patients who did not have IHC performed, there were valid reasons for not performing the stains in eleven cases.

From 2006 onwards, all eight individuals with loss of expression of a mismatch repair gene were referred to the NZFGICR for genetic counselling and six underwent genetic testing (the two others died before testing could occur). Amongst these individuals, one mutation was confirmed, three are awaiting on-going genetic investigations and two have not had any mutation detected.

We have demonstrated that the implementation of guidelines has resulted in a significant increase in the use of IHC in the targeted age group and the majority of IHC testing is now being conducted as part of routine practice. It is unlikely this rate can be improved further due to practical and patient constraints. The implementation of the guidelines has therefore resulted in an effective system for the diagnosis and appropriate referral of potential Lynch Syndrome patients aged 50 or under.

As an additional part of this studentship, a review of current literature revealed a lack of consensus regarding ‘50 years and under’ as an age based criterion. Current international recommendations outline criteria to select some patients over 50 years of age, however many recent studies have demonstrated that testing all patients up to 55, 60 or even 65 years old may greatly increase the capture of Lynch Syndrome cases. It has yet to be determined if this is economically viable, however with IHC methods constantly evolving, it is likely that in the near future this will have ramifications for protocol at Christchurch Hospital.
Rachael Stevenson  
*The Canterbury Methadone Maintenance Model of Care*  
**Supervisor:** Dr Ian Sheerin, Dr David Kerr and Joy Drummond  
**Sponsor:** Pegasus Health

**Introduction:**  
From the 1960’s, New Zealand saw a rapid increase in injected drug use, particularly the opioid heroin. Tougher law enforcement in the 1980’s meant that heroin was difficult to access so the legal opioid, morphine, used for pain relief began to be abused by those addicted to opioids. Addiction to opioids means that if the person stops taking the drug they may experience negative feelings and a severe flu-like illness making it extremely difficult to stop using. As users inject the opioid, 84% were infected with viruses such as hepatitis B and C in the 1990s. The abuse of opioids also increases the risk the person dies by overdose, and that their family, friends, and work will be negatively affected. The average person addicted to opioids in Christchurch costs society $4,960 a month mostly in unsafe and illegal activity such as theft and prostitution as a way of obtaining money to acquire more drugs.

Methadone is a monitored medication for opioid addiction that removes negative withdrawal symptoms but provides no ‘high’ feeling. This may be a lifetime treatment. When patients initially start the Canterbury Methadone Programme (CMP) they must obtain prescriptions from Hillmorton hospital and have daily observed consumption. It can take several months before the person is stable on their methadone dose. Once stable, they can obtain methadone prescriptions from their General Practitioners (GP) in a unique programme to Christchurch called ‘GP Care’.

GP care aims normalize methadone treatment, provide holistic care to patients and reduce the waiting time for other people to start methadone. Over the past 13 years, the waiting time has dropped from 12 months to 3 months as more patients moved to GP Care. This study looks at how both GPs and patients involved find GP Care before potentially expanding nationwide.

**Aim:**  
To investigate the General Practitioners’ perceptions of the Christchurch Methadone Maintenance Model of Care and the perceptions of methadone clients under GP Care.

**Method:**  
Questionnaires were designed and distributed to 48 GPs who had at least one patient on GP Care. Questions focused on; dose adjustments, takeaways, management of other health conditions, prescribing medications that interact with methadone and support and training available. Patient questionnaires were designed to determine how they found GP Care compared to CMP. To maintain patient confidentiality patient questionnaires were sent to each GP’s practice manager. The practice manager asked the GP who these patients were and placed alerts on their screens. When the patient came in for their next monthly meeting an alert would pop up reminding the receptionist to make sure the patient filled out the questionnaire. All questionnaires from GPs and patients were returned with no personal identifying information and results entered into statistical programme; SPSS vs. 17 for analysis. GPs were invited to attend an audio-recorded focus group at Pegasus Health to further discuss issues. This was transcribed and analysed.

**Results:**  
19/48 (40%) GPs returned questionnaires, within a month of receiving them. Three (6%) declined to be involved, and six (12.5%) were known to be away for the entire study period. 84% of respondents had been involved with GP Care for more than two years. Respondents had an average of four patients. Three GPs needed to contact GP Committee to clarify which patients were under their GP Care. Based on the questionnaire:

- 63% became involved to help current patients on methadone wanting to move to GP Care.  
- 68% liked providing holistic care and help manage patient’s addiction.  
- 41% disliked patients not always paying fees and 32% disliked the extra time involved.  
- Half the GPs had patients wanting dose increases and 95% had requests for dose decreases  
- A quarter of the GPs had been asked to prescribe pain relief and a third had been asked to prescribe sedatives that are potentially addictive. Half of the time, GPs felt the request was appropriate.  
- Takeaways are viewed as necessary for the patient having a ‘normal life’, one in four suspect some is diverted and one in ten want all consumption observed at the pharmacy.  
- More GPs preferred having access to advice on issues of treatment rather than more training.
• All had a good relationship with their patients but felt funding and clear boundaries would improve this relationship.
• Two thirds would consider taking on more GP Care patients and 94% would recommend other GPs to be involved.

Eight GPs attended the focus group and the key findings were:
• Seven liked having to refer to GP Care committee before making dose or takeaway increases. This meant they weren’t bullied by patients or seen as the ‘bad guy’.
• Patients are more likely to initiate decreasing their dose than GPs. Whereas a GP is more likely to suggest a dose increase than a patient.
• Cost was a conflicting issue. GPs either charged a decreased fee, their standard fee for all patients or it would vary depending on how long the appointment lasted. All agreed this should be agreed upon with the patient before starting on GP Care.
• The group felt yearly meetings of GPs prescribing methadone would be beneficial, and that more GPs should become involved.
• They perceived GP Care patients as ‘less neurotic’ and more reliable than other patients and perhaps more GPs would be involved if they knew this.

23/137 (17%) of patient questionnaires were returned after 5 weeks. Most (67%) had been on methadone for more than 10 years. Based on these questionnaires:
• All preferred accessing methadone scripts from their GPs rather than CMP.
• For 85% of patients, GP Care had less travel time, impact on family, work and social commitments and improved their quality of life and health compare to CMP.
• Cost of paying for monthly appointments was the main issue.
• 57% wanted more flexibility with takeaways if they proved they were stable reliable patients.
• All were grateful for being on GP Care, and to their GPs for helping them live ‘normal’ lives.

Conclusion:
The available evidence suggests that the Christchurch GP Care programme is well liked by GPs and patients. Future recommendations are that when initially starting the programme, clear rules and boundaries should be decided upon as well as funding options between the patient and GP. GPs should have the opportunity to meet to discuss issues regularly. If more GPs were recruited into the programme it would reduce the current work load and continue to help people overcome their opioid addictions and live ‘normal lives’.
Falls among elderly inpatients are common, especially in rehabilitation units where patients are encouraged to increase their functional independence. Falls can result in adverse consequences for patients such as physical injury, anxiety, loss of confidence, and impaired rehabilitation. Fallers have poorer longer-term outcomes than non-fallers, such as increased length of stay, lower discharge mobility and higher rates of institutional care on discharge. Inpatient falls are also perceived as a marker of poor quality of care by the hospital and its’ staff. Whilst a zero falls rate would be ideal, attempts to reduce falls and subsequent adverse consequences should not be at the cost of the patient’s rehabilitation and gains in their independence. Staff should therefore aim to minimise fall rates whilst maximising patient independence and rehabilitation.

Research supports the assumption that falls have many causes. Our hypothesis was that not all falls and fallers are the same and that different falls may require different fall prevention strategies. The aim of this study was to test an existing categorisation of fall types, developed in a stroke rehabilitation unit, and assess its appropriateness in general rehabilitation and psychogeriatric inpatient populations.

The study was a retrospective (August – October 2010) and prospective (November – December 2010) audit analysis of clinical notes for all falls and fallers on three wards at The Princess Margaret Hospital; two general rehabilitation wards (GRW) and one psychogeriatric ward (PGW). Fallers were identified from incident reports. Data was collected from the patient’s incident report, clinical notes and drug charts. Fall circumstances, faller characteristics and injuries/outcomes were collected for each fall. This information was used to assign the fall into one or more of the existing falls categories, outliers were identified. This existing category of fall types was subsequently modified on the basis of these outliers. The GRW and PGW falls and fallers were analysed together and then independently to identify similarities and differences between the two study groups.

In total there were 164 falls and 86 fallers during the five month study period; 87 falls and 52 fallers on the two GRW and 77 falls and 34 fallers on the PGW. The average faller age was 81 years (range 58 to 102), 45% of faller’s were male and 55% female. It is important to note that almost all (94%) patients that fell had fall prevention assessment documented in their notes prior to the fall. Of those fallers, 93% were assessed as being a high risk of falling prior to their first fall.

There were notable differences between the GRW and PGW populations (figures in the brackets are %fallers GRW, then %fallers PGW); fallers with diagnosis of dementia (33%; 100%) and the number of patients with multiple fall (38%; 47%) were both more common in the PGW. Differences were also evident between the two populations in relation to the circumstances of the falls; falls around bed (47%; 32%), falls in the bathroom (10%; 1%), falls in the toilet (11%; 0%), and falls whilst transferring (39%; 23%) were more frequent in general wards whereas PGW had greater falls occurring in the lounge/dining area (3%; 32%), and whilst walking (17%; 32%).

The two populations were similar in the timing of falls, with 51% occurring between 9pm and 8am. Peaks were evident between 2am and 3am, 9am and 10am and between 9pm and 10pm in the GRW. On the PGW the peak falling times were between 9am and 10am, 1pm and 2pm and also 10pm and 11pm. Falls occurred throughout the admission with 32% of all falls occurring during the first week of admission and 25% occurring in the week prior to discharge.

Only 15% off falls were witnessed by staff. This has implications for the accuracy of staff reporting of cause of falls, as assumptions need to be made from the activity being undertaken just prior. The high prevalence of delirium or dementia may also prevent the patient from explaining what actually happened. Fortunately, only 0.6% of falls resulted in major injury (usually fracture) and there was no injury sustained in 85% of all falls during the study period.

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1 Quality Improvement Event Reporting forms (QIER)
A modified category of fall types and associated definitions were developed to fit these two study groups. It was evident from the data that there were six key categories, with a number of corresponding subcategories. Notable differences were apparent between the GRW fallers and PGW fallers (figures below are %falls GRW, then %falls PGW).

**A. “I’m sick”** Acute medical conditions directly contribute to the fall (31%; 23%)

**B. “It’s the meds”** Medications directly contribute to fall (9%; 34%)

* B(i). “It’s my medication combination” >5 fall risk medications (24%; 34%)

**C. “I shouldn’t have”** Activity is inappropriate to stage of rehabilitation (49%; 29%)

* C(i). “I’m unsteady” The patient is unsteady when mobilising, doing something that is inappropriate to their stage of rehabilitation (28%; 21%)

**D. “I’m giving it a go”** Activity is appropriate to stage of rehabilitation (36%; 69%)

**E. “I was toileting”** The fall occurred during the toileting process (40%; 16%)

* E(i). “I really need to get to the toilet” The fall occurred due to the patient urgently needing to use the toilet (24%; 10%)

**F. “I’m agitated and unsteady”** The patient is both agitated and unsteady when mobilising (24%; 73%)

**G. “Other”** Outlier circumstances contributed to the fall (14%; 12%)

Most of the falls were coded into multiple categories (91%) as they had multiple contributing factors. This multifactorial depiction of falls is supported in falls literature and the basis for many multifactorial fall interventions.

This categorisation highlights a number of key differences regarding the types of falls that occur within the two separate groups. Fall prevention strategies should focus on gait instability and toileting in the GRW. On the PGW fall prevention strategies need to address patient’s gait instability, as well as manage agitation and the fall risk side effects of their medication. Fall prevention strategies need to be weighed up against other potentially competing patient needs such as the need for autonomy and independence in mobility. Thus fall prevention needs to be individualised and rehabilitation will always be associated with some risk of falls.

It is clear that the two populations are different. They have different fall type prevalences and different faller characteristics. This study provides evidence that not all falls or fallers are the same and that different fall prevention strategies may be required to target the prevalent fall types for different units.

Further analysis of the database will be undertaken to find other differences between the two groups. This could include the comparison of our study population with a population of non-fallers. Further refinement of the categorisation is also required as there is some overlap between fall taxonomies. With further research and testing, our classification has the potential to be a helpful tool in predicting and preventing falls in elderly inpatients.
Jessica Taylor

Changing Treatment and Outcomes in Multiple Myeloma for Patients in Christchurch

Supervisors: Dr Peter Ganly, Dr Liam Fernyhough, Dr Barry Hock

Sponsor: Ruth Spearing Cancer Trust (initiated by Barry Mather)

Introduction

Multiple myeloma (MM) is a malignancy of plasma cells, which are the white blood cells that produce antibodies. It has an incidence of about 4 per 100,000 people in most developed countries, with the incidence increasing with age. A significant improvement in the survival of MM patients has been observed over recent years; however conventional treatment still produces unsatisfactory results. Patients eligible for and treated with high-dose chemotherapy and stem cell transplantation (SCT) using the patient’s own stem cells (autograft) have improved outcomes compared with patients treated with conventional chemotherapy. However, both treatment options are unlikely to achieve cure and the disease ultimately relapses. SCT using stem cells from a matched donor (allograft) is considered the only potential cure for MM, although its use is controversial due to the risk of graft versus host disease (GVHD) and high transplant-related mortality. In recent years, the incorporation of novel agents including thalidomide, lenalidomide and bortezomib into treatment regimens has improved outcomes in some patients. However, in New Zealand, access to these novel agents is limited, as they are often only available through clinical trials. Developments in treatment have prompted extensive debate about what is the best treatment strategy.

Purpose

The objective of this retrospective analysis was to describe the patterns of survival for all MM patients treated at Christchurch Public Hospital (CPH) over a 15-year period, with a focus on the impact of SCT and novel agents.

Methods

A total of 443 MM patients (64% male), treated between 1995 and 2009, were identified using the CPH Haematology Department database. Electronic and written medical records were reviewed. For each patient, descriptors of the disease, treatment and outcome were obtained. On the basis of the CPH upper age limit for treatment with SCT, patients were categorised, according to their age at diagnosis, as either < age 70 years (n = 271) or ≥ age 70 years (n = 172). Each age category was independently analysed.

Disease response was evaluated following SCT. Response criteria were based on the reduction in the amount of a particular protein (M-protein) present in the blood. M-protein is present in excessive levels in MM. Complete response (CR) required no detectable M-protein. Very good partial response (VGPR) was defined as a 90% or greater reduction in M-protein and a partial response (PR) as a 50% or greater reduction in M-protein. Stable disease (SD) indicated a response that did not meet the criteria for CR, VGPR or PR. Progressive disease (PD) required an increase of greater than or equal to 25% in M-protein.

Patients were followed up until October 2010. The primary clinical outcome analysed at the end of follow-up was overall survival (OS). For the entire cohort, OS was calculated from the date of diagnosis until death from any cause. In addition, for patients who received a SCT, OS was also calculated from the date of SCT until death from any cause. OS curves were generated using the Kaplan-Meier method. Comparisons of variables were made using standard techniques. Results were considered to be statistically significant if the P-value was ≤ 0.05. The PASW Statistics 18 software package was used to perform the statistical analysis.

Results

The median age at diagnosis of the study population was 66 years (range 32 – 94). 60% of patients were < age 70 years. 31% of patients had received a SCT with 24% having received an autograft only and 7% having received any allograft. 52% of patients had received a novel agent with 49% having received thalidomide. Only 8% of patients had received Lenalidomide and 5% had received Bortezomib.

The median follow-up duration for the entire cohort was 32 months. At the time of analysis, 175 (40%) patients remained alive. The median OS of the entire cohort was 48 months (95% CI 38 – 56). The OS was significantly longer in patients < age 70 years compared with patients ≥ age 70 years (median 72 months versus 20 months; p < .001). Within patients < age 70 years, those who received any SCT had a significantly longer OS than those who did not (median 125 months versus 52 months; p < .001). No difference in OS was demonstrated between patients who received an autograft only and those who received any allograft. Within patients < age 70 years, there was no difference in OS between patients who received novel agents and those who did not. However, within patients ≥ age 70 years, patients who
received novel agents had a significantly longer OS than those who did not (median 32 months versus 14 months; p < .001).

Compared with those who received an autograft only, a greater proportion of patients who received any allograft achieved CR (48% versus 24%; p = .011); whereas a lesser proportion achieved PR (14% versus 49%; p = .010). Similar proportions of patients in both groups had VGPR and SD following SCT. Subsequent to the maximal response, PD occurred in similar proportions of autograft only and any allograft patients. 79% of patients who received any allograft experienced GVHD. 32% of patients who received any allograft were in sustained CR at the end of follow-up.

**Conclusion**

This report summarises the treatment of MM patients at CPH over the past 15 years. The analysis demonstrates that in patients < age 70 years SCT is associated with a significant improvement in OS, but novel agents are not and in patients ≥ age 70 years novel agents are associated with a significantly improved OS. In addition, no difference in OS has been demonstrated between autologous and allogeneic SCT. Considering the controversy that remains about the most appropriate treatment strategy for patients eligible for SCT and for those who are not, these results can assist with local decision-making regarding treatment options.
Matthew Tennant

Double Blind Randomised Placebo-Controlled Trial Subjectively and Objectively Assessing Efficacy/Safety of Topical Lignocaine on Mechanical/Cold allodynia/hyperalgesia in Neuropathic Pain.

Supervisor: Professor Edward Shipton
Sponsor: Canterbury Medical Research Foundation

When asked what lignocaine is I usually tell people that it is what the dentist injects into your mouth so that you cannot feel what he is about to do next. In this study the gel in question is only two percent lignocaine, which is much weaker and is absorbed through the skin not injected. Lignocaine blocks sensory nerves from firing signals to the brain.

Long term nerve-type pain (chronic neuropathic pain) is relatively common. Nerves that have been damaged can become hypersensitive, normal sensations like touch, hot, and cold can be interpreted as pain (allodynia) and normal sensations can be dulled making the area seem numb (hypoalgesia). It is hoped that lignocaine gel could lessen the pain signals and allow the pain pathway to function more normally over a period of time.

Most of the current treatments for chronic neuropathic pain are systemic, which means they affect the whole body. Because lignocaine gel would only be applied to the area where the pain is the side effects should be less common and less severe.

The aim of this study was to determine whether lignocaine 2% gel is effective in decreasing the area affected, and symptoms of chronic neuropathic pain.

The design chosen for the study is a double blinded randomized placebo control trial. The trial is a pilot study and will be used to assess the prospect of a larger study in this area if required.

33 patients were asked to join the project and of these 25 fulfilled the criteria to participate in the trial. These participants were computer randomized into two groups - 13 into an active group which would receive the lignocaine, and 12 into a control group which would receive KY jelly, a placebo. Neither the participants nor the assessors were aware of their group allocation or the gel they received. Both gels are clear, colourless, and of the same consistency. In an initial consultation participants were asked questions regarding patient demographics, pain, mood, and sleep. An area of pain was mapped out on each patient and the area was measured using the Silhouette Mobile system. The participants were then given a jar of gel and told to apply the gel four times a day for the period of the trial. The questionnaire and measurements were then repeated at three weeks and then again at five weeks.

Because of the size of the trial and it being a pilot by nature, it was not surprising that no statistically significant results were achieved. It is therefore not possible to accurately assess the effects of the lignocaine from this trial alone but we can begin to see trends. The pain measurements, including current pain, usual pain, lowest pain and highest pain showed tendency towards slight improvement. Mood measurements also showed a trend towards improvement. Area was on average 19% worse off on the lignocaine than the placebo, however the confidence interval was -23.5%, 84% so the data was inconclusive. On average those in the lignocaine group felt as though they had improved more at three weeks and five weeks than those on the placebo. After five weeks the lignocaine group on average felt their progress was “slight improvement” to “much improvement”.

It must be noted that three individuals in the lignocaine group reported side effects. One individual came in with inflammation and blistering within two days of beginning the treatment. Two reported a mild skin irritation with itchiness. All three were told to stop the treatment immediately.

Although recent research has greatly deepened our understanding of mechanisms of chronic neuropathic pain treatment it is still difficult to clinically manage as current treatment options often have heavy side effects and can be addictive. Topical lignocaine gel may be a useful tool and alternative to add to the current arsenal of treatments.

The trial bares little weight as a standalone study but would make a good starting point for a larger trial. Based on the data of this study a sample of 400 participants would surfeit for all of the subjective measurement to be found statistically significant (Except the sleep index). The mild benefits recorded should also be weighed up against the side effects that were brought to light in the pilot.
Babies that are born prematurely are often very sick during their first few months of life. One reason for this is that premature babies have an underdeveloped immune system and are prone to developing infection. Prior to birth there are no bacteria in the gut, and when these babies first encounter bacteria that can cause infections, their immune defenses may be poor or unable to help them fight off infection.

Many premature babies are fed using a nasogastric feeding tube, which goes through their nose and into their stomach. This allows them to be fed easily, as they are often too little to feed properly from their mother or through a bottle. However, there are worries that bacteria that can cause infection may be able to get into the feeding tube and make babies sick.

This study was carried out to see if there were any bacteria growing in feeding tubes in the neonatal intensive care unit at Christchurch hospital, and if so, find out what kinds of bacteria were growing, and whether they were harmful to the babies in the unit.

After analyzing the feeding tubes in the laboratory, we found that all of the tubes had bacteria growing on them, ranging from low levels right up to high levels of growth. There was a wide variety of bacteria in the tubes – the majority of them were skin bacteria, but there were also a lot of stomach bacteria and some mouth bacteria growing in the feeding tubes. While some of these bacteria are harmless, and some can actually help protect people from infection, many of the bacteria from the feeding tubes can cause disease, especially in young babies or in people who are already sick.

We also compared the information we got from the feeding to tubes to information about the babies. The babies in this study were generally pretty healthy, and there was only one instance where a baby wasn’t feeding properly, and no instances of serious gut problems. There were four times when we found the same bacteria inside a baby’s feeding tube as what was in samples taken from their blood, lungs or eyes.

From this study, we know that babies feeding tubes frequently have bacteria growing inside them, and that these bacteria are ones that commonly cause disease to young babies and people who are already sick. Because of the fact that not many babies got sick during the study, it is difficult to say whether the bacteria found in the babies’ feeding tubes were responsible for making them sick or whether other their sickness was due to other reasons.
Articular cartilage is important to provide shock absorption and a smooth surface for articulation of the joints. This is achieved by the high levels of glycosaminoglycans (GAGs) contained in cartilage that are able to sequester water molecules, creating the mechanical properties of cartilage that makes it so effective in joint cushioning and protection. However, articular cartilage can be easily damaged by sports injuries or disease such as osteoarthritis. Cartilage tissue has only a limited capacity to regenerate and this can restrict the functionality of the tissue after damage. Tissue engineering strategies have significant clinical potential to repair damaged cartilage and restore long-term function. This process involves taking the patients’ cartilage cells or adult stem cells and placing them within a porous 3-D scaffold substrate to stimulate the cells to generate new tissue, which can then be implanted into the site of damage. A number of materials have been investigated for use in this application, some synthetic, such as polyethylene glycol terephthalate (PEGT) and poly(lactic-co-glycolic) acid (PLGA), and some natural, such as collagen. However, finding a scaffold material that is able to replicate the complex zonal organisation of cells and environment found in an in vivo tissue is a challenge. Ovine forestomach extracellular matrix (OFM) is a native and functional biomaterial that has been shown to support cell adhesion and proliferation. The suitability of this biomaterial to support cartilage cells and cartilage tissue growth is not known.

This project aimed to investigate whether the ovine forestomach extracellular matrix (OFM) biomaterial was able to support cartilage tissue growth and differentiation, and if it may represent a potentially useful new tool for remediating cartilage injuries.

The tissue regeneration company Mesynthes Ltd located in Wellington was able to purify ovine forestomach extracellular matrix from the rumen of sheep using sealed transmural osmotic flow (STOF), a process that decellularizes the tissue using an osmotic gradient of detergent solutions that remove the cells from the tissue and allow the distinct tissue layers to be separated from one another. The muscular and epithelial layers of the tissue were removed, leaving the propria submucosa which contains a particularly dense layer of collagenous matrix to be used to produce the OFM biomaterial.

The OFM used in these experiments was lyophilised in sheets and punched into disc shapes of 16mm in diameter, named Endoform™. Pieces of cartilage removed during septoplasty surgery were acquired with informed consent from patients attending Christchurch Hospital for surgery. The pieces of cartilage were digested and the human nasal chondrocytes (HNCs) isolated and expanded in culture over 3 weeks. The HNCs are then removed from culture and seeded on the Endoform™ OFM biomaterial discs in 24-well plates at a concentration of 200,000 cells/well. HNC cell pellets of a cell concentration of 200,000 cells/pellet were formed as comparative controls. The HNCs were grown on the OFM discs for 1, 7 and 14 days, with refreshing of culture medium every 72 hours. After the duration of the culture, the discs were gently washed twice and sliced in half, with one half of the OFM disc reserved for histology and the other half reserved for biochemical analysis.

For histology, the OFM discs used to culture HNCs were fixed in formalin overnight, dehydrated and embedded in paraffin, before being sliced into sections and mounted on slides. The samples on the slides were then stained with Safranin-O, Fast Green, and Haematoxylin, staining cell nuclei blue-black, cartilage orange-red, and cytoplasm blue-green. For biochemical analysis, the DNA content of the digested samples were determined to indicate the number of cells present on the OFM cultures at different time points. OFM cultures were also stained with Calcein AM, a green fluorescent stain that stains live cells, to gain an indication of which side of the OFM disc the cells preferentially adhered to and the density of cells.

It was found that the human nasal chondrocytes were able to adhere to the Endoform™ OFM discs, preferentially attaching to the luminal side of the biomaterial. Live staining with Calcein AM showed viable cells present on both sides of the OFM discs but did not provide much of an indication of which side the HNCs preferred to adhere to. Histology showed that at later time points (day 14) the cells present on the OFM scaffold began to form thin layers on the side of the scaffold on which they were placed. In some instances, the cells migrated into the OFM material. Assays for DNA showed that DNA levels did not significantly rise over the culture period, with the DNA content in the OFM samples about 5- to 6-fold lower.
than that of the HNC pellet controls. This indicates that a low number of cells are adhering to and proliferating on the OFM discs, with some probably being lost at medium changes. There also appeared to be more cells adhered to the luminal side of the OFM compared to be adluminal based on DNA content. However, despite being cultured in media that is proven to be chondrogenic, the cells cultured on the OFM biomaterial did not appear to be producing any GAG, as seen by a lack of Safranin-O staining.

Although human nasal chondrocytes were able to adhere to and proliferate on the Endoform™ ovine forestomach extracellular matrix biomaterial, they did not produce glycosaminoglycans (GAG) and were therefore not in a re-differentiated and chondrogenic state. The Endoform™ OFM biomaterial does not appear to be wholly suitable for cartilage tissue regeneration purposes, but may have significant clinical applications in other areas of tissue engineering and regenerative medicine.
A biomarker is a biological compound present in breath, blood, tissue or other bodily fluids that can indicate the presence of a condition or disease. It can also be used to monitor how well the body responds to treatment. Nitric oxide (NO) is produced in the airways and is present in breath. NO has been shown to be a biomarker for eosinophilic airway inflammation. This type of inflammation is common in asthma and some other airways diseases. When this type of inflammation is present in the lungs, there is a higher concentration of Nitric Oxide found in breath. Subjects without asthma typically have a concentration of NO of 25 parts per billion (ppb) or lower in their breath. Asthmatics that are not using an inhaler typically have concentrations above 50ppb. Devices used to measure fraction of exhaled Nitric Oxide (FE_{NO}) such as the NIOX MINO are used by doctors during treatment of these conditions. Measuring NO in breath has been proven to be useful for assessment and monitoring of asthma and determining treatment effectiveness. However there is still some information that is unknown about NO, especially in relation to the role it plays in the airways and research on this is currently being carried out. NO is only a useful biomarker for eosinophilic inflammation, other types like neutrophilic inflammation cannot be assessed by measuring NO. Different tests would provide more information about the types of airways inflammation.

SIFT-MS is a technique used to measure volatile organic compounds (VOCs). The gas above a sample of blood or urine, or a single breath and the atmosphere can all be tested for lots of compounds using this versatile instrument. This technology is powerful as SIFT-MS can detect VOCs in very small amounts – even as low as parts per trillion, and several VOC can be measured at the same time. What sets it apart from other technologies is the speed that it can deliver these results. Currently, breath research is being carried out using SIFT-MS in relation to different respiratory diseases such as asthma, COPD, and cystic fibrosis and biomarkers that identify them. Carrying out breath research this way is desirable as it is noninvasive, fast and may one day replace blood tests.

Nitric Oxide is difficult to analyse in breath because it is present in very low concentrations (1 part per billion is equivalent to 1mL of water in an Olympic sized swimming pool) and because there are over 200 other compounds present. Currently NO measurement is carried out separately and the machine used can only measure one compound (NO). A SIFT-MS method for measuring NO could become part of a single test for many biomarkers of inflammation. The SIFT-MS test would also provide real-time information including information about the change in concentration of NO during the breath, how fast the breath, and how much breath is being exhaled.

The aim of this project was to develop a breath test to accurately measure Nitric Oxide using SIFT-MS as this has not been established yet.

Initially NO gas at known concentrations was used to develop an accurate test on the SIFT-MS. Once the correct way to measure NO was worked out volunteers were asked to breath directly into the SIFT-MS and their breath was analysed. The breath testing was very simple to complete, it required the participant to take a deep breath and breathe into the SIFT-MS, controlling how fast they breathed out by watching a flow meter on the screen. During the breath test the NIOX concentration that was exhaled and also the rate at which the breath was exhaled was measured. Measuring NO in breath requires breathing in and out in a very particular way. This is because the concentration in the breath is affected by how fast the breath comes out. The faster the person breathes out the lower the NO would be. This is the same as water flowing down a heated pipe. The faster the water flows out of the pipe, the less heated it will be compared to water that flows slower. Keeping the speed at which the breath is blown out is important because the same people were also asked to breath into the NIOX MINO. To be able to compare the amounts of NO measured by the NIOX MINO and the SIFT-MS tests the breaths must be as similar as possible.

The SIFT-MS method was sensitive enough to detect the low amounts of NO in the breath of healthy people and also measured the higher amounts in the breath of asthmatics. The patients' breath test results showed that the amount measured by the SIFT-MS test and the NIOX MINO agreed. This means that the SIFT-MS test could be used as an alternative way of measuring the amount of NO in breath. There is also much more information obtained about the breath when using the SIFT-MS test. This method will prove useful to further
biomarker respiratory research and this project has led the way for more development to occur to obtain a more accurate SIFT-MS test.
Urinary Cystatin C and Microalbuminuria as Biomarkers of Sepsis and Acute Kidney Injury

Supervisors: Dr John Pickering, Professor Zoltan Endre, Dr Geoffrey Shaw
Sponsor: Kidney Health New Zealand

Tom won the award for the ‘Best Presentation in the Clinical Category’.

Acute kidney injury (AKI) is a common condition characterized by a rapid decrease in acute kidney injury (AKI) is a common condition characterized by a rapid decrease in kidney function. In the intensive care unit (ICU), AKI affects about one in three patients and is often fatal. Early diagnosis could lead to better outcomes for patients, yet the current “gold standard” for diagnosis only picks up AKI days after it has occurred. Imagine if the fire service took hours to realise a house fire is in progress! – this is similar to what we’re dealing with here. By the time AKI has been diagnosed, it’s usually too late to do much about it.

Another important condition in the ICU is sepsis. Put simply, sepsis is a nasty infection. Similarly to AKI it is common, often fatal, and hard to diagnose. Many of the signs and symptoms of sepsis are non-specific – that is, they are also present in other, non-infection-related diseases. This is important because different conditions have different treatments: if a patient has sepsis they can be given antibiotics, but this is unnecessary if they don’t have an infection.

Therefore, the discovery of new diagnostic tests for AKI and sepsis could improve the outcomes of many patients in the ICU. This studentship focused on this idea by investigating whether a new urine test could be used to diagnose these conditions. This test measures the urinary concentration of a protein called cystatin C. We suspected, from earlier studies, that urinary cystatin C concentration would be higher in patients with AKI or sepsis than in patients without either condition. We also investigated if a second protein, called albumin, was present in the urine of patients with AKI or sepsis, as it has been suggested that the amount of albumin in the urine can affect the amount of cystatin C, hence modulating the diagnostic accuracy of cystatin C as a test for AKI or sepsis.

To test the theory that urine cystatin C diagnoses AKI and sepsis, and that the accuracy of this diagnosis can be improved by also measuring albumin, urinary concentrations of cystatin C and albumin in 72 ICU patients were measured. Using all available information, each patient was classified as having AKI or not having AKI, and as having sepsis or not having sepsis.

It was found that the average concentrations of both cystatin C and albumin were higher in the AKI group than in the non-AKI group, and higher in the sepsis group than in the non-sepsis group. Therefore, patients with greater amounts of cystatin C or albumin in the urine are more likely to have AKI or sepsis. This can be used as the basis of a diagnostic test.

Further analysis identified that the best diagnostic test for AKI would use the concentrations of cystatin C and albumin, while the best diagnostic test for sepsis would use cystatin C only. Using this information, the best possible diagnostic tests were developed, and the quality of these evaluated.

All diagnostic tests misclassify a proportion of patients – as having the disease when they don’t, or vice-versa. Hence the diagnostic ability of any test is usually assessed by calculating the proportion of patients it classifies correctly. On this basis it was found that 67% of people who tested positive for AKI (using the combined cystatin C and albumin test) actually had AKI, while only 15% of those who tested negative had AKI. That is, if 100 people test positive for AKI, 67 of them will have AKI, but if all 100 test negative for AKI only 15 of them will have AKI. Similarly, if 100 people test positive for sepsis (using the cystatin C only test), 81 will have sepsis, but if they all test negative only 32 will. Therefore, while not perfect, these tests provide valid information that can assist in diagnosis of both AKI and sepsis. In all cases, a positive test is associated with a significantly higher likelihood of having the condition being tested for.

While a lot more research is still required, this studentship has hence made one small step towards enhancing the diagnosis of AKI and sepsis and thus one small step towards improving the health of ICU patients.
It is difficult to predict the post-operative pain relief requirements of surgical patients. The sensation of pain is different for everyone and is mediated by a person’s mood, stress level and thoughts. People also respond differently to the drugs used to alleviate pain; some need much more or less to achieve the same level of relief depending on how sensitive they are to the drug or how fast their body can clear it from their system.

Fentanyl is an intermediate-duration opioid drug commonly given to surgical patients during and after their surgery to manage their pain. This project aimed to document and describe patterns of fentanyl dosing during and after surgery, and to relate those patterns to measures of the quality of short and intermediate term recovery. Identifying any existing relationships could help to better predict how much pain relief surgical patients need and improve their experience and recovery.

Patients having minor/intermediate, laparoscopic, or major surgery were followed through from the beginning of anaesthesia until they left the Post Anaesthetic Care Unit (PACU, where patients wake up and are monitored until they are safe to go back to a normal hospital ward). They were included in the study if the anaesthetist in charge planned to use fentanyl as the only intravenous (IV) opioid drug during the surgery and afterwards in the PACU. In the two instances where that plan changed and patients were given another IV opioid for any reason, their data was still included and analysed along with the rest. The time and amount of each fentanyl dose in theatre and the PACU were recorded and used to model the actual concentration of the drug in the patient’s central nervous system over time. Self-reported pain scores out of five, which are routinely taken by nurses in the PACU, were used as a measure of the quality of short term recovery. To measure the quality of intermediate term recovery, patients were interviewed the next day using the Myles Quality of Recovery (QoR) questionnaire, which generates a score out of eighteen.

Data was collected for 38 people; 17 men and 21 women all over 18 years old. Their average age was 50 years and their average weight was 85 kilograms. On analysis it was found that the more fentanyl a patient received in surgery, the more they received afterwards in recovery. There were also significant positive relationships between both intra-operative and post-operative fentanyl levels and the pain scores reported in recovery. The strongest of these in both cases was the relationship between fentanyl levels and the patients’ worst pain scores. There was no significant relationship between the amount of fentanyl given during or after surgery and patients’ QoR score. There was, however, a significant correlation between low last pain scores and high QoR scores.

The positive correlation between intra- and post-operative fentanyl levels is most likely a reflection of how invasive is the surgical procedure. Major surgery is more invasive, so more fentanyl is needed during the procedure to keep the patient from responding to what is happening. More invasive surgery also causes more pain afterwards, hence the need for more fentanyl post-operatively in the PACU.

The relationship between fentanyl levels and pain scores is not so expected. Essentially, a positive relationship means that the more fentanyl people received, the higher their reported pain scores. This could almost mean that fentanyl causes pain, but probably not. The more likely explanation is again that more fentanyl is given for more invasive or painful surgeries, which in turn need more pain relief afterwards. However these patients are still experiencing more pain than others, so this finding implies that while fentanyl dosing is increased for these types of surgery, it is still falling short of patients’ needs.

It is interesting that QoR scores could not be significantly related by this study to any other measure except the last pain score taken before discharge from PACU. It is possible that this study did not have enough participants to establish a significant relationship between fentanyl levels and QoR. Patients are also more likely to remember the end of their time in PACU rather than the beginning, due to the diminishing effects of the anaesthetic drugs used in surgery. As a result, it seems plausible that the level of pain they feel towards the end of their stay in PACU will colour their experience far more than the rest of their time there.

As an observational study, this project succeeded in describing current patterns of fentanyl use during and after surgery. It throws up a number of questions and further research is needed to establish the validity of the findings suggested here. What it does suggest is that there may be some degree of predictability to
patients’ experience of post-operative pain in the short term. The level of fentanyl given during surgery may be an important guide to PACU staff of how much the patient will need in recovery. There is an implication that for more painful surgeries patients are not currently receiving enough fentanyl to meet their needs. With more research it may be possible to more closely anticipate and meet these needs, improving outcomes for patients.
Introduction
Cardiovascular disease (CVD) is defined as a class of diseases affecting the heart and the blood vessels, which includes heart attacks, angina and strokes. In many cases cardiovascular disease can be prevented yet in New Zealand 40% of deaths annually are from CVD and quality of life can also be affected. Risk factors that can be changed include poor eating habits, lack of exercise, being overweight cigarette smoking and high alcohol intake. Risk factors that cannot be changed include a family history, ethnicity and gender.

Cardiovascular disease risk assessment (CVD risk assessment) is a tool to help general practitioners (GPs) and practice nurses determine a person’s chance of having a cardiovascular event such as a heart attack, or stroke within the next 5 years. CVD risk assessment is encouraged for all adults in New Zealand from 45 years for men and 55 years for women (or 10 years earlier for individuals with various pre-existing risk factors). CVD is, to some extent preventable, so effective management of risk factors will help reduce the possibility of a cardiovascular event occurring. Management can include lifestyle changes, and or medications.

Variations (reported in previous studies) occur between how GPs and practice nurses assess CVD risk and their attitudes towards recording risk, yet the reasons for these variations are not well understood. In order to have a systematic approach to CVD screening it is important to understand the variations and make changes to ensure effective screening tools are used throughout general practice. This study aimed to compare the behaviours and attitudes of GPs and practice nurses towards performing and recording CVD risk assessments.

Method
Structured interviews were conducted with GPs and practice nurses currently working in general practices in Christchurch. All GPs within the Partnership Health Canterbury were invited to take part in this study. A total of 12 GPs and their practice nurses agreed to take part. These GPs were also identified as either high CVD risk recorders or low CVD risk recorders. Topics considered within the interviews included; health practitioners beliefs about the value of doing CVD risk assessments, current systems and processes in place for measuring and recording CVD risk, tools used for performing CVD risk assessment, barriers and enablers to assessing and recording, and support needed to ensure health professionals can effectively assess and record CVD risk. The interview included eight open ended questions facilitating conversation.

Interviews were recorded, transcribed and the results prepared, and thematically analysed, in order to identify common themes. Overall themes were identified within the data, and further analysis showed the similarities and differences between GPs and practice nurses and the reasons for the differences.

Results
The following main themes were identified: “Limitations of the opportunity to perform screening, time, appropriate IT tools, funding and education in how to assess for CVD risk. Differences between behaviours and attitudes of GPs and practice nurses were found within these 5 themes. All GPs believed they conducted CVD risk assessments where appropriate but due to limited opportunities many indicated that the assessments were not routinely undertaken as often as recommended. Some were also not convinced of the clinical merit of performing assessments. Seven of twelve practice nurses either did not attempt or did not conduct full CVD risk assessments as they believed GPs conducted them, or that is was not their role.

Twenty-two of twenty-four practitioners believed time was a limitation to completing CVD risk assessment, due to the difficulty of adding CVD risk assessment into a consultation that was for other issues. GPs stated they are too busy, and practice nurses stated that because they do them infrequently they took a lot of time.

Education that focuses on how to effectively conduct CVD risk assessment was requested by 10/12 practice nurses. One nurse revealed she had never been fully informed about how to conduct CVD risk assessments. And another stated that “Education was probably the big thing for her.” In contrast only one GP requested education related to CVD risk assessments.
Funding was requested by 15/24 practitioners. The majority of GPs believed that CVD risk assessment would become more important if there was a financial incentive. Practice nurses believed that funding was needed to subsidise the patient visit for the assessment. One nurse explained how she thought access to health care was a big issue in NZ, and people who really need to access health care often don’t because of cost. Another nurse believed that if funding for the patient was provided she would be more likely to make an appointment.

Current IT system limitations meant GPs wanted a pre-populating tool (an IT tool that draws in all the relevant information from the data in the patient’s file and then formulates a result without results having to be entered manually) and believed changes needed to be made to the MedTech system for recording. Several GPs experienced problems and expressed frustration when recording CVD risk assessment results in MedTech. CVD risk assessment results give a range eg 5-10% risk of a CVD event in the next 5 years, yet the MedTech tool only allows for a single number to be entered. Other GPs also asked for a more user friendly tool for both assessing and recording. In contrast practice nurses found the MedTech tool used to record CVD risk assessments beneficial and that limitations for them were more related to their IT skills.

Conclusion
This study explored the behaviours and attitudes of GPs and practice nurses towards assessing and recording CVD risk and identified the variations between the two groups. There were particular variations between GPs and practice nurses education requirements.

It is recommended that the themes discussed in this report are considered in order to enable GPs and practice nurses to perform consistent and effective CVD risk assessments.
Abby Zarifeh

*How Effective Do Patients Expect Preventive Interventions To Be?*

**Supervisor:** Dr Ben Hudson, Lorraine Young  
**Sponsor:** Pegasus Health

**Background**

Prevention and early diagnosis of disease are important aspects of general practice. A range of medications and screening tests may be used for this. The aim of this type of healthcare is to reduce the number of cases of disease or reduce the risk of dying of the disease. Many of these types of treatments are effective, but the chance of any one person benefiting from them is usually small. When deciding whether to take a preventive treatment or take part in screening, it is important that patients are aware of the likelihood that they will benefit from doing so. There is little information available on patients’ understanding of how effective preventive interventions truly are. There is also little known about the levels of effectiveness that patients believe would justify participation in interventions with their costs, risks and inconveniences.

**Aims**

The aims for this project were:

i. To investigate public perceptions of the expected effect of preventive interventions  
ii. To investigate the minimum levels of acceptable effectiveness of preventive interventions

**Method**

We designed a questionnaire to assess patients’ expectations of four commonly used preventive interventions in general practice. The interventions included were:

- x-ray screening for breast cancer (mammography)  
- screening tests for bowel cancer  
- medications to decrease the likelihood of broken hips in people with osteoporosis  
- medications to decrease the likelihood of cardiovascular disease (disease of the heart and/or blood vessels) occurring in people from the general population

Patients aged 50-70 years were selected from several Christchurch general practitioners’ lists. This age group was chosen as the preventive interventions illustrated in the survey are largely aimed at those of this age. Participants were asked to indicate the number of deaths or hip fractures they expected would be prevented due to the preventive intervention for a group of 5000 people from the general population treated or screened for 10 years. Participants were also asked to indicate how many lives out of 5000 people over 10 years they thought should be saved, or hip fractures prevented, to justify the costs, risks and inconveniences of the preventive intervention.

**Results**

977 patients were mailed the questionnaire. A total of 323 questionnaires were returned and responses were entered into a database. The average age of participation was 59.5 years with 89% of respondents identifying their ethnicity as New Zealand European and 2.8% as Māori.

Most participants significantly overestimated the number of deaths or fractures that would be prevented by the interventions. For each of the four interventions, over half the respondents expected 500 or more deaths (or fractures) would be prevented. For example over 60% of participants indicated they would expect 500 or more deaths to be prevented out of 5000 women due to screening for breast cancer with mammography. The actual number of deaths prevented based on international evidence is approximately 2.5 deaths out of 5000 women over a ten year period.

The range of responses was wider for the questions looking at what number of lives participants thought should be saved or hip fractures prevented to justify costs, risks and inconveniences of the preventive intervention. However, the majority of participants still gave high estimates of deaths or fractures prevented for these questions.

**Summary**

This study found that participants generally overestimated the benefits of the examples of preventive healthcare we asked about. We also found that many participants would still think the treatments and screening worthwhile even if they prevent a smaller number of deaths or fractures than is believed to be the
This may mean that respondents believe that even a small degree of benefit means that an intervention is worth undertaking.

There are many possible reasons for these findings, but we feel that this information will be useful for healthcare workers to consider when discussing this type of care with patients. We hope that this will help patients to make better informed decisions about whether to use preventive medicines or take part in screening programmes.
5. 2010 / 2011 Photographs from the Presentations

Mr Ernie Poole with student Teagan Hoskin and supervisor Dr Sarah Gunningham

Carole Acheson and Associate Professor Margreet Vissers

Dr Kenny Chitcholtan and Associate Professor John Evans with student Simon Hogg and his parents

Dr Ben Hudson with his student Abby Zarifeh

Dr Scott Stevenson with his son Jonathan Stevenson
Liz Chesterman, CEO of Cancer Society of NZ Canterbury/West Coast Division, with Dr Dean Harris and student Sarah Murphy

Helen Abbott with her mother
Caitlin Boyce with Deborah Snell and Dr Hilda Mulligan

Student Katie Jefferson with her supervisor Kelly Maw and student Monica Johnson with her supervisor Dr David Jardine
Faye Ruddenklau, Marion Pannett and Gwenda Ireland, Representatives from Cancer Society Ashburton Group

L to R: Jasmine Gooda, Joy Drummond (supervisor), Talia Wise, Ronald Puni, Katie Jefferson, Abby Zarifeh, Nofo Puni (Ron’s mother), Rachael Stevenson

Phyl Heal and Jean Burford, from Cancer Society Diamond Harbour Group
Judy Brooks and Shirley C’Ailceta, Representatives from New Zealand Federation of Graduate Women with student Nicole Coman-Wright (centre)

Andrew Gibb with his supervisor Dr Kit Doudney

Ronald Puni with his mother Nofo Puni
Helen Paton (L) and Joy Powell (R), Representatives from Lions Club of Selwyn, with ‘Best Presentations’ prize-winners: (centre) Helen Abbott, Tom Wilkinson and Amanda Polkinghorne

Dr Hilda Mulligan, supervisor, with ‘Best Overall Presentation’ prize-winner Amanda Polkinghorne and Wendy Fulton, CDHB (sponsor) Representative

Colin Dawson, CEO Otago Innovation Ltd with Professor Peter Joyce

Helen Paton (L) and Joy Powell (R), Representatives from Lions Club of Selwyn, with ‘Best Presentations’ prize-winners: (centre) Helen Abbott, Tom Wilkinson and Amanda Polkinghorne
Amanda Polkinghorne (centre), ‘Best Presentation in the Community Category’ and Best Overall Presentation’ prize-winner, with Helen Paton, Shirley C’Aiceta, Judy Brooks and Joy Powell. (Representatives from the sponsors of the prizes, Lions Club of Selwyn and New Zealand Federation of Graduate Women Inc.)

Student James Kennedy and Dr Geoffrey Shaw

Emily Grant, supervisor Dr Gini McIntosh and Gemma Lilly

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