FRONT COVER
Nishat Siddique “Luminal rhodamine”
This is the result of fluorescent rhodamine dye injected into the lumen of a mouse’s oesophagus. The dye is caught in and partially penetrates the stratum corneum in this mouse which has decreased expression of the epithelial transcription factor Grainyhead-like 3.

INSIDE FRONT COVER
Gemma D’Adamo “Phylogenetic tree of cultured isolates and the strength of inflammatory responses initiated”
Phylogenetic tree of cultured isolates displaying the distribution of isolates among the four main phyla – Bacteroidetes (green ring), Firmicutes (blue ring), Proteobacteria (red ring) and Actinobacteria (yellow ring). The overlay shows isolates cultured from inflamed mucosal samples (red bars), isolates classified as a putative novel species (black bars), the site of biopsy in the colon (shades of brown), and the intensity of inflammatory gene activation, in relation to the 12 genes investigated (shades of yellow and red), being IL6, IL8, IL12, IL17A, IL17F, IL23, CXCL10, TNF-a, STAT3, EPCAM, TREM1, IFN-y. Each ring around the phylogenetic tree represents one of the genes investigated.
Message from the BMedSc(Hons) Course Management Committee

Dear BMedSc(Hons) Students,

Congratulations on completing your BMedSc(Hons) degree! Well done, it is a very significant achievement.

The Course Management Committee would like to thank you for choosing to embark upon a formal year of research in BMedSc(Hons). We hope that the BMedSc(Hons) year has challenged you both personally and academically. The Honours year is meant to give you a new appreciation of how much more there still is to learn about medicine, about how new knowledge is created, how medical research is translated into changes in clinical practice and how important evidence-based medicine is for ensuring that changes to practice are justified. By the end of the year most students will feel like they have undergone an exponential learning curve, not just in their research area, but also in their confidence to critically evaluate new research findings, to communicate in written and oral formats and in their ability to work independently, as well as a member of a team. We hope that your Honours year has equipped you with all of these skills and many more.

We would also like to express our thanks to your supervisors and to the large number of unsung heroes who have devoted their time this year to help you learn. The Course would not be possible without them. We are also very grateful to the large number of examiners who willingly volunteer their time every year to assess the oral and poster presentations, literature reviews and theses. Thank you also to the MRSS committee, particularly your BMedSc(Hons) Chairperson Stephanie Davies. Stephanie has worked hard to organize information nights and to feed back your questions and comments, helping to improve your own experience as well as that of future cohorts.

On behalf of the BMedSc(Hons) Course Management Committee, we wish you all the very best for a bright future.

Dr Megan Wallace, Director of Medical Student Research

Message from MRSS

Congratulations to the BMedSc(Hons) Class of 2018 on completing the year!

As I am sure you are all aware this is no mean feat. There have certainly been some highs and lows for all of us. You should all be proud of what you have achieved during this year, whether it was trying something new, writing a paper or just getting through that never ending workload.

The advantage of the BMedSc is that everyone’s experience is different. No two projects are the same and the outcomes even more so. The diversity of the projects in this yearbook is a testament to this.

I hope that you have all gained something unique and valuable from this year as well as a passion to answer the big questions of medicine. I am sure you will go on to do great things in the future and I wish you all the best of luck!

Stephanie Davies, BMedSc(Hons) Representative
Background

Macrophage Migration Inhibitory factor (MIF) was one of the first immune active molecules discovered in the 1960s, and while it has been shown to be associated with multiple inflammatory pathologies, the exact role of MIF in such diseases remains unclear. Despite this, MIF is known to influence several biological processes, including (but not limited to) apoptosis, inflammasome activation, autophagy/mitophagy, pattern recognition receptor signalling, cytokine activity and immune cell proliferation and migration. However, some contention regarding the role of MIF as a cytokine exists, with numerous studies pointing to CD74, CD44, chemokine receptors CXCR2 and CXCR4 being the protein’s physiological receptors. However, there are multiple aspects of MIF biology pointed toward it being an intracellularly acting protein as opposed to a traditional cytokine. The goal of this project was to determine whether MIF has a wide range of intracellular interacting partners - the MIF interactome.

Method

WT (wildtype)/Mif-/- /GFP-LC3 (cells stably expressing GFP-LC3) iBMM (immortalised bone marrow mouse macrophages) and THP-1 cells (human monocyctic cells from a patient with acute monocyctic leukaemia) were cultured. These cultured cells were stimulated in several conditions: inflammatory (lipopolysaccharide and/or nigericin), autophagy inducing (starvation, Bafilomycin A1, Torin1) and MIF-inhibiting (using a small molecular inhibitor – 4-IPP). The cells were then lysed and MIF was then immunoprecipitated out of the lysates, and the samples were either run on sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) gels (for Coomassie stain/Western blot) or sent for liquid chromatography mass spectrometry analysis.

Results

Co-immunoprecipitation (Co-IP) was successful in iBMM using RIPA buffer and abcam175189 -MIF antibody and in THP-1 cells using the Biolegend -MIF antibody/Abcam175189 -MIF antibody. Co-IP coupled Coomassie stain/Western blot analysis demonstrated NLRP3, vimentin (inconsistently) and LC3 (inconsistently) as binding partners of MIF in WT iBMM, whilst CD74 was not present. Co-IP coupled mass spectrometry analysis demonstrated 299 binding partners for MIF, with a broad array of functions. LPS was found to have an effect on the binding partners of MIF in the Co-IP coupled mass spectrometry analysis. Variation was also observed between the Co-IP coupled mass spectrometry results and the Co-IP coupled Western blots.

Conclusions

MIF is likely not a traditional cytokine, since many of the proteins with which it interacts are involved in the maintaining basic cellular functions. The binding partners of MIF may be affected by the treatments used during culturing and the MINOR THESIS BMedSc (Hons) 10 | P a g e elution protocol during the immunoprecipitation process. Further experimentation is required to determine the definitive biological role of MIF.

I decided to commence a BMedSc (Hons) year after completing Yr 4 since I thought it would be best to pursue research after completing my major exams. I chose my project since I have been interested in Rheumatology for a few years now and decided that it would be good to get a taste of what it is like to be in the specialty before committing who knows how many years of my life to it down the line! In retrospect now that the year is complete, I can firmly say that I have a greater understanding of what the specialty stands for, what the average day as a Rheumatology fellow is and what lab-based Rheumatology research is like.

In addition, I learnt several life skills, ranging from dealing with adversity and maintaining focus and determination in the face of repeated failures and challenges. It was a very transformative year and I sincerely hope that you consider taking on the challenge for yourselves!
Resolution of Hypertension with Weight Loss

Professor Wendy Brown, Centre for Obesity Research and Education, Department of Surgery, Central Clinical School, Monash University
Professor Michael Cowley, Monash Obesity and Diabetes Institute, Department of Physiology, Monash University
Dr Stephanie Simonds, Monash Obesity and Diabetes Institute, Department of Physiology, Monash University

ABSTRACT

Background
Cardiovascular disease is the leading cause of death in the world and hypertension is one of the major risk factors. Obesity, in turn, is an important risk factor for hypertension. Leptin is a hormone produced by adipocytes and is secreted in proportion to the adipose tissue mass. It is postulated that leptin contributes to the development of hypertension in people with obesity. Substantial weight loss improves obesity-related diseases and its components, including hypertension and leptin concentration. Laparoscopic adjustable gastric banding (LAGB) is a bariatric surgical procedure which may allow patients to achieve substantial weight loss. This study aims to understand the relationship between the resolution of hypertension and changes in leptin level by studying changes in a cohort who underwent LAGB surgery. The study also aims to determine the percentage of total body weight loss (%TBWL) needed for the resolution of hypertension.

Method
This was an observational study using prospectively collected data of obese patients who underwent an LAGB procedure between April 2009 and March 2010. Demographics, comorbidities, and anthropometrics, along with blood tests measuring the causes and complications of obesity as well as for gut hormone assessment were performed before surgery. Patients were reassessed, including repeating blood tests, monthly for the first 9 months, then 3-monthly until 24 months after the surgery. Radioimmunoassay was performed to determine the leptin concentration.

Results
89 patients were eligible to participate in the study, 83 of which had hypertension at baseline. There were 56 (62.92%) women and 33 (37.08%) men in this study. The mean age of all participants was 48.23±10.75 years. The mean weight loss 24 months after LAGB was 18.37±7.6% TBWL (48.73±23.51% EWL). Leptin level was reduced to 69%, from 46.19 (26.34–71.74) ng/mL to 14.31 (4.22–33.53) ng/mL, 12 months after surgery (p<0.0001). A correlation between leptin and systolic blood pressure (SBP) was seen in males without antihypertensive medications (p=0.0265). This correlation was shifted when analysing leptin and SBP in males with antihypertensive medications (p=0.0541). The median time for the resolution of hypertension was 5 months. The odds ratio for the resolution of hypertension with 22.5–25% TBWL was 2.99 (p=0.021). A higher weight loss showed an increased probability for the resolution of hypertension to occur.

Conclusions
Leptin showed no correlation with the resolution of hypertension after LAGB in all patients, but had a correlation with SBP in males with antihypertensive medications (p=0.0541). The median time for the resolution of hypertension was 5 months. The odds ratio for the resolution of hypertension with 22.5–25% TBWL was 2.99 (p=0.021). A higher weight loss showed an increased probability for the resolution of hypertension to occur.

Hi, I’m Nadya, a fourth-year medical student from Universitas Indonesia. This Honours year at Monash University is one of the best years of my life. First, I was so lucky to have the chance to work with amazing and really great (or the best) people in their fields who also happened to be really supportive and helpful during the program. These people were my supervisors and my colleagues who really inspired me a lot to do and give my best in my career in the future. Second, I got to experience both lab work (radioimmunoassay) and clinical observations (bariatric surgeries) during the program. Both were new for me and were really cool! Third, this Honours program helped me to improve not only my writing but also my presentation skill. Last, living abroad and meeting new people were really priceless experiences for me. By the end of the course, I was really amazed at what I have achieved so far. For future students, I really hope you enjoy your Honours year as much as I do. I never regret any second I spent during this Honours year because surely it was one of the best times of my life!
How can we transform primary care? Areas of improvement in trans and gender diverse primary care: Client and GP perspectives

Dr Riki Lane, Dr Chris Barton
Department of General Practice, School of Primary Health Care, Monash University

ABSTRACT

Trans, gender diverse and non-binary (TGDNB) people identify as a gender differing from what is expected of their sex assigned at birth, with various gender expressions that may not fit into the traditional gender binary. The health disparities experienced by the TGDNB community suggests this is one of the most vulnerable and marginalised groups in Australia and internationally. Primary care plays an important role in reducing these health disparities. GPs can provide specific healthcare for TGDNB clients, and also holistic care as for any other client. However, primary care for TGDNB people is not optimal, and there is a lack of in-depth research focused on primary care provision for this group in an Australian context. Evaluation of client experiences is necessary to identify possible barriers to providing high quality healthcare. GP perspectives can further facilitate identifying these barriers. A combination of perspectives can enable identifying appropriate and practical solutions, increasing positive engagement with primary healthcare for this community.

Aims
This study aimed to explore the perceived barriers to providing high quality primary care to TGDNB people, from a GP and a client perspective. The secondary aim of this study was to use these perspectives and understanding to build recommendations for overcoming these barriers.

Methods
This study consisted of semi-structured qualitative interviews with GPs and TGDNB clients, using a phenomenological approach and drawing on feminist research principles. The research plan and question schedule were developed with a TGDNB Community Advisory Group. Interviews were transcribed, and the data analysed using Braun and Clarke’s Approach to Thematic Analysis. NVivo 12 was used for data management. The resultant codes were then organised using the socio-ecological model of health provision, into three major themes: socio-structural influences, interpersonal influences and intrapersonal influences.

Results
This research found perceived barriers to providing high quality primary care on a socio-structural, interpersonal and individual level. Socio-structural influences included societal and political influences on healthcare provision, the healthcare system and related structural barriers. Interpersonal influences centred on the client-clinician relationship, and effects of a GP’s knowledge, and perceived role in providing safe primary care. Intrapersonal influences included individual characteristics of the TGDNB clients, including their diverse intersections of identities, and perceptions, knowledge, and expectations of primary care.

Conclusions
TGDNB clients had variable experiences with GPs, with many clients finding inadequate GP knowledge to be a barrier in providing comprehensive care. However, TGDNB clients stressed the importance of practicing patient-centred care, identifying that GPs could be considered safe if they were empathetic and willing to learn. GPs highlighted the importance of protecting their clients from harm, which was complicated by different perspectives of what constitutes harm. Open and honest communication is important to mediate these tensions. Other recommendations for improving care provision included increasing education for GPs, increasing funding to medical and community services for this population, and updating medical software to more accurately identify TGDNB clients. Overall, this study suggests that with structural support and education, any GP has the capacity to provide high quality care to TGDNB clients.
Interconception care in general practice: a qualitative study

Professor Danielle Mazza¹, Dr Cathy Watson¹
¹ Department of General Practice, School of Primary and Allied Health Care, Faculty of Medicine, Nursing and Health Sciences, Monash University

ABSTRACT

Background
Interconception care (ICC) aims to reduce the effect of maternal risk factors on subsequent pregnancies, particularly if a poor outcome has occurred in a first pregnancy. General practitioners (GPs) are leading providers of care for women between pregnancies yet there is a knowledge gap regarding GP understanding and experiences of ICC in the literature. To address this gap, we aimed to explore GPs’ knowledge, perspectives and experiences of ICC using qualitative interviewing.

Method
18 GPs from metropolitan Melbourne were recruited using purposeful sampling from the Monash Practice-Based Research Network (MonRen). Semi-structured telephone interviews (30 to 60 minutes) were conducted. Interviews were audio-recorded and transcribed verbatim. The software NVivo 11 was used for data management and generation of codes. Data were analysed using thematic analysis guided by the Framework Method.

Results
Participants were unfamiliar with the term ‘interconception’. Most GPs conceptualised ICC as routine care of childbearing age women as opposed to interventions aimed at improving health for a subsequent pregnancy. GPs reported some key ICC activities reflected in existing literature but described providing this care opportunistically after the scheduled postpartum visit. GPs perceived a lack of engagement in ICC from mothers with high competing demands. Participants questioned whether women prioritise health optimisation for a subsequent pregnancy whilst raising a young child. Participants attributed this absence of prioritisation on ICC by women as a result of general lack of awareness on the importance of pre-pregnancy health optimisation. GPs also reported time constraints in general practice and a lack of clarity on the content and timing of ICC as provider barriers.

Continuity of care and education materials for women and GPs were viewed as facilitators to ICC by participants.

Conclusions
Our findings indicate that GPs do not conceptualise ICC as a particular subset of their practice but rather routine opportunistic care for women. GPs also perceived many patient barriers to the delivery of ICC, including a lack of awareness on the value of pre-pregnancy care. Further research to evaluate patient perspectives on ICC may be necessary before a complex intervention to improve ICC in general practice can be developed, trialled and evaluated.

With an interest in women’s health and primary care, I decided to do a BMedSc at the Department of General Practice after completing my fourth year. I wanted to gain insight into the world of research and experience the other side of medicine after having done two years of clinical placements. From interviewing participants to using NVivo software and analysing data, I have gained valuable experience in performing qualitative research which I’d not previously encountered in medical school. I would definitely recommend the Department of General Practice to anyone considering an honours year – it is a friendly, supportive environment where everyone is willing to help you, even if they are not directly involved in your research! If anyone has any further questions, feel free to send me an email at ember2@student.monash.edu.
Comparison of a one and two-tiered trauma activation protocol at a Metropolitan Trauma Service

Nadia Bogatzke

ABSTRACT

Background
Early assessment of trauma patients in the emergency department (ED) by multi-disciplinary teams has improved patient outcomes. Trauma teams are triggered when patients meet defined physiological, injury pattern or mechanism of injury (MOI) criteria. However, trauma team activations are resource intensive. Research at major trauma services report that two-tiered trauma responses reduce resource consumption without adversely affecting patient outcomes. Smaller ED-based teams manage physiologically stable patients with MOI criteria, as this subgroup is low risk for major trauma. The safety of a two-tiered trauma response at a level two, Metropolitan Trauma Service (MeTS) is unproven.

Study Aim
To determine if the safety of a two-tiered trauma response at a Melbourne MeTS is non-inferior to a one-tiered system.

Methodology
An observational, non-inferiority study was conducted at Dandenong Hospital, a MeTS within the Victorian State Trauma System. Outcomes during a retrospective one-tier period (1 June to 12 August 2017) were compared with a prospective two-tier period (1 June to 12 August 2018). Patients triggering a Trauma Call in the one-tier period, and a Trauma Call (first-tier) or Trauma Alert (second-tier) during the two-tier period were included; performance and timing of a CT scan was noted. The primary outcome measure was time to CT scan (TtCT). This was chosen as safety relies on timely diagnosis, and diagnosis is confirmed on CT. Non-inferiority required the upper 95% confidence limit of the mean TtCT in the two-tier period to be <30 minutes longer than the mean TtCT in the one-tier period. Secondary outcomes including length of stay (LOS) and disposition from ED were compared between periods, and between the Trauma Call and Trauma Alert subgroups of the two-tier period. The primary comparison of mean TtCT included only patients who had a CT scan; baseline data and most secondary outcomes compared all Trauma Response patients from both periods.

Results
Of the 140 and 172 eligible patients from 2017 and 2018, 61% [95%CI: 53-70] and 55% [95%CI: 48-63] were male; mean ages were 37 (95%CI: 34-40) and 41 (95%CI: 38-44) years. The mean TtCT for the 100 patients who had a CT scan in each period were 146 (95%CI: 135-157) and 154 (95%CI: 140-168) minutes respectively. The upper 95% confidence limit in 2018 was <30 minutes longer than the mean TtCT in 2017, meeting the a priori definition for non-inferiority. From 2017 to 2018, ED LOS was non-significantly reduced (6.6 [95%CI: 5.9-7.4] to 5.8 [95%CI: 5.1-6.6] hours), as was that for admitted patients (15.7 [IQR 5.4 – 36.8] to 6.5 [IQR 2.9 – 31.0] hours). The discharge rate was similar between periods (30% [95%CI: 23-38] vs 38% [95%CI: 30-45] respectively), but from 2017 to 2018 the Short Stay Unit (SSU) admission rate increased significantly (28% [95%CI: 19-39] vs 53% [95%CI: 43-63], p<0.01) while the inpatient ward admission rate decreased significantly (88% [95%CI: 58-78] vs 45% [95%CI: 35-55]).

Conclusions
At a Melbourne MeTS, the safety of a new two-tiered trauma response system was non-inferior to the previous one-tiered system. Apparent LOS benefits warrant further investigation.
Decisions about withdrawal of life support for infants are predominantly made through consensus between physicians and parents. Occasionally, disagreement results in controversial legal battles. Medico-legal precedent is for withdrawal of treatment only if it is in the best interests of the child, and the burdens of life outweigh the benefits. However, it is unclear how we evaluate when life is no longer worth living for an infant, and public attitudes towards treatment withdrawal and the role of parents in decision-making have not previously been assessed.

Aims
The empirical component of this study aims to assess public attitudes towards when life is no longer worth living for an infant, and whether this justifies treatment withdrawal. The ethical analysis aims to evaluate these public views in comparison to key principles within the bioethical discourse.

Methods
An online survey was conducted with a sample of the UK public (n=130). Participants were asked to judge the benefit of life for seriously ill infants in a series of case scenarios, as well as their views on treatment withdrawal and the role of parents in decision-making. Statistical analysis was conducted on IBM SPSS Statistics version 25 for Mac. The null hypothesis was rejected at p<0.05. The data gathered was compared against ethical principles identified in the literature review.

Results
The majority of participants agreed that at a certain level of wellbeing, an infant’s life may have no benefit (93.8%) or be worse than death for the infant (87.7%). This belief varied significantly between cases: for the most severe case, 89.2% of participants did not believe life was of benefit, while for the least severe case, 13.9% of participants did not believe life was of benefit. Participants seemed to place most value on the objective goods of awareness and capacity for basic relationships when making this judgement. A significant proportion of participants in each case (up to 50%) believed it was permissible to continue or withdraw treatment for each case. Participants were reluctant to disagree with parents being allowed to continue treatment indefinitely for their child: in 5 of 6 cases, a majority of participants believed parental autonomy should be allowed.

Conclusion
Despite the controversy generated by similar legal cases and quality of life judgements, our findings indicate that there is a level at which most people reach consensus that life is not worth living: one where cognition is so limited that the infant has no awareness of themselves or their surroundings, even if suffering is minimal. The defining feature of a life that the majority believed to be worth living was a level of cognition that allows for basic relationships and a small chance of future communication. Significant support for permissible withdrawal of treatment (where it is not morally obligatory to either withdraw or continue) in the most divisive cases as well as prioritisation of parental autonomy may be useful when constructing robust guidelines for clinical practice. Further research is needed to ensure reproducibility and to investigate more specifically the factors behind these beliefs.
Evaluating the impact of pneumococcal conjugate vaccine against paediatric pneumonia and empyema in children

Main supervisor: Angela M McCullagh 1
Co-supervisor: Rosemary SC Horne 2

1 Monash Children’s Hospital, Melbourne, Australia
2 The Ritchie Centre, Department of Paediatrics, Monash University and Hudson Institute of Medical Research, Melbourne, Australia

Abstract

Introduction
Pneumonia is a lung infection that can be complicated by empyema, defined grossly as pus in the pleural space. Pneumonia is most commonly caused by Streptococcus pneumoniae.

Pneumococcal conjugate vaccines (PCV) have been used to decrease the burden of these diseases. After the introduction of PCV7 in 2001, paediatric pneumonia rates decreased, however empyema rates paradoxically increased. This was due to “serotype replacement”, where non-vaccine serotypes became more prevalent and were more likely to progress to empyema. To address this, PCV13 was released in 2011.

The aim of this study was firstly, to identify the bacterial aetiologies and S. pneumoniae serotype prevalence in pneumonia and empyema patients after the introduction of PCV13. Secondly, we aimed to identify patient factors which could predict the development of empyema in children.

Methods
63 pneumonia and 44 empyema patients were prospectively recruited from Monash Children’s Hospital between November 2015 – July 2018. These groups were compared with respect to demographic and clinical features and underlying bacterial aetiologies.

Nasopharyngeal swabs, blood and pleural fluid were tested for underlying bacterial aetiologies using PCR and cultures. Pneumococcus positive samples were then serotyped. Demographic and clinical factors were compared between the groups.

Serotype prevalence was compared with the serotype prevalence prior to PCV13 introduction (Strachan, 2011).

Results
S. pneumoniae was the most commonly identified pathogen in the entire population (41.1%). Furthermore, infections more associated with empyema included S. pneumoniae (68.2% vs. 22.2%; p<0.05), S. pyogenes (22.7% vs. 0.0%; p<0.05) and a viral co-infection (17.5% vs 36.4%; p=0.047).

PCV13 serotypes 19A (2.3%) and 3 (41.9%) were still identified. The proportion of serotypes 1 and 19A have fallen significantly since PCV13 introduction, however the prevalence of serotype 3 has not changed.

In a multivariate analysis, S. pneumoniae (OR 19.5; 95% CI 4.3-88.9), CRP on admission over 120mg/L (OR 8.45; 95% CI 2.1- 33.4) and use of ibuprofen during hospital admission (OR 9.81; 95% CI 1.2-76.7) were predictors for empyema.

Conclusions
PCV13 appears to be effective at against caused by serotype 1 and 19A, however is ineffective against serotype 3.

Clinical predictors for the development of empyema from pneumonia include S. pneumoniae, CRP >120mg/L on admission, and use of ibuprofen during hospital stay.
Daniel Chepurin

Bony Stress in the Lumbar Spine

Dr Ashish Diwan: St George & Sutherland Hospital Clinical School
Dr Uphar Chamoli: St George & Sutherland Hospital Clinical School
Dr David Scott: School of Clinical Sciences Monash University

ABSTRACT

Background
The lumbar spine motion segment has multiple components that interact during normal and pathological function. Bony stress in the lumbar spine is recognised as a factor in the process of pars defects and stress fractures in the lumbar spine, but its prevalence and relationship with intervertebral disc degeneration and other pathology is not well understood.

The primary aim of this project was to explore the relationship between bony stress in the lumbar spine and disc degeneration. Secondary outcomes include prevalence of bony stress, facet osteoarthritis, lower back pain and anatomical parameters.

Method
Data were collected from a sample of patients under the age of 25 who had a lumbar MRI conducted at three radiology centres between March 2015 and March 2018. All patients (n=493) had their images screened for bony stress. Association between outcomes of interest were assessed using two case-control studies; the first study had one control group of patients without bony stress (n=75), and the second study had two age and sex-matched control groups; one with disc degeneration (n=51) and the other without disc degeneration (n=51). Images for all cases were retrospectively examined for disc degeneration, lumbar anatomical parameters and other pathology. Radiology reports were also read for the indication for MRI. The groups were analysed using Pearson’s Chi Square and logistic regression, and risks were estimated as odds ratios.

Results
Bony stress was visible on MRI in 11% (55/493) (95% CI [8.4% - 14.5%]) patients. Bony stress was missed on routine assessment by radiologists in 36% (20/55) (95%CI [22.2% - 54.7%]) of cases.

The odds of disc degeneration being present among patients with bony stress was 2.3 times higher than in patients without bony stress (OR 2.3 (95% CI [1.1 - 4.8]). The odds of pain being an indication for MRI among patients with bony stress was 5.3 times higher than in patients without bony stress (OR 5.3 95% CI [2.11 – 13.3]). Facet osteoarthritis was not significantly associated with bony stress (p=.07). There were no clinically substantial differences in anatomical parameters between bony stress patients and control patients.

Conclusions
These findings suggest there is an associative relationship between bony stress in the lumbar spine and intervertebral disc degeneration and pain as an indication for MRI. Bony stress is likely to be undiagnosed in many cases which may have clinical consequences given it may be a cause of cryptogenic lower back pain. Further temporal studies need to be conducted to clarify the cause and effect of bony stress on lumbar pathology.

I started the BMedSc year after completing year 4C of the MBBS for a number of reasons. I was incredibly lucky to have been given the opportunity to conduct the year back home, in Sydney, with some of the most supportive and helpful supervisors. Of course, the chance to spend a whole year doing work in the field that I wanted, being able to control which path my work went down and seeing results from the whole journey was amazing for me to experience. Overcoming constant challenges, like teaching myself statistics from scratch in a very small time-frame, and balancing self-motivation throughout the year can only be described as fun.

Throughout a lot of school and university, you come across many topics that make you question whether you will ever actually need or use this. After finishing this year I can confidently say that I will use the skills I’ve learnt this year for the rest of my career. This year transformed my mindset from being a university student to being part of a medical team, and I believe it’s set me up to launch into a medical career very well.

I

ABSTRACT

Background

Method

Results

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I started the BMedSc year after completing year 4C of the MBBS for a number of reasons. I was incredibly lucky to have been given the opportunity to conduct the year back home, in Sydney, with some of the most supportive and helpful supervisors. Of course, the chance to spend a whole year doing work in the field that I wanted, being able to control which path my work went down and seeing results from the whole journey was amazing for me to experience. Overcoming constant challenges, like teaching myself statistics from scratch in a very small time-frame, and balancing self-motivation throughout the year can only be described as fun.

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Determining the Surface Levels of the Thrombin Receptor, PAR4, on Human Platelets

A/P Justin Hamilton, Australian Centre for Blood Disease (ACBD), Monash University
Dr Shauna French, Australian Centre for Blood Disease (ACBD), Monash University

ABSTRACT

Background & Aim
Cardiovascular disease (CVD) is the major cause of death in the world. The most common manifestations of CVD are myocardial infarction and stroke, both of which are caused by formation of platelet-rich thrombi in major arteries. Due to the poor efficacy of current treatment options, potential new therapeutic targets are being examined. The examples of these targets are the protease activated receptors (PARs), PAR1 and PAR4. Vorapaxar is the only clinically approved drug that targeting PAR1. However, Vorapaxar has limited clinical utility due to a high risk of bleeding. Therefore, PAR4 has recently become a prime target for the development of novel anti-thrombotic therapies. One potential limitation in developing robust PAR4 antagonists is the existence of a single nucleotide polymorphism (SNP) in PAR4 (rs773902) that impairs the efficacy of existing antagonists. PAR4 can either have an alanine or threonine at amino acid position 120 (Ala120 or Thr120) and the Thr120 sequence variant has increased sensitivity to agonists and decreased sensitivity to antagonists. The mechanism underlying this altered PAR4 function is unknown. In order to address this, this study investigated whether there is a correlation between rs773902 genotype and the absolute number of PAR4 on the platelet surface.

Method
PAR4 surface level expression was measured by quantitative flow cytometry on the platelets of 49 individuals, which were subsequently genotyped rs773902 using a Taqman SNP genotyping assay.

Results
The average number of PAR4 on the human platelet surface was 1093 ± 63 receptors/platelet. Importantly, individuals expressing the Thr120 PAR4 sequence variant had significantly more PAR4 on their platelets (1799 ± 378) than either of those expressing the Ala120 PAR4 sequence variant (1010 ± 64) or heterozygous individuals (1065 ± 89).

Conclusions
This study is the first to quantify platelet PAR4 expression level. These findings may explain the altered receptor sensitivity to agonists and antagonists of the Thr120 PAR4 variant and may therefore be an important consideration for any future efforts to target PAR4 for anti-platelet drug therapy.
Isabelle Claxton

Pre- and Post-Migration Factors Associated with Resilience Among Refugees in Australia

Prof Grant Russell, Department of General Practice, School of Primary Healthcare, Monash University
Dr Joanne Enticott, Department of General Practice, School of Primary Healthcare, Monash University

ABSTRACT

Background
Australia’s refugee and asylum seeker population is a vulnerable population at risk of both physical and mental health issues. Current refugee mental health research has focussed on risk factors for mental illness, and mental health assessment and intervention methods. Despite over 90% of refugees reporting exposure to trauma, about 50% of refugees develop mental illness. This means that 50% remain mentally healthy, exhibiting resilience in the face of potentially traumatic events. We examined the pre- and post-migration factors that are associated with resilience among refugees.

Method
We used the first three waves of data from the Building a New Life in Australia (BNLA) study, an ongoing, nationwide, longitudinal study conducted by the Australian Institute of Family Studies. The first wave of data collection included 2399 refugees aged 15 and over, who were granted permanent humanitarian visas between May and December 2013. The three data waves used in this study were collected between October and March of 2013-14, 2014-15 and 2015-16. Resilience in this study was defined as Kessler-6 and Post-traumatic Stress Disorder 8 items within normal limits in all three waves of data.

Results
30.0% of refugee participants demonstrated resilience and 37.1% of refugee families contained members who all demonstrated resilience. Financial hardship has the greatest influence on odds of resilience in individuals and families, with an OR of 0.333 (95% CI 0.267-0.415) among individuals and 0.396 (95% CI 0.329-0.478) among families for 3-6 financial hardships per day compared to no financial hardships per day. Long-term disability or illness (OR 0.408 for individuals and 0.493 for families) and exposure to trauma pre-migration (OR 0.476 for individuals and 0.497 for families) also had significant influence on the odds of resilience.

Discussion
This study is the first to examine resilience among refugees, determined by those refugees with K6 and PTSD-8 results below the clinical threshold in each wave of the BNLA data. Our study differs from previous studies in refugee mental health as we have used a longitudinal dataset of a large, nationally-representative sample of refugees. We found several factors that significantly influence refugees’ odds of demonstrating resilience. While some factors are fixed and cannot be altered to increase resilience, we have identified other factors that can be modified to promote resilience. We are also able to compare the relative effect that each factor has on resilience, so can determine which factors have the greatest influence on refugees’ mental health outcomes.

In the future, these predictors of resilience represent targets for intervention that can be used to assist refugees to maintain good mental health.

I finished fourth year last year and decided to do a BMedSc (Hons) project as a chance to not only learn some research skills, but also to explore an area that’s been an interest of mine for a while: refugee health. It’s not too often you get the chance to focus solely on one topic and learn about it in great detail, and this year has provided the opportunity to do so. Not only have I learned how to conduct literature searches, use data analysis software and write a scientific thesis and paper, but I have also learned more about refugees and refugee health than I ever expected I would.

Doing my project at the Department of General Practice has been great, as I had access to many researchers, not just my two supervisors, for advice. Working with such a supportive team, I have discovered my interest in research and in the future, I hope to do further research as part of a Master of Public Health.
ABSTRACT

Background
Oesophageal atresia (OA) is a life-threatening congenital disease which affects 1 in 3500 children. There are five main sub-types (Gross classification: Type A – Type E). Oesophageal atresia is diagnosed on the first days of life with surgical repair occurring on an emergency basis. Improvements in treatment have increased survival, which has changed the focus to morbidity management. Dysphagia, gastro-oesophageal reflux disease (GORD), oesophageal dysmotility, as well as, quality of life (QoL), are the main areas of interest in current OA research.

Method
Patients with repaired OA were identified from The Royal Children’s Hospital OA database. Eligibility criteria included type C OA children who had undergone surgical repair and whose parents consented to the study.

Data on their demographics, previous admissions and interventions were organised in a Microsoft Excel 2016 (Washington State, USA) spreadsheet. High resolution impedance manometry (HRIM) was performed with an 8-French solid-state catheter with 32 pressure sensors, inserted from a nostril, through the oesophagus into the stomach. Children swallowed a minimum of five 5mL sips of Standardised Bolus Media (SBM) solution IDDIS4 (thin solution) and five 5mL sips of SBM IDDIS4 solution (extremely thick solution). The catheter registered pressures in the oesophagus and plotted them in topography-pressure plots. Images were then stored for further analysis and the catheters were sterilised. The child’s dysphagia symptomatology questionnaire (Dakkak) was completed by the parents.

Oesophageal manometry analysis was performed using AIMplot software (Flinders University, Adelaide). Dakkak symptomatology analysis was performed with Microsoft Excel 2016 (Washington State, USA) and GraphPad Prisma 7 (California, USA). Studies were compared with 17 retrospective HRIM studies of children investigated for suspected GORD without a history of OA repair. A review of the literature was performed to evaluate the effects of radiation in children with OA, as well as the standardised imaging regimens currently being utilised.

Results
Forty-one children with type C OA were contacted; 17 patients underwent oesophageal manometry. Ten patients were male and 7 were female (age: 3 months to 3.5 years old).

Manometric assessments demonstrated three motility patterns: distal contraction pattern, aperistalsis, and pressurisation. No statistically significant correlation was found between oesophageal motility type and Dakkak questionnaire score (p = 0.44).

Children with OA had less effective oesophageal body peristalsis and bolus clearance than controls. No statistically significant difference in lower oesophageal sphincter relaxation was found.

Radiological imaging currently performed exposes children with OA to a higher amount of radiation dose than the general population, putting them at an estimated 130-fold increased cancer risk.

Conclusions
Children born with OA demonstrated objective oesophageal dysmotility, with less effective oesophageal contractions and bolus transport than patients with GORD. Information about oesophageal motility, reflux and appropriate diet was gained with HRIM. No guidelines regarding standardised follow-up regime for children born with OA and recommended maximum radiation exposure exist.
Identification of novel bacterial species in paediatric inflammatory bowel disease through direct mucosal sampling.

Gemma D’Adamo

ABSTRACT

Background

Inflammatory bowel disease (IBD) is a chronic, incurable inflammatory condition, comprised of Crohn's Disease (CD) and Ulcerative Colitis (UC). The manifestation of IBD during childhood (paediatric IBD; PIBD) ensures that genetic variants predispose to immune dysregulation, in response to environmental triggers and microbial factors.

Methods

Mucosal samples were collected from 38 PIBD patients during endoscopy at Monash Children’s Hospital. Biopsies were taken from three colonic regions (Terminal Ileum, Caecum and Rectum) and cultured using YCFA culturing techniques. Taxonomic classification of isolates was based off partial-length 16S rRNA sequences. Additionally, mucosal-associated inflammatory responses were investigated, through assessment of 12 genes (IL6, IL8, IL12, IL17A, IL17F, IL23, CXCL10, TNF-α, STAT3, TREM1, EPCAM, IFN-γ). Correlations between the inflammatory cascades initiated and microbiota present were identified to detect novel therapeutic candidates.

Results

Mucosal samples were collected from 38 patients, across three colonic regions (RNA analysis: 95 samples, microbial analysis: 107 samples). The cohort comprised a roughly equal distribution of males (52.6%) and females (47.4%); however, most patients were 11-18 years of age (65.8%), and Caucasian (57.9%). Additionally, most samples were histologically non-inflamed (69.5%). Culturing allowed 1748 bacterial isolates to be picked, which generated 1209 high-quality sequences. We identified 415 known and 325 putative novel species. Enrichment and depletion analyses were performed and correlated with the strength of inflammatory responses initiated, which identified four therapeutic candidates. Future functional characterisation and experimental validation of these candidates will be required to assess their potential roles in disease exacerbation and control.

Conclusions

We applied novel YCFA1 culturing techniques to culture the mucosal-associated microbiota from PIBD patients for the first time. A significant number of known and novel species were cultured, and several therapeutic candidates for future functional characterisation were identified. This workflow should enable characterisation of microbial signatures implicated in the pathogenesis of PIBD, and various intestinal and extra-intestinal diseases, thereby permitting translation to other conditions.
Antiepileptic drugs (AEDs) are key causes of cutaneous adverse drug reactions (ADRs), which are categorised as type IV hypersensitivity reactions and mediated by T cells. Cutaneous ADRs range from mild, maculopapular exanthema (MPE), to severe, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The mild reactions are characterised by a rash, which may extend to organ involvement in drug reaction with eosinophilia and systemic symptoms (DRESS). The severe reactions (SJS/TEN) are characterised by epidermal detachment and significant morbidity and mortality.

Carbamazepine is the AED most strongly associated with cutaneous ADRs. The mechanism proposed for the presentation of carbamazepine to T cells is via pharmacological interaction of the drug with the immune receptors, known as the p-i concept. This interaction is non-covalent and labile. Associations have been made between cutaneous ADRs and human leukocyte antigen (HLA) molecules, which are responsible for presenting peptides to T cell receptors (TCRs) for T cell activation. The most established correlations are HLA-B*15:02 with carbamazepine-induced SJS/TEN and HLA-A*31:01 with carbamazepine-induced MPE.

MPE is not as well characterised as the severe reactions and the association with HLA-A*31:01 is not as strong as HLA-B*15:02 with SJS/TEN. This project hypothesised that specific AED-responsive TCRs may also be associated with MPE. The aims were to i) characterise drug-specific T cell responses in MPE patients, ii) investigate cross-reactivity between structurally similar AEDs and iii) identify the associated TCR signatures.

In this study I was able recapitulate carbamazepine-induced immune reactions T cell responses in HLA-A*31:01+ drug hypersensitive patients who had exhibited MPE as well as drug-naive HLA-A*31:01+ individuals. Additionally, carbamazepine-induced T cell responses were also observed in individuals with HLA alleles from the wider HLA-A19 subgroup. This novel observation suggests that drug hypersensitivity may also extend beyond HLA-A*31:01 to other members of the HLA-A19 supertype.

T cell cross-reactivity between carbamazepine and other structurally related molecules (ECBZ and oxcarbazepine) was observed, supporting current findings in the literature. Additionally an incidence of cross-reactivity between carbamazepine and lamotrigine was also observed.

Lastly variable polyclonal T cell responses were observed in most MPE patients. A clonal T cell response from carbamazepine-specific TCR clonotypes was observed in one MPE patient. The clonotypes identified were patient-specific but appeared to be cross-reactive between HLA-molecules. This suggests a private TCR response occurs in individuals with MPE.

The findings of this study corroborate previous reports of HLA association and cross-reactivity. It also provides areas for further exploration of the mechanisms underlying carbamazepine-induced MPE, namely the possibility of an association with the HLA-A19 subgroup and alternative mechanisms for activation of T cell responses namely direct interaction of the drug-TCR interaction.
ABSTRACT

Background
Abortion is sometimes restricted by law beyond the point when fetuses are ‘viable’. However, viability is poorly defined and relies on access to technologies which vary temporally and geographically. Moreover, new technologies such as ectogestation—a way of extending gestation using an artificial womb—may improve outcomes for extremely premature infants who would be non-viable without this technology. Ectogestation thus appears to shift the borderline of viability. This raises questions as to whether ectogestation should impact on access to abortion.

Aims
The aim of this study was to combine empirical results with ethical analysis to investigate whether by shifting the gestational age of viability, ectogestation should result in changes in access to abortion.

Methods
Two principle methods have been adopted: theoretical analysis of ethical issues and a survey of doctors on their views and practices with regards to management at the borderline of viability.

The ethical analysis sought to explore the key arguments linking ectogestation, viability and abortion, to determine whether ectogestation should lead to changes in access to abortion.

The online survey involved consultants and fellows in obstetrics or neonatology working in Victorian tertiary hospitals who were recruited via a ‘snowballing’ technique. They were presented hypothetical scenarios relating to extremely premature labour in the light of current technology and ectogestation, before being asked about the appropriateness of abortion, Caesarean section, resuscitation and non-resuscitation, and to respond to general questions about abortion, ectogestation and the nature of viability. Results were presented descriptively and statistical analysis (using Chi-square and t tests) was adopted to compare the views of doctors who work in obstetrics and neonatology.

Results
The ethical analysis found consistency (treating ‘like’ cases like) to be the best argument in support of restricting abortion post-viability. However, a woman’s autonomy represents a morally significant difference between a fetus and infant that justifies different treatment.

Ninety-one doctors completed the survey (response rate 64%). When asked directly, 69% of doctors said that viability related to the possibility of survival at a particular gestation, however they did not apply this definition: 69% of neonatologists and 89% of obstetricians did not believe that a 22+3-week infant was viable, even though survival is possible at this gestation. Surveyed doctors believed that ectogestation would shift the gestational age of viability (88% agreeing that an infant is viable with ectogestation at 22+3 weeks). Over half (55%) of respondents neither agreed nor disagreed that ectogestation should become common practice. Forty-one percent of respondents agreed that this technology would influence their views on termination of pregnancy, while 48% disagreed.

Conclusion
I conclude that ectogestation does not warrant changes in access to abortion. However, this does not exclude other reasons for limiting abortion after a certain gestation as a compromise. Surveyed doctors agreed that ectogestation will alter the point of fetal viability (a conclusion that I independently reached) however, there was contention as to whether access to abortion should be limited beyond viability. Qualitative studies are needed to determine the reasons behind such contrasting views.
Background
Cerebral palsy (CP) is a permanent, non-progressive motor disorder that can result from brain injury during the perinatal period. It is a complex disorder that often causes low quality of life in the patients. One of the most easily identifiable causes of CP is hypoxic ischemic encephalopathy (HIE). HIE is a brain injury due to severe acute deprivation of oxygen in infants around the time of birth. It affects 2 to 3 out of 1000 live births in the developed countries. HIE can lead to either postnatal death or in surviving patients, permanent neurophysiological disabilities. The key point of HIE treatment is to reduce inevitable brain inflammation and restore functional brain structures. The only treatment available for HIE is therapeutic hypothermia which principally reduces body temperature of infants to delay the disease progression. However, it is found to be ineffective in the majority of patients.

Recently, the use of mesenchymal stem cells (MSCs) has been proposed as a new treatment for HIE and CP. MSCs treatment has already been shown to be beneficial to treat adult brain injury. MSCs can be collected from many sources, and MSCs have been found to be safe in both preterm and term animal models. However, the way to maximize the potency of MSCs and their mechanism of actions in HIE, remain unclear. Our study aimed to reveal the therapeutic benefits of MSCs therapy in treating HIE. Moreover, our project explored the potential of human umbilical cord tissue-derived MSCs (UC-MSCs) and intranasal administration route, both of which have not been tested yet.

Method
In this project, we isolated MSCs from human umbilical cord tissue collected from consented term cesarean section deliveries. Hypoxic-ischemic (HI) injury was performed using postnatal day 10 rat pups through permanent ligation of their left carotid artery, followed by a hypoxic challenge at 8% oxygen for 90 minutes. Seven days later, negative geotaxis test to analyse their behaviour was performed, followed by post mortems to collect brains for histological analysis and immunohistochemistry for detection of neurons, microglia, and astrocytes, cell tracking.

Results
We found the brains were smaller and had less number of neurons in the hippocampus after HI injury. Administration of UC-MSCs significantly increased the brain mass and neuronal cells in the hippocampus. Furthermore, we found that HI exaggerated brain inflammation. The improvement of brain inflammation was detected through significant reduction of astrocytes and microglial counts in the hippocampus after UC-MSCs treatment.

Conclusions
In conclusion, this study demonstrated that UC-MSCs treatment improved brain injury following HI by restoring neuronal cell numbers and reducing brain inflammation in the hippocampal area. Further improvements are needed to advance the limitations in this study including the small sample number, the histological cutting method, and the use of an unstable cell tracking marker. Future studies also need to include more complex behavioural studies, other brain areas for histological analysis, cytokine analysis, and test different UC-MSCs administration dosages, times, and routes. Finally, we have shown that UC-MSCs have potential as a therapy for HIE during neonatal period.
Short- and Long-term Outcomes Following an In-hospital Cardiac Arrest

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ABSTRACT

Background
The rate of event survival and survival to hospital discharge following an in-hospital cardiac arrest (IHCA) is poor, worldwide and in Australia. Worldwide there is little data about survival outcomes beyond hospital discharge and even less in the Australian context. Many factors relating to the patient and the arrest have been previously shown to positively or negatively influence survival at different points, unfortunately little investigation has been done into how these factors influence survival beyond hospital discharge. This study aimed to measure survival outcomes following IHCA in the short (event survival and survival to hospital discharge) and long-term (survival beyond hospital discharge) and investigate how patient and arrest factors may influence outcomes.

Method
single-centre retrospective longitudinal study was done of all adult patients (aged 20 years and over) who had a cardiac arrest inside the Bendigo Hospital between the 1 February 2000 and 31 December 2017. Patient and arrest data were sourced from the existing hospital’s Code Blue Database. Long-term survival outcomes were ascertained by linking the hospital data to the death data in the Victorian Death Registry on the 31 January 2018. All patient and arrest variables were included in multivariate logistic regression to determine adjusted association with survival of the event and survival to hospital discharge. A Cox regression including all variables then determined associations with long-term survival. Finally, the long-term survival of all patients that survived to hospital discharge was compared to that of a standard Australian population matched on age and sex.

Results
A total of 682 patients were included in the analysis, the median age was 73.01 years and 59% were males. Twenty six per cent of arrests were of a shockable type (Ventricular Fibrillation or Ventricular Tachycardia) and the median duration of resuscitation was 10 minutes. Fifty four per cent of patients survived the cardiac arrest and 32% survived to hospital discharge. Shockable rhythms and arrests that occurred in recent years were independently associated with an increased rate of survival to hospital discharge as were arrests occurring in the Emergency Department. An increasing resuscitation duration and the patient having a not for resuscitation order were associated with a decreased rate of survival to discharge. When compared to the standard Australian population cohort, the annual risk of death was significantly higher for the first three years-post arrest for the IHCA group. Beyond this time there was no significant difference in mortality. Younger age was independently associated with a decreased hazard of death whereas cardiac rhythm, being Ventricular Tachycardia or Pulseless Electrical Activity, and increasing resuscitation duration were associated with an increased hazard of death in the Cox regression analysis.

Conclusions
Around half of patients who suffer an IHCA survive the event and around a third survive to hospital discharge. Over time the impact of the arrest on survival decreases. This is the first ever Australian study to investigate IHCA survival beyond 1-year post arrest and has the longest patient follow-up period following the arrest in the literature worldwide.
ABSTRACT

Background
Generating an artificial immune response by against glioblastoma by administering vaccines stimulating CD8+ T-cells to generate tumoricidal cytotoxic T-lymphocytes (CTLs) could improve tumour clearance. Vaccines have been trialled in the GL261 model of glioblastoma, syngeneic to C57BL/6 strain of mice. Whole GL261 vaccine with alpha-galactosylceramide (aGC) produced protective effect, yet this intravenous formulation produced some toxicity requiring reformulation. Alternatively, bioinformatics pipeline approaches have identified targeted GL261 neoantigens which could be used alongside nanoparticle-based adjuvant (nanovax) capable of producing peptide-specific CD8+ T-cell responses. Our group has also derived CD4+ T-cell epitopes (long peptides) which could also be used. Ultimately, the immunogenicity of these neoantigens is unknown and requires evaluation. To evaluate the potential efficacy of these vaccines, we had three aims:

1. To develop an immunogenic vaccine against GL261.
2. To evaluate subcutaneous and intracranial GL261 tumour growth kinetics, calibrating anti-tumour effect.
3. To develop an immunogenic vaccine based formulation produced some toxicity requiring reformulation.

Method
We performed IFN- enzyme linked immunosorbent spot (ELISpot) to determine systemic immunogenicity of neoantigens based vaccine formulations. To confirm irradiation inactivated GL261s, we irradiated GL261 samples to 150Gy, and evaluated growth in vitro, ensuring that 150Gy irradiated cells could be used in vaccine formulations. Following these experiments, immunogenic and theoretically functional vaccines were formulated. To test the protective effects of these vaccines, we optimised a subcutaneous model of GL261 to test vaccine formulations. Finally, we performed prophylactic vaccination experiment, vaccinating mice 7 day prior to implanting subcutaneous GL261 per optimised model, to evaluate the protective effect of vaccine.

Results
To formulate vaccines, we first confirmed immunogenic neoantigens of greatest immunogenicity. Greatest immunogenicity was observed when pool of longer CD4+ T-cell epitopes (long peptides) were administered with nanovax. In particular, greatest CD8+ T-cell response was observed upon administration of CD4+ T-cell epitope peptide 4, which showed largest response upon re-stimulation with CD8+ T-cell restricted epitope of peptide 10. Therefore, long peptide pool and peptide 4 would be useful vaccines to trial. 150Gy irradiated GL261s were definitively inactivated in vitro and could therefore also be formulated into vaccines for use.

Having identified useful formulations (long peptides, peptide 4, and 150Gy irradiated GL261s), we optimised a subcutaneous (SC) model of GL261. We found that 1x10^6 live GL261 administered subcutaneously generated tumours reliably and in a workable 20-day time frame, in C57BL/6 mice.

We then evaluated the prophylactic protective effect of these vaccines, observing prophylactic vaccination with irradiated GL261s (with or without aGC) produced statistically smaller tumours (p<0.0001) as compared to vaccine naïve mice. Long peptides pool produced no significant effect, but single peptide 4 did show statistically smaller tumours (p=0.0001). Nonetheless, survival was only observed to be superior in mice prophylactically vaccinated with irradiated GL261s (with or without aGC).

Conclusions
Our study demonstrated the systemic immunogenicity of neoantigens peptides in combination with nanovax adjuvant. Furthermore, we observed intradermal irradiated GL261 (with or without aGC) produced protection against growing SC GL261, but protection not clearly conferred by single peptide vaccine. This gives insight into the formulation of vaccines against glioblastoma.
Nic Ensor

Negative Pressure Wound Therapy in Pilonidal Surgery (N-PIPS): A Multicentre Randomised Controlled Trial
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Mr Maurizio Pacilli – Monash Children’s Hospital, Monash University

ABSTRACT

Background
Pilonidal sinus disease (PSD) is a localised inflammatory reaction secondary to the implantation of loose hair within the intergluteal (natal) cleft. Surgical excision with off-midline primary closure is the most accepted definitive treatment method. However, it is limited by high rates of postoperative wound complications, namely surgical wound dehiscence (SWD). Negative pressure wound therapy (NPWT) reduces rates of SWD in other high-risk wounds, though it has not previously been investigated for closed PSD excisions.

Aim
Our primary aim was to investigate whether the use of a NPWT dressing (versus a conventional passive (CP) dressing) reduces the rate of SWD for primarily closed PSD excisions. Our secondary aims were to establish whether NPWT improves wound healing, short-term recurrence rates, patient quality of life (QoL) and the time taken return to normal activities.

Method
A prospective, multicentre randomised controlled trial (RCT) was conducted at 3 Australian hospitals. Patients, aged 12-40 years, with primary PSD requiring excision with primary off-midline closure were eligible for this study. The sample size of 100 patients was powered to detect a 35% reduction in SWD (power=0.9, significance=0.05). Patients were randomised by computer minimisation to receive a CP (PrimaporeTM or OpsiteTM) or NPWT (SNAPTM) dressing. Patients were followed-up on postoperative days 3, 7, 10, 14, and then weekly until wound healing. Data was collected on: the time to wound healing, analgesia utilisation, SWD, surgical site infection (SSI), and return to normal activity. De-identified photographs were taken of the dehisced wounds and classified as superficial (depth<5mm) or deep (depth≥5mm). Patients were followed-up at 2-months postoperatively with an online survey to assess: time taken to wound healing, time taken to return to normal activity, postoperative pain, patient satisfaction, and overall health. Patients will be followed up at 6-months to screen for short-term PSD recurrence.

Results
At this interim analysis, 13 patients were recruited into the study. 10 patients received surgical treatment and were randomised; there were 5 patients in each group. Six patients completed the 2-month follow-up. There were no significant differences in patient demographics or surgical variables. One SWD occurred in each group. The dehiscence rate in both groups was 20% (p>0.9). The SWD in the CP group (superficial) occurred on postoperative day 14 and the SWD in the NPWT group (deep) occurred on day 21. Both cases of SWD were associated with SSI, despite intraoperative antibiotic prophylaxis. There were no differences in median time to wound healing (p=0.9) or postoperative analgesia use (p=0.5). Furthermore, no difference was found in the median time taken to return to normal activity (p=0.8), though this time was longer in the NPWT group for all-but-one outcome. There were no changes in pre- and postoperative self-reported health ratings in either group (p>0.9).

Conclusions
This was an interim analysis of a trial with ongoing recruitment. There were no statistical differences in any outcome between the CP and NWPT groups in our unpowered cohort. Based on our current findings, continuation of this RCT is feasible and necessary to reveal any significant differences.
As the prevalence of chronic, lifestyle-related diseases continues to grow, the focus of many health campaigns has shifted towards individual responsibility for ill health. There is some evidence to suggest that individuals’ role in disease may become a more common healthcare rationing criterion. With developments in lifestyle-tracking technology, it may soon be possible to monitor many behaviours which result in lifestyle-related diseases. Much of the debate regarding individual responsibility in healthcare focuses on retrospective (or backward-looking) responsibility. Prospective responsibility is an alternative framework for if responsibility is to become a healthcare rationing criterion. Public attitudes towards prospective, lifestyle contract models of responsibility, and towards using mobile health technology to assess responsibility for disease, have not previously been studied.

An online survey was conducted on members of the UK general public using the crowdsourcing platform, Prolific (n=81). Participants were invited to respond to a series of statements on responsibility in healthcare, both retrospective and prospective, and on using mobile health technology to assess responsibility for disease, have not previously been studied.

Findings included that participants disagreed significantly more with the notion of intrinsic desert (M=1.9877, SD=1.14558) than of extrinsic social benefit (M=2.5802, SD=1.30254) as a justifiable rationale for holding people responsible for past behaviours (t(80)=-6.400, p<0.001). There was greater support for lowering healthcare priority on the grounds of multiple failed lifestyle contracts than either non-specific patient responsibility (MD=0.716, SE=0.137, p<0.001) or a single failed lifestyle contract (MD=0.568, SE=0.111, p<0.001). Furthermore, participants approved more of using mHealth technology to monitor adherence to a lifestyle contract (M=3.2593, SD=1.37639) than of determining whether past behaviour contributed to illness (M=3.0123, SD=1.21957), t(80)=-1.958.

Prospective responsibility is preferable to retrospective responsibility in the context of healthcare rationing. A reasonably achievable lifestyle contract model is less vulnerable to many of the objections commonly used against retrospective responsibility in healthcare. Our study found evidence that the public supports consequentialist allocations of scarce healthcare over retributivist frameworks, and that they believe good intentions have some moral worth. They also preferred lowering healthcare priority after multiple violated lifestyle contracts over non-specific responsibility. These views are better aligned with a prospective model of responsibility. Furthermore, developments in mHealth technology are likely to produce specific and accurate monitors that can reduce the time and personnel required to support the prospective model.
Factors affecting vitamin D status in infants

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Dr Rachel Peters, Murdoch Children’s Research Institute
Dr Jennifer Koplin, Murdoch Children’s Research Institute

My name is Charlie: I chose my project through my supervisor, which I would recommend. I met Prof. Allen, who’s working on several projects, and chose vitamin D in HealthNuts because I am interested in common problems in medicine. Katie also was a great choice of supervisor because she was very keen to set out the year as a way of learning skills (e.g., academic writing, data analysis, epidemiology). My advice to future students would be a) pick a supervisor who you can easily get along with, and b) try to make clear goals about what you want to learn (there’ll always be more; you don’t know what you don’t know), rather than what you want to achieve. Everyone is lovely in research-land, they have lots of time to show people around, but also things move more slowly there, so plan ahead and try to give as much time as possible for every step of your project. Everyone’s always on leave, and everything takes longer than expected.

A BMedSci(Hons) is a great experience, one in which you can learn a lot about research in a short period of time, and a great way to dip your toes in the water.

ABSTRACT

Background
Vitamin D is a micronutrient essential for normal growth and development in infancy, the first two years of life. Recognised for its effect in calcium and phosphate metabolism and skeletal mineralisation, there is also emerging evidence that vitamin D may be important for other body systems. Large RCTs in progress, such as the Vitality trial, are assessing the non-osseous benefits that vitamin D may have. Despite the importance of vitamin D, the factors which determine vitamin D status in infancy remain incompletely understood. Although some associations between vitamin D status and formula intake and UV exposure have been observed, many more relationships have yet to be fully understood, such as ethnicity and socioeconomic status. The published studies vary widely in the ages and the factors assessed; only one study has investigated 1-year-olds alone, and none have investigated 2-year-olds alone. Additionally, no studies have used paired samples to assess how the determinants of vitamin D status may change over time. The purpose of this study is to assess the factors determining vitamin D status in infancy and the factors which affect the change between these two ages.

Methods
Vitamin D deficiency in this study is defined as less than 50 nmol/L of serum 25-hydroxyvitamin D. It uses vitamin D measurements from the HealthNuts study, which was a population-representative, longitudinal study in Melbourne between 2007-2011, with the aim of assessing the prevalence and potential risk factors of food allergy, including vitamin D deficiency. This study includes 851 1-year olds and 125 2-year olds.

Results
At 1 year of age, the factors which affected risk of vitamin D deficiency were formula intake (aOR = 0.21 for fully-formula feeding vs. exclusive breastfeeding), UV exposure (aOR = 0.08 and aOR = 0.01 for highest vs. lowest quintile of ambient and personal UV exposure respectively), ethnicity (aOR = 1.68 for Asians vs. Caucasians), socioeconomic status (aOR = 0.42 for highest vs. lowest quintile), and gestational age at birth (aOR = 0.54 for post-term vs. term birth).

At 2 years of age, Asian ethnicity and UV exposure both had stronger associations with vitamin D status than at 1 year of age (aOR = 3.40 for Asian vs. Caucasian ethnicity; aOR = 0.01 for highest vs. lowest quintile of ambient UV radiation); and the relationship with formula intake was seen to be weaker.

In the change between these ages, risk factors for developing a new deficiency were formula intake (aOR = 10.64 for exclusive formula feeding vs. exclusive breastfeeding) and Asian ethnicity (aOR = 3.76 for Asian vs. Caucasian ethnicity), while increased UV exposure remained protective (aOR = 0.26 for increasing ambient UV radiation).

Conclusions
Regarding the factors affecting vitamin D status at 1 year of age, the findings of this study supports current evidence. With 2-year-olds, and the use of paired samples to explore the factors affecting the change in vitamin D status between 1 and 2 years of age, the study is entirely novel. The findings of these analyses suggest new avenues for research and could point to children at risk of developing vitamin D deficiency in the first two years of life.
Background
Musculoskeletal disorders (MSD) have a major impact on the population’s health and productivity, leading to a substantial economic burden. The recently published productivity-adjusted life year (PALY) is a new measure to estimate the productivity impact attributable to a disease or condition at a population level. To date, no studies have examined the productivity impact of two of the most prevalent MSDs low back pain and osteoarthritis using PALYs.

Aims
This study aims to investigate the burden of low back pain and osteoarthritis with regards to quality-adjusted life years (QALYs) lost, PALYs lost, and the economic cost of productivity loss in Australia.

Methods
Life table modelling was employed to hypothetically simulate the experiences of the 2016 Australian working-age population. The sample comprised Australians aged 20 to 69 years, who were followed up to 70 years of age or death. Separate life tables were constructed for those with the MSD under study (low back pain and osteoarthritis) based on prevalence data. Mortality rates, utility and productivity indices were applied. The life tables were then duplicated, assuming the population did not have the conditions of interest, and the utility and productivity indices were updated accordingly. QALYs and PALYs were summed for each life table. The difference in total QALYs and PALYs between each MSD, and assuming the MSD under study did not exist, provided the health and productivity impact of each MSD. The economic cost of this productivity loss was estimated by multiplying each PALY lost to the gross domestic product (GDP) per equivalent full-time worker (EFT).

Results
Our modelling shows that in those aged 20 to 69 years, followed up to 70 years of age, low back pain reduces the total number of QALYs by 18.3% and PALYs by 0.8%, compared to if low back pain did not exist. While osteoarthritis reduces QALYs by 10.8% and PALYs by 9.2%, compared to if osteoarthritis did not exist. The economic burden of low back pain and osteoarthritis on workforce participation over the remaining working lifetime of Australians currently living with these MSDs is estimated to be $34.8 billion and $147.8 billion in lost GDP, respectively. When considering additional work impairments of absenteeism and presenteeism, low back pain reduces PALYs by 17.8% and osteoarthritis by 17.5%, resulting in $652.7 billion lost GDP due to low back pain and $232.0 billion lost GDP due to osteoarthritis.

Conclusions
MSDs such as low back pain and osteoarthritis are associated with reduced quality of life and work productivity, which can be quantified as a reduction in QALYs and PALYs. This study provides an indication of the size of the economic loss to society conferred by these conditions and illustrates the potential increase in GDP if these conditions are to be better managed and prevented in the long run. Results found in this study will allow cost-benefit analysis on the management and prevention strategies implemented.
Maylyn Goh

Identifying and addressing osteoporosis knowledge gaps in women with Premature Ovarian Insufficiency (POI) and Early Menopause (EM)

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ABSTRACT

Background
Premature Ovarian Insufficiency (POI) and Early Menopause (EM), menopause before age 40 and 45 years respectively, affects up to 10% of women. The prevalence of POI/EM is expected to rise as increasing numbers of women develop iatrogenic POI/EM. POI/EM is associated with an increased risk of osteoporosis, a condition with significant adverse impacts upon one’s quality of life. Many women with POI/EM have unmet information needs, which may lead to sub-optimal health-related behaviours and outcomes. Even though osteoporosis is a major concern for women with POI/EM, little is known about women’s knowledge, beliefs, information needs and behaviours regarding osteoporosis.

Study’s Aims
I. To evaluate women with POI/EM’s current understanding and practices regarding bone health.
II. To assess current online consumer resources regarding POI/EM and bone health.
III. To co-design a bone health factsheet for women with POI/EM.

Method
This mixed-method study involved two phases: (I) An initial needs-analysis which informed (II) The development of an acceptable factsheet.

The needs-analysis compromised: (A) A quantitative survey of women, recruited from the community and hospital with a self-reported diagnosis of POI/EM, assessing demographics, medical history, calcium intake, exercise, factsheet information needs, osteoporosis knowledge (OKAT), beliefs and self-efficacy (validated scales) and (B) An assessment of the quality and readability of current online consumer resources related to POI/EM and bone health.

Using the results of the needs-analysis, a bone health factsheet was developed and refined, using semi-structured interviews involving women with POI/EM. Data analysis involved descriptive statistics, logistic regression (SPSS) and thematic analysis (NVivo) of interview transcripts.

Results
Needs-Analysis
The median age of survey respondents (n=316) was 54 years (IQR: 47-63) and 75.7% had a post-school qualification. Median age of menopause was 40 years (IQR: 38-43) and iatrogenic POI/EM affected 55.6% of women. According to current guidelines, most women reported inadequate dietary calcium intake (98.7%) and exercise (65%). Osteoporosis was diagnosed in 19.3% of women. The median OKAT score was 8 (IQR: 6-10)/19 and main areas of knowledge gaps were related to osteoporosis risk factors, treatment options and post-menopause bone loss. OKAT, adjusted for age and education, predicted calcium intake [OR 1.126 (CI 1.035-1.225); p=0.006] and screening [OR1.186 (CI1.077-1.305); p=0.001]. All factsheet topics were considered Very Important/Essential to include (>75% of women).

Significant shortcomings exist in current resources regarding POI/EM and bone health. Quality assessment, using the DISCERN tool, demonstrated that 54% of resources were of a moderate quality or lower (Score ≤3). None of the assessed resources had a readability consistent with current recommendations (Grade 8 or lower).

Development of factsheet
Two rounds of interviews were conducted (n=10 each). The five main themes that emerged included: content, design, perceived usefulness, emotional responses and clinical considerations.

Conclusions
This is the first Australian study to identify women with POI/EM’s knowledge, beliefs, information needs and health-behaviours regarding osteoporosis. The co-designed factsheet addresses women’s information needs and may facilitate discussions with health professionals and self-care of condition. Further investigations exploring the effectiveness of the factsheet in improving women’s knowledge, health-related behaviours and health professionals interaction is needed.
Christopher Hardy

Trends in condomless anal sex and drug and alcohol usage amongst Men who have Sex with Men in Melbourne, Australia; A retrospective case analysis from 2011 to 2017

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2. Central Clinical School, Monash University, Melbourne, VIC 3004, Australia

ABSTRACT

Background
The rates of STI infection have been rising for a decade in Men who have Sex with Men. The aim of this paper is to see if trends in sexual risk factors have been increasing over the same period to determine if they may potentially explain the increase in STI infection.

Method
Data from clinical consultations at Melbourne Sexual Health Centre (MSHC) from January 1st 2011 to December 31st 2017 were reviewed. Only those who completed CASI were included in the analysis. Logistic regression analysis using generalised estimating equations was conducted to explore the risk factors associated with condomless anal sex during drug use, alcohol use, and with health issues. Risk factors included number of casual sexual partners, overseas birth, PrEP use, a positive HIV status, and having a regular sexual partner.

Results
There were 134 614 consultations in MSM in the study period of which 22, 255 were included for analysis. The number of consultations with MSM reporting condomless anal sex with casual sexual partners in the past 12 months increased from 1686 in 2011 to 5635 in 2017. Condomless anal sex during and/or after drug use increased significantly by 5% per year (adjusted odds ratio [AOR] 1.05; 95%CI 1.03-1.08, p<0.001). Condomless anal sex during and/or after alcohol use and with health issues showed no change.

Conclusions
The finding of increases in condomless anal sex over time has been previously described but the finding of increases in drug use among men practicing condomless anal sex is new. Given drug use increases other activities such as group sex it may explain some of the rises in STIs. Further research is needed in this area to clarify further risk factors, and continual surveillance of MSM will be required to monitor their sexual health into the future.

Hey there! My name is Chris, and I decided to undertake BMedSc(Hons) project after completing my fourth year of the MBBS degree. I have always been incredibly interested in sexual and LGBTQIA+ health, so I thought a project at MSHC would be perfect for me.

This year has been challenging; a lot of blood, sweat, and (mostly) tears have gone into writing the literature review, the thesis, and my article. But, it has also been an incredible year that has allowed me to explore another aspect of medicine whilst also making some incredible friends and contacts.

Working with a large dataset, using statistical analysis software, and learning how to get things published have been skills that I will no doubt be using further on in my career. A huge thanks to Dr Eric Chow and Prof Kit Fairley for their patience with me, and thank you to MSHC for welcoming me in with open arms!

If you have any questions or queries please email me: cahar25@student.monash.edu.
Alexander Herdyanto

Cardial Procedural Outcomes During the Festive Season

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ABSTRACT

Background
Previous studies have suggested that there are seasonal impacts on CVD outcomes. In the northern hemisphere where Christmas time falls in winter, an analysis by Phillips and colleagues found that deaths from heart disease increased in the winter season, but that there were also spikes in cardiac mortality around Christmas and New Year. Relatively fewer studies have been conducted in the Southern Hemisphere (where Christmas and New year occur during summer). This study by Knight and colleagues looked at out of hospital cardiac death and found that even though there was lower mortality during the summer season, there appeared to be a small increase over the Christmas New year holiday period relative to surrounding time periods. The aim of this study was to use VCOR data to determine whether there are differences in PCI outcomes for patients having procedures during the Christmas-New Year holiday period compared to another non-holiday summer period.

Method
Data obtained from the Victorian Cardiac Outcomes Registry, or VCOR. VCOR was established in 2013, and the aim of the registry is to improve quality of care for patients. The study examines PCIs performed during the period 2013-2017. The festive season period was defined as 24th December to 1st January and non-festive defined as 8th November to 17th November and 20th February to 28th February. Temperature data obtained for day of procedure from the Bureau of Meteorology.

Categorical variable (gender, history of diabetes, CABG, PCI, peripheral vascular disease, cerebrovascular disease, public/private hospital, and number of stents) analysed by chi-square, while continuous variable such as age and BMI were analyzed by t-test. Multivariate logistic regression modelling with backward step was used to examine predictors outcomes between Christmas/New-Year’s Holiday and the selected non-holiday periods.

Results
The majority of patients were male, with no difference in proportions of males and females between time periods. here were significant differences in 30-day mortality and major cardiac and cerebrovascular events (MACCE) between the festive and non-festive season periods. Moreover, analyses identified some risk factors that may contribute to 30-day mortality. Age, ventricular function, myocardial infarction status and temperature were significantly associated with 30 day mortality. This was also seen in MACCE that age, ventricular function, sick on-hospital cardiogenic shock, and maximum daily temperature were associated significantly towards MACCE outcomes.

Conclusions
In summary, there are differences in 30-day mortality and MACCE outcomes between festive and non-festive season periods. Analyses suggest that patients having PCI in the holiday period have poorer pre-procedural ventricular function. In addition, Regression analyses indicate that festive season itself is not a significant predictor of outcome, but patient age and maximum daily temperature are associated with adverse outcomes post-PCI.
Dispensing trends and medication use behaviour of SGLT2 inhibitors versus other glucose-lowering drugs in older adults: The Australian perspective.

Supervisor: Dr Ken Lee Chin
CCRE Therapeutics, Department of Epidemiology and Preventive Medicine

Co-supervisor: Professor Danny Liew
CCRE Therapeutics, Department of Epidemiology and Preventive Medicine

ABSTRACT

Background
The therapeutic landscape in diabetes has changed rapidly in recent years. Whether or not dispensing patterns of glucose-lowering drugs (GLD) in Australia are in accord with recently published data is unclear. The present study sought (i) to compare the dispensing patterns of sodium-glucose cotransporter-2 (SGLT2) inhibitors versus other GLD and its associated costs from the Australian perspective; and (ii) to evaluate adherence and persistence of use in patients who received GLD.

Methods
A retrospective cohort study was performed using the Australian Pharmaceutical Benefits Scheme (PBS) databases, covering a 10% random sample of the Australian population. The yearly prevalence and incidence use of GLD was assessed by descriptive statistics. Adherence was assessed using proportion of days covered (PDC) and GLD discontinuation was defined as the first ≥90 days without GLD coverage.

Results
Data from a total of 175,125 patients who received GLD were analysed. In the time period 2013-2016, metformin (84%) and sulfonylurea (33%) were the most commonly dispensed GLD, while SGLT2 inhibitors were dispensed to 3% of the patients. Patients were most commonly initiated with metformin (77%). The incidence of patients newly initiated with SGLT2 inhibitors increased 24-fold from 0.8 per 1,000 in 2014 to 19.3 per 1,000 in 2016, while the incidence for metformin initiation decreased from 774.1 per 1,000 to 750.9 per 1,000 during the same period. In 2016, 18% of patients were initiated with a GLD that was inconsistent with contemporary diabetes guidelines. In 2006, the Australian government subsidised a total of AUD $1.2 million on GLD, largely attributed to metformin (52%) and sulfonylureas (41%). By 2016, the cost increased by AUD $480 million/year to AUD $6 million and is projected to reach AUD $8.5 million by 2020. Only 58.8% of the patients were considered adherent using metformin (PDC≥80). A total of 55.2% of patients dispensed with SGLT2i were considered adherent.

Conclusion
Despite decreasing trends from 2012 to 2016, metformin remained the most commonly dispensed GLD during the study period. 18% of the patients were not initiated with first-line therapy as recommended by contemporary guidelines. Annual costs of glucose-lowering drugs are expected to continue rising.
Ryan Hirsch

The SITAR study: SIRT versus DEB-TACE identifying good prognostic indicators
Supervisor: Prof Amanda Nicoll: EHCS Monash University and Eastern Health
Co-Supervisor: Dr Rohit Sawhney: Eastern Health

ABSTRACT

Background
The treatment of Hepatocellular Carcinoma (HCC) is generally guided by the Barcelona Clinic Liver Cancer (BCLC) staging system. However, this is a guide and with the constant evolution of non-curative therapies many cases have treatments other than those recommended. Indeed, despite not being part of the BCLC algorithm the use of selective internal radiation therapy (SIRT) is increasing, however there is limited data that can be used to discern which patients would be the best candidates for SIRT. We aimed to catalogue the use of SIRT within Victoria and identify which characteristics were associated with superior response within the SIRT cohort, as well as determine specific groups that may be more suited to SIRT or Dr g Eluting Bead Trans-arterial Chemoembolisation (DEB-TACE).

Methods
A retrospective multicentre study, with the SIRT cohort consisting of patients from five major liver centres within Victoria, and the DEB-TACE cohort consisting of patients from a single site. Participants were identified by a search of each site’s HCC database and were supplemented by electronic patient records. The endpoints used were overall survival from the time of diagnosis and from time of treatment, time to progression and radiological response.

Results
The SIRT cohort had significantly more advanced tumour burden, despite this there was no significant difference in overall survival or time to progression between the two cohorts either from first DEB-TACE or SIRT or from diagnosis. Subgroup analysis conducted on covariates considered pertinent demonstrated patient characteristics more suited to each treatment modality.

Conclusion
This research is the first to catalogue the experience of using SIRT in HCC in an Australian population, and the largest study to compare SIRT and DEB-TACE. This study suggests there may be subgroups of patients with HCC that are more suited to DEB-TACE or SIRT and highlights the need for further research to establish the optimal roles for these treatments.
Smell perception in Motor Neurone Disease

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ABSTRACT

Background
The discovery of hyposmia as a common feature of Parkinson's Disease (PD) and Alzheimer's Disease (AD), has generated increasing interest in the area of olfactory dysfunction (OD) in neurodegenerative disorders. It’s early presentation in PD and AD has led to the proposal of olfactory testing as a potential diagnostic tool for these disorders.

It has been established that people with Motor Neurone Disease (MND) can suffer from non-motor problems. OD has been observed through anecdotal evidence and small sample studies, with some suggesting possible correlations with bulbar, frontotemporal, and respiratory impairment. However, the evidence remains conflicting and there’s a paucity of studies assessing correlations with clinical subtypes, important clinical parameters and the diagnostic utility of smell impairment.

Method
This is a cross-sectional study (still in progress) at Calvary Health Care Bethlehem that aimed to examine the prevalence of smell abnormalities in the MND population, and determine whether they correlated with clinical phenotype, stage of disease, disease severity, cognitive impairment and respiratory decline. Furthermore, it aimed to assess the clinical usefulness of the smell test in differentiating MND patients from a healthy control group.

We have thus far, analysed olfactory performance in 60 MND patients and 20 age and gender-matched controls. All participants were screened for sinonasal problems, questioned for self-perceived smell and taste changes and impacts on QOL, and assessed with a cognitive test and a smell test. Additional MND patient data was collected on clinical phenotype, disease stage and severity, behavioural dysfunction, disease duration and respiratory function. We performed non-parametric statistics and receiver operating characteristic (ROC) curve analyses.

Preliminary Results
Findings show 31.7% of MND participants displayed smell abnormalities. Median B-SIT scores were mildly but significantly lower than controls (MND=9/12 vs. Controls=11/12, p<0.05). Median B-SIT scores didn’t differ between bulbar and limb-onset phenotypes. Olfactory or gustatory changes was self-reported by 63.2% of MND patients that demonstrated abnormal smell performance. Half of those that self-reported changes reported an impact on quality of life (QOL). There was no notable correlation between olfactory performance, and frontotemporal changes, disease duration, disease stage, severity nor respiratory decline. The sensitivity of the B-SIT in identifying MND was 0.32. ROC analysis additionally showed poor diagnostic accuracy (area under curve=0.58).

Conclusions
OD was significantly more common in MND patients, but impairment appeared to be only mild thus far. This suggests that olfactory structures may be involved in the MND disease process. Our findings so far do not support smell testing as a useful clinical biomarker, nor a method of early screening. The lack of correlation between OD and other clinical parameters further deducts from its potential clinical utility.

Our findings suggest OD can contribute to poorer QOL in MND patients, which highlights an area that should be addressed by clinicians in practice. We aim to study more patients and controls to validate our findings. Further larger sample studies, longitudinal studies and pathological studies would assist our understanding of OD in MND and its relationship with clinical variables and the underlying neuropathology.
ABSTRACT

Background
Familial Hypercholesterolaemia (FH) is an inherited disorder that predisposes patients to increased cardiovascular risk. Achilles tendon (AT) xanthoma represents lipid deposition in the AT and is a pathognomonic feature of FH. It is associated with increased risk of premature cardiovascular disease.

The role of imaging in the detection of xanthoma has been explored and ultrasound has been deemed to be superior to X-ray, computed tomography (CT) and Magnetic Resonance Imaging (MRI). However, there is limited data regarding the accuracy of physical examination in the detection of xanthoma, compared to ultrasound. Scarcity of data also exists regarding the frequency of xanthoma in the Australian FH population.

Method
Between March 2017 and June 2018, 42 patients with possible, probable or definite FH according to the Dutch Lipid Clinic Network Score from a lipid clinic based at MonashHeart (Melbourne, Australia) were included in the study. The baseline demographics, medication and pathology results were obtained from medical records, pathology services and phone calls to GP clinics.

The physical examinations were performed by the same examiner with expertise in lipidology. The patients were considered to have xanthoma on physical examination if the tendon felt thicker than normal subjectively or nodular lesions could be palpated. The ultrasound imaging were performed at Monash Imaging and analysed from the database by an expert radiographer. Xanthoma was considered to be present if the tendon was thicker than normal or if discrete hypoechoic lesions could be observed.

Statistical analysis was performed on Microsoft Excel, version 16.16.1 and Stata/MP 14.0 2015 for Mac (StataCor, College Station, TX). Distribution for variables was determined by the Skewness-Kurtosis test. Categorical variables are reported as number (n) and percentages (%). Continuous variables are expressed as mean ± standard deviation (normal distribution) or median and Interquartile Range (IQR) (skewed). p value <0.05 was considered significant.

Results
Mean age was 47.7 years, mean Low Density Lipoprotein Cholesterol (LDL-C) was 4.76mmol/L and 47.6% of the subjects were male. The frequency of xanthoma was 73.8% by ultrasound and the median antero-posterior diameter was 5.15mm (IQR 4.7mm-5.7mm). Physical examination had a sensitivity of 38% (95% Confidence Interval (CI) 24.7% to 52.8%) and a specificity of 73.5% (95% CI 55.6% to 87.1%) in xanthoma detection. No single factor demonstrated significant association with xanthoma. There was a trend of association of Arcus Cornealis with the presence of xanthoma (OR=4.5, 95% CI, p=0.18). No association between age and xanthoma was observed.

Conclusions
The frequency of xanthoma in our FH population was 73.8%. Ultrasound, used in conjunction to physical examination increased the accuracy of xanthoma detection. No association between xanthoma and age was observed. We observed a trend of association between xanthoma and Arcus Cornealis.
Sleeve gastrectomy is currently the most commonly performed bariatric surgery used to treat morbid obesity. Gastro-oesophageal reflux disease (GORD), is an important issue following sleeve gastrectomy due to its prevalence, adverse effects on quality of life and potential role as a driver of Barrett’s oesophagus and oesophageal carcinoma. GORD is a major cause of re-operation following sleeve gastrectomy. Following the gastric sleeve procedure, there are contrasting views regarding the occurrence of gastro-oesophageal reflux disease, with the majority of reports suggesting sleeve gastrectomy promotes GORD, while another view proposes that sleeve gastrectomy can alleviate GORD symptoms. Despite multiple investigations from various studies, the physiology of gastro-oesophageal reflux disease following sleeve gastrectomy procedure remains poorly understood.

In this study we sought to determine: 1) the expected pattern of gastro-oesophageal reflux following sleeve gastrectomy, using nuclear scintigraphy. 2) The expected symptoms of reflux and associated gastrointestinal symptoms following sleeve gastrectomy. 3) To describe how reflux symptoms and nuclear scintigraphic appearance of reflux change over the first two years following sleeve gastrectomy. 4) To define how the pattern of gastro-oesophageal reflux differs in patients suffering severe adverse symptoms.

Method
Sleeve gastrectomy patients with minimal symptoms from The Alfred hospital were recruited into the study. They were classified into different cohorts base on their following months after surgery. Early(0-4 months), Intermediate(5-15 months), and Established(>15 months)
Pattern of emptying, gastric emptying half-time, quality of transit, and oesophageal transit property data were taken using nuclear scintigraphy study. Series of questionnaires were used to assess patient’s reported reflux symptoms, dysphagia, Quality of Life, and depression. Seventeen “optimal patients” with minimal symptoms and have matched nuclear scintigraphy and questionnaires were selected from the whole cohort. Another separate cohort of patients with significant reflux symptoms following the surgery will be recruited as a comparison to the asymptomatic group.

Results
We obtained a total of 30 patients for the asymptomatic group, 17 optimal patients, and 7 patients with significant reflux symptoms that has done nuclear scintigraphy scans. Majority of the patients had reflux, with 67% and 76% from the asymptomatic group and the optimal group were detected to had reflux.

We found that there was a significant increase of gastric content retained in the oesophagus and sleeve at the end of nuclear scintigraphy in patients with significant reflux(p-value: 0.048 and 0.0445). This event could indicate the association of impaired gastric clearing with severe reflux symptoms.

We observed that there is no significant decrease in quality of life in sleeve gastrectomy patients in comparison to community norms. However, there is a significant decrease in physical function in established group patients compared to early and intermediate group(p-value: 0.0357 and 0.0160).

Conclusions
We identified that around the time of a meal, reflux appears to be expected following gastric sleeve procedure. There are potentially three patterns of GORD following sleeve gastrectomy that is associated with altered gastric anatomy and physiology. Further delineating these patterns and linking them specifically with symptoms will be an important future research endeavour.
Prostate Cancer Pattern of Presentation and Treatment in Jakarta and Victoria

Associate Professor Sue Evans – Head of Prostate Cancer Outcomes Registry
Fanny Sampurno – Prostate Cancer Outcomes Registry
Professor Rainy Umbas – Faculty of Medicine, Universitas Indonesia

ABSTRACT

Background
Prostate cancer (PCa) is the fourth most common cancer in Indonesia and the most common non-skin cancer in Australia. Although the number of PCa incidence rate is higher in Australia, but the five-year mortality rate in Indonesia is nearly as high as the Australian rate. This study aims in gaining understanding regarding the pattern of treatment and presentation of men with PCa in Jakarta, Indonesia, the timeliness to treatment as well as the factors affecting the choice of treatment and compared it to Victorian men with PCa.

Method
Data were extracted from two databases; Prostate Cancer Outcomes Registry – Victoria and database from Department of Urology, Cipto Mangunkusumo National Central General Hospital in Jakarta. Descriptive, univariate and multivariate logistic regression analyses were used.

Results
This cohort consisted of 448 men from Jakarta and 16,738 men from Victoria diagnosed with PCa. The mean age at diagnosis of men in our Jakarta cohort was 67.0 years of age and in Victoria was 66.4 years. Our study found that most men in the Jakarta cohort were diagnosed with metastatic risk disease (51%). Whereas most men in Victoria were diagnosed with intermediate risk disease (45%). Over half of men in Jakarta (65%) were diagnosed with PSA level >20 ng/mL and on the contrary, most men in Victoria were diagnosed with PSA level 4.01-10.00 ng/mL (54%). In Jakarta, most men were diagnosed with Gleason score of 8-10 (53%) while in Victoria, most men were diagnosed with a Gleason score of 7 (46%).

Conclusions
To our knowledge, this was the first study that directly compares pattern of diagnosis and treatment for PCa between Indonesia and the developed country of Australia. The results of this study can be used to support the development of updated comprehensive treatment guidelines in Indonesia. Moreover, to provide an indication of the importance of developing a national PCa registry and contributing to a Global PCa registry.
Vivien Lai

Systemic Treatments for Alopecia Areata: The Efficacy of Cyclosporin

Prof. Rodney Sinclair, Sinclair Dermatology;
Prof. Douglas Gin, Alfred Hospital;
Dr Gang Chen, Monash Centre for Health Economics

ABSTRACT

Background
Alopecia areata (AA) is a T-cell mediated autoimmune disease of the hair follicle resulting in acute or chronic patches of non-scarring hair loss, which may progress to loss of total scalp hair (alopecia totalis, AT), or universal loss of hair over the entire body (alopecia universalis, AU). Systemic treatment for extensive disease has been poorly investigated. Despite widespread use of steroid-sparing agents, particularly cyclosporin, in the treatment of moderate to severe AA, there are no randomised, placebo-controlled trials evaluating its efficacy. Case series indicate the response rate to cyclosporin is in the range of 33% - 55%.

Aims
To evaluate the efficacy of cyclosporin compared to placebo at 3 months in patients aged 18 to 65 years with moderate to severe AA.

Methods
A double-blind, randomised, placebo-controlled trial was conducted. Adults aged 18 to 65 years of age with moderate to severe AA were randomised in a 1:1 ratio to receive 3 months of cyclosporin (4mg/kg/day) or matching placebo. The study was powered to detect a 50% reduction in SALT score in 50% of participants. Blinded assessments were conducted monthly and included: physical examination, blood biochemistry, photography, quality of life measurements and efficacy evaluation using Severity of Alopecia Tool (SALT) score, eyelash and eyebrow assessment scales. A per protocol interim analysis was performed for participants completing 3 months of treatment.

Results
28 participants (cyclosporin: 13; placebo: 15) were analysed. At baseline, the mean SALT score was 79.4% and approximately half of participants in each group had AT or AU. The mean duration of current AA episode was 6.5 years. While the cyclosporin group had a greater mean change in SALT score (-10.3% versus -2.6%; p=0.59) and greater proportion of participants achieving at least a 50% reduction of SALT score (23.1% versus 6.7%; p=0.216) compared to placebo at 3 months, this did not achieve statistical significance. Only the proportion of participants achieving a 1 grade improvement in eyebrow assessment scale was significantly different between cyclosporin and placebo (23.1% versus 0.0%; p=0.049). Quality of life assessment did not show any statistically significant change for each group at the end of treatment compared to baseline.

Conclusion
This is the first randomised, placebo-controlled, prospective clinical trial investigating the effectiveness of 4mg/kg/day cyclosporin monotherapy in the treatment of moderate to severe AA for 3 months. Interim results of 28 participants did not reveal a statistically significant difference between cyclosporin and placebo in reduction of scalp hair loss at 3 months of treatment. The trend for continued response over time suggests that trials employing a larger sample size and longer treatment duration may allow detection of lower response rates. These results suggest that any potential benefit associated with cyclosporin treatment is likely to be slower in onset than other inflammatory skin diseases, such as psoriasis and atopic dermatitis. These results may be interpreted for a cohort of patients with moderate to severe, long-standing AA and will guide clinicians in their choice of second-line agents for this patient cohort.

I decided to pursue a Bachelor of Medical Science (Honours) following 5th year medicine. Having always had an interest in furthering medical knowledge, I desired a greater, more enriching experience in research prior to beginning work as a junior doctor. This year, I had the exciting project of conducting a clinical trial at Sinclair Dermatology Clinical Trials Centre, in a disease area that has often been overlooked. I am greatly appreciative of the skills, friendships, insights and inspiration I have gained and I look forward to continuing to build on these in the years to come. I would like to thank my supervisors, Prof. Sinclair, Prof. Gin, Dr Chen for all their support this year!
Factors improving outcomes of the artificial pancreas during pregnancy in women with type 1 diabetes

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ABSTRACT

Background
Even with myriad advances in diabetes technology, the majority of pregnant women with type 1 diabetes struggle to meet the recommended glycaemic targets during pregnancy. Maternal and neonatal outcomes remain suboptimal with one in two pregnancies being complicated by pre-term delivery, large-for-gestational-age infants and neonatal intensive-care admissions. Outside of pregnancy, the novel approach of a closed-loop insulin delivery advice (artificial pancreas) has been shown to improve glycemic control. To date, our group has performed two studies assessing its efficacy in type 1 diabetes during pregnancy; one overnight study (Closed-Loop in Pregnancy 03) and one day-and-night study (CLIP 24/7). These randomised-crossover trials compared the closed-loop device to sensor-augmented pump therapy (SAP) – the women completed 4 weeks of closed-loop (intervention) and SAP (control) in random orders. The efficacy and safety of the device during pregnancy was demonstrated, but with a high degree of variability in glycaemic responses.

Method
This study aimed to assess factors that predict women’s glycaemic and psychosocial response to the closed-loop technology. This pre-specified secondary analysis examined data from CLIP 03 and 24/7. The combined dataset (n=32) includes women from Cambridge, Norwich and Ipswich, UK. Our primary endpoint examined factors predictive of a positive composite outcome of biomedical and psychosocial response. A positive psychosocial response was defined as an improvement in the participants’ attitude to the technology from their baseline qualitative interview to their follow-up interview. The effects of multiple variables on the biomedical and psychosocial efficacy of closed-loop was examined using a range of qualitative and quantitative outcomes.

Result
Overall, 28 women (87.5%) experienced a positive composite outcome with 22 women experiencing a biomedical response and 13 women experiencing a positive psychosocial response to the technology. Women with a lower baseline HbA1c had a more significant biomedical improvement (p=0.014) and women with a higher baseline HbA1c had a more significant psychosocial response with the device (p=0.018). Baseline demographic factors such as age, body-mass index, duration of diabetes, location of treatment and previous usage of insulin pumps or multiple-daily injections, had no effect on the biomedical or psychosocial efficacy.

Conclusion
For women with strong peri-conceptual glycaemic control, the closed-loop device may enable them to achieve an even more stringent level of glycaemic control. In contrast, the women with a higher baseline HbA1c may derive more psychosocial benefit from the technology as the device may provide a way to mitigate the burden of type 1 diabetes. It is important that clinicians paint a detailed and accurate picture of the capabilities of the technology to properly manage women’s expectations prior to its use. We eagerly await the results of the upcoming, large, randomised trial assessing the closed-loop device in type 1 diabetes pregnancies before any robust conclusions can be made.

I’m extremely grateful that I had the opportunity to complete a BmedSci. I was fortunate enough to have completed my project in Cambridge, UK. It’s been an incredible adventure and exposed me to a wide depth of scientific knowledge and a wealth of passionate individuals. I believe the ability to think critically has been the most valuable skill I’ve learn this year. I’ve also been fortunate to have had exceptionally supportive supervisors and believe this to be a key component to a successful year. I would be happy to discuss my project. Feel free to contact me at yrlef1@student.monash.edu
Investigating if ibuprofen could improve antenatal respiratory function in preterm infants

Eva Matthews Staindl

ABSTRACT

Background
Preterm infants are amongst the most vulnerable members of our society and despite major advances in respiratory support methods, they suffer from high rates of respiratory insufficiency – a major cause of morbidity and mortality. Current management of respiratory insufficiency includes respiratory support at birth with injurious ventilation methods, and postnatal stimulation of breathing using caffeine. These methods largely ignore the neural control of respiration – found in the brainstem respiratory centres, which are vital for sufficient breathing.

Inflammation, which affects a large proportion of preterm infants in utero, is known to affect these brainstem respiratory centres, and also affects fetal breathing movements. In particular, inflammatory mediator prostaglandin E2 (PGE2) has been shown to reduce fetal breathing and has an inhibitory effect on the brainstem. Intratracheal inflammation can be reliably induced using lipopolysaccharide (LPS). COX-inhibitors such as ibuprofen are known to reduce inflammation and PGE2 levels, as well as stimulating fetal breathing movements (FBMs), however these concepts have never been studied simultaneously.

Aims
Our aims were to assess the effects of LPS-induced inflammation on ovine FBMs and brainstem PGE2 levels, and to determine if antenatal ibuprofen could decrease localised PGE2 expression in the brainstem and stimulate FBMs.

Methods
Pregnant ewes at 120 days gestation underwent surgery to instrument the maternal vein, uterus and the fetal veins, arteries, and trachea to allow for monitoring of FBMs and the delivery of LPS/saline/ibuprofen. On days 1-3 of the experiment, fetuses received intravenous LPS (escalating doses: 300ng, 600ng, 1.2ug) or saline. On days 4-5 saline or ibuprofen 5mg/kg twice daily was delivered. Throughout the experiment, FBMs were continuously monitored, and fetal blood and plasma were collected for analysis. At the conclusion of the experiment, both ewe and fetus were euthanized and fetal cerebrospinal fluid and brainstems were collected for analysis.

Results
Incidence of FBMs was reduced by up to 63% following LPS administration on day 1 which was sustained for 6 hours then returned to baseline. There was a reduced response in FBMs on day 2, and no significant difference across groups on day 3. Lactate, partial pressure of oxygen, oxygen saturations, and partial pressure of carbon dioxide followed the same pattern of decreasing responses to LPS over the 3 days of LPS. Whilst the ibuprofen group had limited animal numbers, ibuprofen appeared to transiently stimulate FBMs. Preliminary tissue analysis indicated that animals that received LPS + saline (compared to saline controls and LPS + ibuprofen animals) had: increased PGE2 immunoreactivity in brainstem respiratory centres, increased cytokines and cell death markers in the medulla oblongata, and increased PGE2 levels in the cerebrospinal fluid.

Conclusion
LPS significantly reduced FBMs however the effect was transient – we suspect the fetuses developed a tolerance to LPS. This theory was supported by blood gas data that showed a similar pattern of response and recovery. Tissue analysis appears to support the theory that PGE2 plays a role in the respiratory inhibition observed however further analysis of more animals and of plasma PGE2 and cytokines will help to provide a clearer picture.
Fadhil Muhammad

A Retrospective Study of the Effect of Nivolumab on Overall Survival in Non-small Cell Lung Cancer

John Zalcberg – Cancer Research Program division of SPHPM Monash University
Rob Stirling – Allergy, Asthma & Clinical Immunology Clinic of Alfred Hospital

ABSTRACT

Background
Most of lung cancer patient is not detected until the disease is advanced. In 2006 Australian data, Advanced Non-Small cell lung cancer (NSCLC) patients had very poor survival, which was 7.8 months. This number was associated with the therapies for advanced patients, which was standard chemotherapy, EGFR inhibitor, and ALK inhibitor. In 2014, there was a new drug called nivolumab which showed the survival benefit in clinical trials studies (Trials 017 and 057). The median survival of trial study (057) was 12.2 months, which was 4.4 months longer than the previous data. Although the trial result showed a promising result of this treatment, the real-world study of nivolumab is limited.

The objective was to assess the impact of nivolumab use in stage III and IV NSCLC in an Australian hospital and evaluate the impact of nivolumab on overall survival.

Method
This study was a retrospective, observational and single-site study that used medical records as primary data and survival analysis as an illustration of the survival benefit of nivolumab. Two survival analyses were conducted to confirm the aim of this study. The first survival analysis was to illustrate the survival differences among nivolumab, chemotherapy and no anti-tumour therapy groups. The second survival analysis was to validate the survival benefit of nivolumab as second-line therapy. Lastly, the regression model was generated based on prognostic factors of NSCLC patients to confirm the survival result of second survival analysis.

Results
Data collection was finished. Three hundred and forty patients were included. The first survival analysis showed that patients with nivolumab (21.2 months) had longer survival than chemotherapy patients (13.5 months) and no anti-tumour medication patients (4.6 months). Then, the second survival analysis showed that patients with second-line nivolumab had the median survival of 19.8 months, whereas the median survival of patient treated with second-line chemotherapy was 10.1 months. The confirmation of the second survival result was by analysing factors including age, sex, smoking status, tumour types, sites of metastases, mutation status (EGFR, ALK), PDL1 result, surgery, radiotherapy, and targeted therapy using Cox regression method. Among all factors, the adenocarcinoma of Tumour types played a significant role in patient survival, which was showed by significant p-value (0.027) and significant hazard ratio (0.08).

Conclusions
Despite the low number of patients and higher treatment effect showed in this study, it was revealed that this real-world study supported the survival benefit of nivolumab of the previous clinical trials studies (Trials 017 and 057). This study also can become the reference to the clinician who seeks the evidence of nivolumab use in real-world patients. With the limitations and strength of this study, future directions for real-world nivolumab study should include exploration of the adverse event of therapy and complications occurred due to the treatment. Also required is an investigation of quality of life between nivolumab and chemotherapy patients.

Hi everyone! My name is Fadhil Muhammad and I am from Indonesia. This honour program is part of my study program from Universitas Indonesia and I finished my pre-clinical years before underwent this honour degree.

Well, it was an outstanding experience to do research which I interested on, cancer. The friendly environment and clinical type of research were the reasons why I chose this research. My research was drafted by myself from scratch with the help of my supervisors and other staffs during my honour years.

There were countless benefits of taking the honour degree, but I could simplify for the newcomers into 3 things: critical thinking in how we appraise the problem and come up with an idea of research, we learn a specific topic of research, and we get a chance to form up our own research from draft. Those advantages were worth for one-year degree program.

If I may suggest to newcomers, spend a year to learn and make a good quality research needs hard-work and good time management but enjoy the whole process. If you have further queries about honour degree or my research, feel free to contact me through email: dr.fadhilm@gmail.com.
Ari Mushin

Predictors of Cardiovascular Disease in HIV

Professor Jennifer Hoy, Director of HIV medicine, Department of Infectious Diseases, the Alfred Hospital and Monash University

Doctor Anna Hearps, Deputy Program Director, Healthy Ageing (Expansion Program), Burnet Institute

ABSTRACT

Background
People Living with HIV in the developed world have seen increased lifespan since the introduction of antiretroviral therapy. As the life expectancy has increased, an increase in serious non-AIDS events including cardiovascular disease has been identified. It is not known whether this increased risk is due to HIV infection and the changes it causes, exposure to antiretroviral therapy, traditional risk factors, or a combination of these.

Method
A retrospective case control study was designed. HIV patients with a diagnosis of CVD were identified from the Victorian HIV Database as cases and matched by age and gender to HIV patients without a diagnosis of CVD as controls. Data on the history of the HIV infection (including duration of known infection, contemporary and nadir CD4 counts, CD8 counts and viral loads) and the antiretroviral therapy used to treat HIV (including length of exposure to ART, current regimen, and previous drugs used) was collected, as were data on traditional risk factors (including blood pressure, lipid profile, and current prescriptions).

Results
172 cases and 344 age- and sex-matched controls were identified. Analysis of traditional risk factors revealed that

- History of hypertension (but not current systolic or diastolic blood pressure) was associated with CVD
- High density lipoprotein levels were associated with lower rates of CVD, and triglyceride levels were associated with higher rates of CVD
- Current smoking and history of smoking were both associated with CVD
- Diabetes was associated with CVD
- Prescriptions for hypertension, dyslipidaemia, and anticoagulation were all associated with CVD

The analysis of HIV factors revealed no statistically significant associations.

The analysis of ART factors showed an association between NNRTI use with lower rates of CVD, current use of abacavir and dolutegravir with higher rates of CVD, and historical use of lamivudine with lower rates of CVD.

Conclusions
This study showed a risk factor profile different to that which might be expected. While the elevated risk of CVD may be explained by higher rates of traditional risk factors, further research is warranted to determine the physiological changes caused by ART that may modify the risk of CVD.

I decided to do a BMedSc(Hons) year after finishing 3rd year. I was lucky enough to find a project in the field I find interesting; Infectious Diseases and in particular, HIV. Through this project I have had the opportunity to work with both the clinical and lab teams at the Alfred Hospital and the Burnett Institute, covering a wide range of research techniques and clinical applications. I learnt more than I could have hoped, not just about the particulars of my project, but about the process of developing, implementing, revaluating and refining research projects. I also had a fantastic time in the Infectious Diseases department, which id full of great people and learning opportunities.

The full scope of my research wasn’t completed by the end of the BMedSc(Hons) course so I am still working with the team on continuing the research, which is fantastic and will hopefully allow me to stay engaged with this part of the medical world throughout the rest of my medical degree.

Feel free to email me at mushinari@gmail.com with any questions about the project or BMedSc(Hons) in general; I am happy to talk and provide any insight I can.
Cameron Naidu

Developing a Model to Elucidate Dendritic Cells in Colorectal Carcinomas
Professor Eva Segelov
Dr Maja Green
Translational Oncology Research Group at MHTP

ABSTRACT

Background
Dendritic cells (DCs) interact with both innate and adaptive immune systems, functioning as a crucial mediator of the natural anti-tumour response. Recently, it has been found that DCs up-regulate the immune checkpoint programmed cell death protein 1 (PD-1) in response to inflammatory stimuli as well as potentially in the tumour microenvironment itself, the same immune checkpoint targeted by anti-PD-1 immunotherapeutic medications. Additionally, it appears as though certain DC functions, specifically production of the cytokine interferon (IFN)-λ may be regulated by this checkpoint. Despite this, minimal research has been conducted on how these crucial cells are affected by these immunotherapies. Mismatch repair-deficient (MMR-D) colorectal carcinomas (CRCs) are known to be more responsive to anti-PD-1 immunotherapies than mismatch repair-proficient (MMR-P). However, in searching for explanations as to why this is the case, the role of dendritic cells has been largely overlooked.

We aimed to identify the presence and abundance of DC subsets infiltrating MMR-D and MMR-P CRC tumour microenvironments as well as their expression of the PD-1 immune checkpoint and the anti-cancer cytokine IFN-λ. Hypothesising that MMR-D tumours would exhibit increased cDC1 dendritic cells, PD-1 and IFN-λ compared with the MMR-P cancers. Ancillary, we aimed to assess the effect of anti-PD-1 therapy over time on the expression of IFN-λ within serum samples of melanoma patients, hypothesising that circulating levels would increase throughout treatment.

Method
Antibodies directed towards PD-1, IFN-λ and human leukocyte antigen-DR isotype (HLA-DR) were optimized through immunohistochemistry (IHC) on MMR-D and MMR-P CRC tumours. Subsequently, preliminary series staining MMR-D and MMR-P CRCs for HLA-DR and IFN-λ infiltration were performed and analysed for comparison. Immunofluorescence (IF) was performed on these antibodies and a number of additional antibodies to distinguish the distinct dendritic cell subsets.

Results
Antibodies directed towards PD-1, IFN-λ and HLA-DR were identified and optimized for future use in IHC and IF for IFN-λ and HLA-DR. Comparative series of MMR-D and MMR-P CRCs revealed average percentage tumour area staining of 11.49% and 11.50% for HLA-DR (p=0.34) and 1.01% and 0.38% (p=0.29) for IFN-λ.

Conclusions
This study was an important first step in assessing the role of DCs in anti-PD-1 immunotherapies. Preliminary findings from this work suggest MMR-D and MMR-P CRCs exhibit distinct patterns of IFN-λ expression prior to treatment. However, further antibody optimization and immunofluorescence must be performed to assess DC infiltration. Testing of larger sample sizes is necessary in order to draw distinct conclusions. Circulating levels of IFN-λ must also be assessed throughout treatment.

In 2018 I undertook a Bachelor of Medical Science (Honours) degree after completing my fourth year of medical school. I hoped to learn about the processes of how research goes from the translational stage to eventually being implemented into clinical practice. I find the breakthroughs in oncology research to be fascinating and was excited to see how things function at the cutting edge of medical research.

The Translational Oncology Research Group proved to be a great group, allowing me to experience all aspects of the research process, from establishing a project to conducting and analysing the results myself. I would highly recommend future students consider them for honours projects in the future.

In 2018 I undertook a Bachelor of Medical Science (Honours) degree after completing my fourth year of medical school. I hoped to learn about the processes of how research goes from the translational stage to eventually being implemented into clinical practice. I find the breakthroughs in oncology research to be fascinating and was excited to see how things function at the cutting edge of medical research.

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Atrial Fibrillation at a Victorian tertiary metropolitan hospital

Professor Danny Liew
School of Public Health and Preventive Medicine
Chair of Clinical Outcomes Research, Monash University
Head of the Division of Clinical Epidemiology, Monash University
Co-Director of the Centre of Cardiovascular Research and Education (CCRET)
Consultant physician at the Alfred Hospital in Clinical Pharmacology and General Medicine.

ABSTRACT

Background
Atrial fibrillation (AF) is the most common cardiac arrhythmia and a significant cause of morbidity and mortality. The pathophysiology, outcomes and classification remain disputed, and while hospital data and epidemiological information exist for the condition, there are many gaps in understanding, particularly in an Australian context.

Method
This study was a retrospective cohort study, utilising administrative data from The Alfred Hospital collected from 1 January 2013 to 30 June 2018. The primary analyses used inpatient admissions as the units of measure. Descriptive analyses were undertaken of patient characteristics (sex, age, Charlson comorbidity index), burden of care (length of stay and costs), and outcomes (readmissions, complications, and mortality). Central tendency and variance of numerical data were described using medians and interquartile ranges (IQR), given the strong positive skew of data. Categorical data were described by percentages. In ‘associative analyses’, the positive skew of outcome data meant that negative binomial regression was used for non-binary outcomes, while logistical regression was used for binary outcomes. Secondary analyses were performed using individual patients as the units of measure.

Results
There were 10,251 admissions of interest in the study period, involving 7,387 unique patients. A higher percentage of admissions were for men (56.63%), with the median (IQR) age at admission being 75 (65, 84) years, and the median (IQR) and mean (standard deviation (SD)) Charlson comorbidity index score being 1 (0, 2) and 1.37 (1.93), respectively. The median (IQR) LOS was 4 (1, 9) days, with a median (IQR) cost of AUD $6,258 ($3,331, $11,884). All admissions involved at least one in-hospital complication, with the median (IQR) number of complications being 9 (5, 15). Of the admissions, 11.65% resulted in death, and 7.14% of admissions involved readmissions for AF within 30 days of discharge. A higher Charlson comorbidity index score was predictive of longer LOS, higher costs, a higher number of in-hospital complications and in-hospital death, while being male was predictive of higher costs, a higher number of in-hospital complications and in-hospital death. Increasing age was predictive of longer LOS, lower costs, a higher number of in-hospital complications and in-hospital death.

The results of the secondary analyses (based on individual patients) were similar to those of the primary analyses. Among the study patients, 75.96% only had a single admission during the study period, 6.00% had a readmission for AF of any classification within 30 days of whom 92.43% readmitted with a primary diagnosis of AF; 18.43% within a year, with 94.00% readmitted with a primary diagnosis of AF. Analyses of longitudinal outcome data found that 16.43% of admissions involved at least one in-hospital complication, with the median (IQR) number of complications being 9 (5, 15). Of the admissions, 11.65% resulted in death, and 7.14% of admissions involved readmissions for AF within 30 days of discharge. A higher Charlson comorbidity index score was predictive of longer LOS, higher costs, a higher number of in-hospital complications and in-hospital death, while being male was predictive of higher costs, a higher number of in-hospital complications and in-hospital death. Increasing age was predictive of longer LOS, lower costs, a higher number of in-hospital complications and in-hospital death.

Conclusions
AF imposes a large, and growing, burden of hospitalised care in Australia, with high risk of morbidity and mortality. The consistent association of Charlson comorbidity scores with burden of care and outcomes highlights the importance of recognising comorbidities in this patient population.
Background

Imaging has played an increasingly dominant role in the diagnosis and localisation of prostate cancers. Prostate Specific Membrane Antigen (PSMA) ligands in PET imaging show superior results compared to traditional prostate cancer imaging techniques. These have mostly been studied in the context of recurrent staging of prostate cancers. Simultaneous PSMA PET/MRI is an emerging modality yielding strong initial results in the localisation of primary prostate cancers.

Objectives: To compare the diagnostic accuracy of multiparametric MRI, PSMA PET/MRI and PSMA PET/CT to whole-mount histopathology for localisation of primary prostate cancer.

1. Localisation and characterisation of significant primary prostate cancers on PSMA PET/MRI compared to PSMA PET/CT and multiparametric MRI.

2. Compare the accuracy of these modalities to whole-mount prostate histopathology specimens.

Method

A prospective database for patients who underwent mpMRI in our group urology practice since 2013 was used. 13 patients underwent mpMRI, 68Ga-PSMA PET/CT, 68Ga-PSMA PET/MRI and subsequent radical prostatectomy with whole-mount histopathology. Imaging was reported based on PIRADS sector maps, with results analysed by dividing the prostate into 12-sectors. The histopathology was matched to imaging with the 12-sector prostate map. Diagnostic performance of each modality was assessed using sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio and accuracy. Receiver Operating Characteristics analysis was used to compare modalities. Significant cancer defined as greater than or equal to Gleason 3+4=7 (Grade Group 2).

Results

Analysis was based on 156 sectors from 13 patients. Whole-mount histopathology reveals significant cancer in all 13 patients, with positive tumour detection in 59 of 156 sectors (37.8%).

mpMRI detected lesions in 36 sectors, of which 31 were true positives, and no lesion in 120 sectors, of which 92 were true negatives. 68Ga-PSMA PET/CT demonstrated avidity in 32 sectors, of which 25 were true positives, and no avidity in 124 sectors, of which 90 were true negatives. 68Ga-PSMA PET/MRI demonstrated avidity in 36 sectors, of which 32 were true positives and no avidity in 120 sectors, of which 93 were true negatives. The overall accuracies were 71%, 63% and 75% respectively.

mpMRI, 68Ga-PSMA PET/CT and 68Ga-PSMA PET/MRI each conferred a sensitivity and specificity of 50.85%/94.85%, 42.37%/92.78% and 54.25%/95.88% respectively.

Conclusions

In this pilot study involving high selected patients undergoing prostate mpMRI, 68Ga-PSMA PET/CT, 68Ga-PSMA PET/MRI and subsequent radical prostatectomy with whole-mount histopathology, 68Ga-PSMA PET/MRI outperformed both mpMRI and 68Ga-PSMA PET/CT in accurately detecting and localising significant primary prostate cancer. As a diagnostic technique, pelvic PSMA PET/MRI is an emerging modality, and as such requires further investigation and cost-effectiveness analysis. Expansion into whole-body 68Ga-PSMA PET/MRI imaging could lead to an all-in-one diagnostic and staging modality for prostate cancer.
Laura Panozzo

Communication and Implementation of Advance Care Planning in Regional Victoria.

Dr Bernadette Ward – Monash School of Rural Health
Ms Pam Harvey – Monash School of Rural Health
Dr Dennis O’Connor – Monash School of Rural Health
Dr Jason Fletcher – Bendigo Health

Relocating to Bendigo to complete my BMedSc(Hons) project was a big leap faith – and it most certainly paid off. The support from all staff at the School of Rural Health was sensational. In particular, I would like to extend my gratitude to my academic supervisors, Dr Bernadette Ward and Ms Pam Harvey. The scope of this project was not feasible in a metropolitan setting; it was fantastic to have the opportunity to interact with both the ICU and all general practices in the local area. This year has reignited my passion for high-quality, regional healthcare while engaging my interest in continuing with research in the future. I would strongly recommend that any future student who is considering a BMedSc(Hons) project consider completing a project with the School of Rural Health.

ABSTRACT

Background
Advance Care Planning (ACP) is a process that can empower competent individuals to make decisions regarding their future medical care. An Advance Care Plan (Plan) is a written declaration of these wishes which can be referenced by health practitioners so that medical care is provided in alignment with that individual’s preferences and values. The prevalence of Plans in Australia is low, and it is unclear how these ACP documents are communicated from their recommended point of uptake in general practice to a hospital service. The content of Plans and whether preferences are implemented when an individual loses decision-making capacity has had very limited research. The aim of this project was to measure the prevalence, communication and implementation of ACP documents for decedents aged 75 years and over in a regional setting in 2016 – 2017.

Method
Three consecutive retrospective decedent medical record audits with feedback were conducted. These assessed the uptake (prevalence), communication and implementation of ACP alerts and documents for decedents aged 75 years and over who died in the study hospital between 1 January 2016 and 31 December 2017. For the purposes of this study, an ACP document could include: a Plan; a Refusal of Treatment Certificate; an Enduring Power of Attorney (Medical Treatment); or an Enduring Power of Guardianship. The prevalence of Plans in Australia is low, and it is unclear how these ACP documents are communicated from their recommended point of uptake in general practice to a hospital service. The content of Plans and whether preferences are implemented when an individual loses decision-making capacity has had very limited research. The aim of this project was to measure the prevalence, communication and implementation of ACP documents for decedents aged 75 years and over in a regional setting in 2016 – 2017.

Results
Of the 536 decedent hospital records audited, the majority did not have any ACP alerts (n=110; 79.5%) or documents (n=96; 82.1%). Only 9.7% (n=52) of hospital decedent records contained a Plan. Of those with no hospital record ACP alert, 14.6% of decedent general practice records with a GP in the immediate surrounding local government area contained at least one ACP document that was created, but not communicated, to the study hospital. This included four Plans.

The content of the Plans that were available in hospital records were divided in their preference for (44.2%) or against (50.0%) life-prolonging treatment. In some cases, Plan preferences were not implemented. This included cases where a Plan explicitly preferenced against a treatment and it was given, including intubation, surgery, antibiotics and medication.

Conclusions
The use of ACP to ensure a patient’s preferences and values are respected is currently hindered by low Plan prevalence, inconsistent communication of documents from general practice to a hospital service and variable Plan implementation. By refining medical record systems and proposing methods of consistent communication, existing ACP documents can be identified and referenced during end-of-life care. Future work should include identifying populations that could benefit most from having a Plan, such as those who are socially isolated and do not have a substitute decision-maker.
Jessica Paynter

A multicentre comparison of the contemporary management of Dupuytren’s disease.

Associate Professor David Hunter-Smith
Professor David Warren
Department of Plastic and Reconstructive Surgery, Peninsula Clinical School.
Central Clinical School, Monash University.

ABSTRACT

Background
Collagenase Clostridium Histolyticum (CCH) is a novel treatment for Dupuytren’s disease (DD) within Australia. However, the delivery of CCH as a therapeutic is believed to be variable within the public sector. The effectiveness and safety of CCH for treating DD has not been assessed or documented within the Australian public health sector, nor the Victorian population itself.

Method
This ongoing multicentre, observational comparative study included a consecutive cohort of adult patients with DD being treated with CCH within the Victorian public health system. The exclusion criteria varied according to each individual clinic. Assessment occurred at three time-points; injection, manipulation and follow-up. Injection was day one across all clinics, yet the manipulation and follow-up time-point varied and formed a part of this investigation. Assessment of the therapeutic effect of CCH was made objectively using the Total Passive Extension Deficit (TPED), clinical success and clinical improvement. Patient perception of CCH effectiveness was subjectively assessed using three Patient Reported Outcome Measures (PROMs); Unite Rheumatologiquedes Affections de la Main (URAM), Southampton and the Canadian Occupation Performance Measure Patient Set Questionnaire (PSFS). Analysis was undertaken using median values, analysis of variance and mixed effects logistic regression to determine if CCH outcomes were affected by clinic design.

Results
Qualitative analysis
The delivery of CCH is variable across all Victorian public health clinics. Differences are observed at injection, manipulation and follow-up of people with DD. At injection the adoption of anaesthetic, assessment of disease severity, technique and monitoring differs across all clinics. Manipulation is variable by time frame (two to seven days), location (outpatients or theatre) and anaesthetic use itself. Follow-up is different across all clinics via both length and time.

Quantitative analysis
Seven public clinics were observed across this project; 30 clinics at Frankston Hospital, two at Dandenong Hospital, three at Austin Hospital, two at Maroondah Hospital and one at Northern, Box Hill and Geelong Hospital. Currently only patient data for Frankston and Dandenong Hospital is available for analysis. 209 and 36 patients respectively at Peninsula Health (PH) and Monash Health (MH) were treated with CCH. Clinical success was achieved in 42% of the Frankston and 35% of the Dandenong cohort. Clinical improvement was achieved in 78% of the Frankston and 86% of the Dandenong cohort. A statistically significant reduction in all three PROMs was observed at both the Frankston and Dandenong cohorts. A two way repeated measures for effectiveness (clinical success, clinical improvement, TPED and PROMs) across both centres found nil statistical significant difference between the two cohort’s results. CCH clinic design does not impact upon outcomes.

Conclusions
The delivery of CCH is variable across public hospital clinics in Victoria. CCH clinic design does not impact upon the effectiveness of CCH at first review. CCH is effective and safe for treating people with DD in Victoria, Australia. CCH results in improved patient reported functional outcomes. Furthermore, it has led to reduced contracture degree, as reported by the outcomes of clinical success, clinical improvement and TPED.
Regularity Learning in Schizophrenia and Psychosis

I chose to undertake a Bachelor of Medical Science following my fourth year of Medicine to experience a different side of the medical profession. I have always been interested in psychiatry, in particular improving outcomes and quality of life for those experiencing mental illness. This project not only allowed me to contribute to research that may help to improve these outcomes, but also provided me with valuable clinical experience on a psychiatric ward. I learned important techniques in data collection and analysis that have given me a good foundation for future research practice. In all, I found this to be a highly enjoyable and rewarding year, which I would definitely recommend to future students!

**ABSTRACT**

**Background**

Schizophrenia is a disabling psychiatric illness, characterised by delusions and hallucinations. These symptoms may cause significant distress and impaired functioning in affected individuals, however their pathology is not well understood. Recent theories in computational psychiatry have proposed that these symptoms may arise from an impaired ability to store, and use knowledge of regularities in the sensory environment to influence current perception. However, no previous study has specifically examined ‘regularity learning’ in schizophrenia. Moreover, the relationship between regularity learning and psychotic symptoms remains poorly defined. We therefore aimed to examine whether regularity learning is impaired in schizophrenia, and if this impairment is associated with the severity of psychotic symptoms. In addition, we aimed to examine if regularity learning deficits are associated with the occurrence of ‘psychotic-like’ experiences in healthy individuals and across other psychiatric diagnoses.

**Methods**

44 psychiatric inpatients (22 schizophrenia spectrum disorder, 22 non-psychotic controls) and 22 healthy controls were administered an auditory regularity learning task. Psychotic-like traits were assessed for all participants. Psychotic symptom profiles of inpatients were also scored.

**Results**

Participants with a schizophrenia spectrum disorder made significantly more errors in regularity learning than healthy controls. Regularity learning errors were positively associated with the severity of positive ‘psychotic-like’ traits occurring in all study participants.

**Conclusions**

These results suggest that regularity learning is impaired in schizophrenia. In addition, they suggest that regularity learning deficits may be involved in the pathology of psychotic symptoms, such as delusions and hallucinations. This finding was not specific to schizophrenia, and may point to a similar mechanism underlying psychotic experiences at both the subclinical and clinical level. However, larger trials are necessary to better define this relationship.
How does age of trauma exposure influence the relationship between early life adversity and dissociation?

Professor Jayashri Kulkarni – Monash-Alfred Psychiatry Research Centre, Monash University
Dr Caroline Gurvich – Monash-Alfred Psychiatry Research Centre, Monash University
Dr Natalie Thomas – Monash-Alfred Psychiatry Research Centre, Monash University

ABSTRACT

Background
Borderline Personality Disorder (BPD); a diagnosis now recognised to be on a stress-trauma spectrum along with complex Post-Traumatic Stress Disorder (cPTSD) is a condition which has debilitating effects on everyday quality of life, and for which there are few effective treatment options. This is in part attributable to the heterogeneity of the condition, with many different symptoms leading to the same diagnosis. Dissociation is often associated with BPD, and better understanding of key symptoms, and the development of BPD helps to better define the condition and consequently improves treatment outcomes. Early life trauma is thought to play a significant role in the development of dissociation, and this study explores this relationship; specifically the age at which early life trauma was experienced and the type of trauma experienced.

Aims/Hypotheses:
The aims for this study were to a) determine whether the age of an individual at the time of trauma affects the severity of dissociation as an outcome, b) identify whether the type of trauma affects the severity of dissociation as an outcome, and c) conduct an exploratory analysis to ascertain if there are specific age groups within each category of trauma which affect the severity of dissociation as an outcome. It was hypothesised that the results would show differences in long term outcomes different types of trauma experienced and between trauma experienced at different ages.

Method
Twenty-five participants were recruited, all of whom had experienced early life trauma as determined by the Maltreatment and Chronology of Exposure (MACE) scale, and dissociative symptoms as recorded using the Dissociative Experiences Scale (DES). These participants also completed the Life-Experiences Checklist (LEC-5) to determine whether the participants felt that they had experienced trauma to compare with their MACE scores. Dissociation scores (DES) were then compared across different age groups, and different trauma types to test if there were any significant factors of trauma exposure that were influencing dissociative outcomes. Statistical analyses were conducted using Generalised Linear Models (GLMs) and Mann-Whitney U tests to test for significance.

Results
We found that early life trauma occurring between 6-18 years, was significantly associated with the development of dissociative symptoms in adulthood. Moreover, the trauma categories of parental verbal and physical abuse, emotional neglect and peer emotional abuse were also significantly associated with dissociation. The exploratory analysis considering the age that each trauma type is experienced, suggested that experiencing parental physical abuse between 6-10 years and peer emotional abuse between 11-18 years was significantly associated with dissociation.

Conclusions
The findings from this study support the existing literature, in that there is a link between early life trauma and the development of dissociation, and that the age that trauma is experienced as well as the type of trauma experienced both have a significant impact. It is important to understand the roles that these factors have in the aetiology of dissociation, a symptom of BPD and cPTSD, allowing us to better characterise the diagnoses and more effectively treat patients with these diagnoses.

Sai Ponnaganti

I chose to undertake my Bachelor of Medical Science (Honours) at the Monash-Alfred Psychiatry Research Centre with the Women’s Mental Health Team after completing 4th year. Psychiatry has always been a field that has fascinated me and after completing my mental health rotation at The Alfred, the impacts and consequences of childhood trauma stood out as an area of interest that I wanted to learn more about. My project was clinical and allowed me to practice skills such as history taking and phlebotomy which I greatly enjoyed.

While there were ups and downs over the course of the year, I can confidently say that I have developed several skills that I had not experienced during medicine, such as designing a clinical study, writing a research paper, and learning to conduct statistical analyses. I also want to stress the importance of choosing a lab and supervisor who you feel comfortable with! It absolutely defines how great your year will be, and I was fortunate enough to work with an amazing team.

It has overall been a very rewarding year, and I wholeheartedly recommend undertaking a BMedSc(Hons) to anyone considering one! Don’t hesitate to contact me if you have any questions (spon13@student.monash.edu).
Kirby Qin

Extended Peripheral Intravenous Catheters in Paediatric Surgery: A Randomised Controlled Trial (The EPIC Trial)

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ABSTRACT

Background

In paediatric surgery, many children require multiple days of intravenous (IV) therapy after an operation. Intravenous therapy is generally administered through a peripheral intravenous catheter (PIVC). PIVCs are widely used and readily available, however, there is growing evidence to suggest that they are inappropriate for more than 48 hours of therapy. As a result, a longer, more durable catheter has been developed: the long peripheral catheter (LPC). They are 6-15cm long compared to PIVCs which are 2-6cm. Randomised controlled trials (RCTs) have shown LPCs to have superior outcomes compared to PIVCs in adults. Paediatric research is limited to observational studies which have shown that LPCs are safe and well-tolerated.

The aim of this study was to determine if LPCs would demonstrate improved duration of action, reduced failure rates, reduced postoperative IV cannulations and increased patient satisfaction.

Methods

This was an open-label RCT involving paediatric surgical patients requiring >48 hours of postoperative IV access. Participants were randomised to receive either a standard PIVC or an 8cm 22G LPC, inserted intraoperatively under general anaesthesia. The allocated catheter was used to deliver IV therapy on the inpatient ward. Throughout their admission, participants were monitored daily to assess catheter function. If the allocated catheter failed on the ward, participants were subsequently treated with PIVCs. In addition, cost-effectiveness analysis was performed and parental satisfaction was assessed by means of a questionnaire. Parametric data is presented as median [range] and non-parametric data is presented as mean ± standard deviation.

Results

Although recruitment is still ongoing, 50 patients are documented in this interim analysis – 26 in the PIVC group and 24 in the LPC group. Gender, age, weight and emergency status were similar between groups. The median duration of IV therapy was 5.1 days [2.1-16.1]. The mean duration of PIVCs and LPCs was 3.8 ± 1.9 days and 4.3 ± 1.4 days respectively (p=0.38). Patients in the PIVC group received a median of 2 [1-4] catheters compared to 1 [1-3] in the LPC group (p=0.005). Furthermore, patients with LPCs were more likely to complete postoperative treatment with a single catheter (70.8% vs. 38.5%, p=0.02). The rate of catheter failure was higher for PIVCs than for LPCs (65.4% vs. 29.2%, RR 2.2, p=0.01; 170 vs. 71.1 failures per 1000 catheter-days). Infiltration was the most common complication; 34.6% of PIVCs infiltrated compared to 4.7% of LPCs (RR 8.3, p=0.007). Parental satisfaction was higher for LPCs for all domains, although only ‘Pain and discomfort due to IV access’ (p=0.007) and ‘Overall satisfaction’ (p=0.02) were significant. The average cost of insertion (including theatre costs) was $97.50 AUD for PIVCs and $263.00 AUD for LPCs.

Conclusions

In children receiving surgery, intraoperative insertion of LPCs is a feasible and effective procedure. Preliminary results indicate superior outcomes in the LPC group. LPCs succeeded in reducing postoperative IV cannulations and the incidence of catheter failure. Patients also indicated a clear preference for the LPC.
Camilla Sophi Ramadhanti

The Role of Nox5 in the Akita Mouse Model of Diabetic Nephropathy

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Dr Jay C Jha

ABSTRACT

Background
Diabetic nephropathy (DN) is one of the most common diabetic complications and the leading cause of end stage renal disease worldwide. DN development and progression is contributed by metabolic and hemodynamic changes, which inevitably increase the production of reactive oxygen species (ROS). NADPH oxidase is the major source of ROS in the kidney, with several Nox isoforms have been identified for their role in the progression of DN. Based on recent evidences, Nox5 expression is found to be upregulated in diabetes, suggesting its possible role in DN. However, Nox5 is expressed in humans, but not in rodents. Therefore, there is a paucity of data regarding its role in DN.

Aim
To investigate the role of Nox5 in the development and progression of DN using endothelial cell specific (using VE-cadherin promoter) Nox5 transgenic Akita mice in the absence or presence of diabetes.

Method
Nox5 transgenic Akita mouse with Insc gene mutation was used to create spontaneous T1DM. After 10 weeks, urine and blood sample were collected for metabolic data and renal function measurement. Kidney tissues were collected and assessed for renal structural injury as well as gene and protein expression of pro inflammatory, pro fibrotic, and oxidative stress parameters.

Result & Conclusion
Metabolic parameters showed a decrease in body weight, elevated blood glucose and glycated haemoglobin, an increase in food and water intake as well as urine output in diabetic mice groups compared to the respective control groups, with no difference observed among the diabetic groups when subjected to Nox5 expression. Significant increase in albuminuria and expression of pro fibrotic and pro inflammatory genes (collagen III, fibronectin, α-SMA) were observed in VEcad+Nox5+ groups compared to VEcad+Nox5- in the presence of diabetes. Nox5 expression selectively in endothelial cells worsen the renal function and upregulated the expression of pro-inflammatory and pro-fibrotic genes in the renal cortex of diabetic mice.
Teenage pregnancy is associated with negative outcomes for both mother and child. While the rates of teenage pregnancy in Australia have declined, there are still areas of relative high-risk in Victoria. Effective contraception can prevent unintended pregnancies and general practitioners (GPs) are the first-line providers of prescription contraceptives. In high-risk areas for teenage pregnancy, GPs may face additional barriers accessing and providing contraceptive counselling to teenage women. The aim of this study is to explore GP insights into the provision of contraceptive counselling and to determine if GPs perceive any additional challenges when providing contraceptive counselling in the context of a high-risk area for teenage pregnancy.

Method
A qualitative study design was utilised for this project using a constructivist grounded theory approach. Semi-structured, in-depth telephone interviews were conducted with 18 GPs purposively sampled from high-risk local government areas as defined by the Victorian Women’s Health Atlas. Interviews were transcribed verbatim and imported to NVivo 11 for management. An inductive and iterative data analysis approach was used to develop themes.

Results
We identified three major themes from the interviews. Firstly, GPs believed they provided best-standard care when delivering contraceptive counselling to teenagers; however, many did not offer all contraceptive options which may have impacted a teenager’s ability to make an informed, empowered contraceptive choice. Secondly, most GPs recognised that the teenagers in their area were a vulnerable group and required targeted contraceptive counselling that also addressed wider social issues. There were additional challenges reported in engaging this group in contraceptive counselling as

Conclusions
Our study explores GPs’ insights into providing contraceptive counselling within high-risk regions for teenage pregnancy. GPs reported additional challenges at a patient and structural level and their own biases and misperceptions, which can be targeted with interventions to improve the standard of contraceptive counselling and potentially reduce teenage pregnancies. Our findings also suggest there is limited knowledge of the high-risk for teenage pregnancy amongst GPs in high-risk areas. Educating GPs to improve awareness of the high-risk for teenage pregnancy may improve the delivery of counselling and help target vulnerable teenagers.
A Qualitative Analysis on the Perceived Barriers and Enablers to Falls Prevention Implementation in the Acute Hospital Setting

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ABSTRACT

Background
Studies examining the effectiveness of falls prevention programs have been the focus of research attention as falls remain the most common adverse event in the hospital setting. However, there is limited research exploring the barriers and enablers to the implementation of falls prevention programs. 6-PACK was a nurse-led falls prevention program implemented in six hospitals in Australia. The 6-PACK RCT was the world’s largest falls prevention falls prevention trial. Unfortunately, the trial results demonstrated that 6-PACK did not reduce in-hospital falls. To understand the contextual factors impacting on the trial results, this study collected qualitative data from senior hospital staff and nurses post-implementation of the 6-PACK program.

Aim
To explore the perceived barriers, enablers, and sustainability factors to implementation of the 6-PACK program.

Method
Seven focus groups with nurses and 13 interviews with hospital senior staff. Data analysis was guided by the COM-B framework. This framework includes capability, opportunity, and motivation factors that interact to create behaviour change.

Results
Small hospital rooms, belief that falls were inevitable, privacy issues during bathroom supervision, insufficient staffing levels, lack of resources to implement 6-PACK strategies, ineffectiveness of 6-PACK facilities, and staff juggling multiple projects were identified as barriers to 6-PACK implementation. Enabling factors included one-on-one education during ward round, senior staff leadership and support, nurses’ positive attitudes towards 6-PACK, provision of audit-feedback-reminder, and staff held accountable for program implementation. In order to sustain the program, the hospitals must continue ward-champion role as project leader, introduce 6-PACK to future nursing staff, provide ongoing audit and feedback, encourage staff involvement in 6-PACK implementation, and adopt 6-PACK for hospital-wide implementation.

Conclusions
This study identifies the perceived barriers, enablers, and sustainability factors to falls prevention program implementation from the perspective of hospital staff. These results can be used in the design future falls prevention programs and implementation strategies.
Antonia Rowson

Single-cell RNA Sequencing to Understand Inflammatory Disease Mechanisms

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ABSTRACT

Background

The pathophysiology driving inflammatory diseases such as giant cell arteritis (GCA) is incompletely understood, preventing the development of targeted therapies. As such, glucocorticoids and other non-specific anti-inflammatory medications are the principal treatments for many inflammatory conditions, with a host of subsequent adverse effects. Single-cell RNA sequencing (scRNA-seq) provides a means of characterising the activity levels of every gene within a cell. Hence, scRNA-seq offers an unparalleled means of asserting the specific contribution of each gene to a pathological cellular state, instead of merely documenting correlations between specific alleles and disease states. We aimed to compare the gene expression profiles of individuals with systemic inflammatory disease with individuals of non-inflammatory phenotype via scRNA-seq in a Caucasian population.

Methods

1,010 participants provided demographic data on sex, age, gender, smoking status, and ethnicity, and gave a peripheral blood sample. After initial scRNA-seq preparation and assessment of cell count and viability, samples were outsourced for further genomic and scRNA-seq analysis; this analysis is still ongoing. Meanwhile, data was retrieved from medical records available for 550 participants regarding health status and medications. A sub-group of 45 individuals with systemic inflammatory disease was identified, and demographic details of this group were compared with the rest of the cohort. A temporal artery tissue sample was taken from one patient with GCA, in addition to a blood sample, and enzyme dissociation of this temporal artery tissue was attempted as an initial step in comparative analysis of cells from the temporal artery and peripheral blood cells.

Results

Of the non-inflammatory cohort of participants, mean age was 63.55 years, and 42.90% were male. Of the inflammatory sub-group, mean age was 70.84 years, and 35.56% were male. Age was statistically significant between the two groups (p = 0.0036), and conformed to a normal distribution. There was no significant difference between groups with regard to sex (p = 0.3583) or smoking status (p = 0.3945). Following scRNA-seq preparation, peripheral blood mononuclear cell samples of the non-inflammatory cohort yielded on average 3.452 x 10^6 cells each, with a mean 91.86% of cells viable. Mean cell count of the inflammatory group was 3.703 x 10^6, with average viability of 91.82%. Neither cohort was significantly different by these two outcomes (p = 0.6306 for cell count, p = 0.7920 for viability). Temporal arterial tissue dissociation was unsuccessful, with a cell count of 1.23 x 10^5 and 0% viability.

Conclusion

As genomic and scRNA-seq data is as yet unavailable, we are currently unable to assess the aims of our study. However, consideration of demographic data allows us to posit the validity of the awaited study results. Based upon normal distribution of age and relative similarity with other demographic factors of the Australian population generally, the study cohort is likely a fairly representative sample from which to draw conclusions about normal cellular gene expression, and the similarity between the inflammatory and non-inflammatory subgroups, except as regards mean age, also suggest a fair basis for comparison.
Improving the prediction and diagnosis of pre-eclampsia: validation of a novel biomarker assay

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I completed fourth year in 2017, and thought a BMSci would be a good change of pace from clinical medicine. I chose an Obstetric clinical/lab project mainly because of how much I enjoyed O&G last year.

It’s been a fantastic year, but if you do something lab-based it can be a very different skill set, so you’ve got to be prepared to learn new things and work quite hard, depending on the demands of the project. That said, the Ritchie Centre is a great place to do a lab-based project, because there are lots of other students working there who will help and support you. Also, if you don’t know something in the lab, Googling it works more often than not from personal experience.

Your supervisor and team are very important, and I was incredibly lucky in mine. If you’re unsure whether or not you want to do one, my advice would be to go for it.
Heart Failure (HF) is a complex clinical syndrome characterized by the reduced ability of the heart to pump blood to complete the needs of the body. In this study we will focus on chronic heart failure and defined HF as chronic heart failure. HF is associated with multiple comorbidities that leads to or may affect the development of HF and the patients’ outcome. Moreover, comorbidities also appear as an important determinant of health care cost. Although there are a number of studies on the prevalence and incidence of HF, however relatively few studies have described data on common comorbidities in HF patients, particularly in the Australian primary health care setting.

Method
This study used a cross-sectional study design. Data was obtained clinical practice software of n=676 GPs from across all states and territories of Australia pertaining to their patients with HF treated in the period 2011-2016. De-identified patient information regarding age, sex, risk factors and comorbidities was obtained for patients recorded as having HF.

Results
This study found that hypertension is the most common comorbidity (33.1%) among nine selected comorbidities (i.e. hypertension, arthritis, diabetes, hyperlipidaemia, renal disease, depression, chronic obstructive pulmonary disease (COPD), anaemia, and chronic pain) and most common across all age groups in 7093 HF patients ranging in age from 18-115 years. Significant gender difference were found for arthritis, diabetes, renal disease, COPD, depression and chronic pain (p<0.01). Further, significant differences between age groups were observed for proportions of patients with arthritis, renal disease and COPD. We also found that hypertension and arthritis is the most common comorbidity pairs in our study. Increasing number of GP visits were observed with comorbidity burden ranging from an annual average of 17 visits for those with two comorbidities up to an annual average of 24 visits for more than five comorbidities.

Conclusions
Management strategy for HF patients with comorbidities in Australian primary setting should be considered particularly for HF patients with hypertension and HF patients with hypertension and arthritis.
IDENTIFICATION OF PREDICTORS OF CRITICAL BLEEDING IN CARDIOTHORACIC SURGERY PATIENTS AND VARIATIONS IN PATIENT BLOOD MANAGEMENT

Australian and New Zealand Massive Transfusion Registry and Australia and New Zealand Society of Cardiac and Thoracic Surgeons Cardiac Surgery Database Data Linkage

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ABSTRACT

Introduction
One Australian dies every 12 minutes due to cardiovascular disease (CVD). Cardiothoracic surgery (CTS) is a common intervention for treating serious CVD. Critical bleeding (CB), which necessitates massive transfusion (MT), is one of many risks of CTS. A study on prediction of CB/MT, using the MT definition of ≥5 RBC units transfused in any 4 hours, with an Australian CTS cohort has not been done. The aims of the project were to identify: 1) patient or procedure variables that can predict CB in CTS, and 2) variations indicative of differences between hospitals in perioperative patient blood management (PBM) and transfusion strategies by conducting a data linkage with the ANZ-MTR and ANZSCTS databases.

Methods
Inclusion criteria for the total cohort were: patient ≥18 years of age at time of CTS, underwent CTS indicated by ACHI procedure codes, data came from hospitals participating in both ANZ-MTR and ANZSCTS databases. Test cohort (MT patients) were CTS patients listed in ANZ-MTR (received MT). Control cohort (non-MT patients) were CTS patients not listed in the ANZ-MTR, but from the same sites and same timeframe. Final MT cohort consisted of 665 CB/MT cases from 11 sites between January 2011 to December 2017; and final non-MT with 29,010 cases. Initial variables were chosen based on statistical significance of univariate analysis (significant at p<0.001). The final model used binomial logistic regression. The model was adjusted for site and year of procedure. Statistical significance for categorical variables was determined by the Chi-Square test and the Mann Whitney U test for continuous variables. P-value <0.001 was considered statistically significant for difference between sites and p<0.05 for difference between cohorts within sites.

Results
Patient-related factors predisposing to CB were: lower Body Surface Area (OR 0.38); infective endocarditis at presentation (OR 2.96); worse heart failure, classified as NYHA class IV (OR 1.78); Increased number of diseased vessels (OR 1.24); lower renal function based on eGFR (OR 0.986) (all p<0.001).

Procedural factors included in the model were having aortic procedures (OR 2.83, p<0.001); using Cardiopulmonary Bypass (CPB) (OR 2.52, p=0.003), and having more complex procedures (i.e. Valve surgery, Valve+CABG surgery, and Other CTS) (OR 2.4, 2.11, 2.15 respectively, p<0.001) and any increased urgency of procedure (reflecting patient status and readiness of the surgery team), (OR 2.10 (urgent), 2.88 (emergency), 8.455 (salvage); p<0.001).

Variation between sites was significant for all variables included in the model with indication of significant differences within the sites between MT and non-MT cohorts.

Conclusions
Patient and procedural factors can predict for CB/MT for the population used in this study; patient characteristics and comorbidities appear to be the most important factors that affect rate of CB/MT; mostly impacting complexity and length of procedure and not many of them are modifiable by the surgeon. Variation was apparent between sites, but insufficient data was available to assess differences, if any, in PBM and transfusion strategies. Aims of this project were achieved; but variation due to perioperative blood management could only be partly proven and will require more detailed PBM-related data to be made available.
ABSTRACT

Background

Epilepsy is a serious chronic neurological disease characterised by an enduring predisposition to seizures. Up to 90% of people with epilepsy living in resource-poor countries do not receive antiepileptic drug (AED) therapy. This phenomenon is described as the “treatment gap” and is generally attributed to socioeconomic reasons. However, there has been scant study of this phenomenon in resource-rich specialised settings and the reasons for patients not receiving treatment is not well understood.

The objective of this thesis is firstly to evaluate the scale of untreated epilepsy in a cohort with newly diagnosed epilepsy. Secondly, to examine the risk factors associated with not being treated with AEDs at diagnosis, and finally, understand the individual reasons why patients did not commence with treatment.

Method

Adult patients seen at hospital-based First Seizure and Neurology Clinics for evaluation and management of seizures between 1 May 1999 and 31 May 2016 were screened. Patients with epilepsy diagnosed by the managing neurologist were identified and had their medical records reviewed. Reasons for not being treated and eventually commencing therapy if applicable were captured. Factors that influenced the likelihood of treatment initiation were statistically assessed via penalised logistic regression models.

Results

Of 1317 patients presenting with one or more unprovoked seizures, 611 were diagnosed with epilepsy (61% male; median age at diagnosis: 40 years [IQR: 24-57]). 421 (69%) commenced AEDs at diagnosis. During follow-up (median 5.6 years, IQR: 1.8-8.9), 118 (19%) subsequently commenced AEDs, while 72 (12%) remained untreated by the end of follow-up.

Patients treated at diagnosis were older (OR=1.02, 95% CI: 1.01-1.03) and had lower socio-economic status (OR=0.42 95% CI: 0.18-0.98) compared to those who commenced treatment at diagnosis. An epileptogenic lesion on neuroimaging (OR=1.95 95% CI: 1.16-3.27) and a greater number of seizures prior to diagnosis (OR=2.63 95% CI: 1.39-4.97) were associated with treatment initiation at diagnosis. Among the 427 patients who had more than one pre-diagnosis seizure, those having at least one seizure per year were more likely to be treated compared to those with less than one seizure per year (OR=5.15, 95% CI: 2.53-10.47). Epilepsy type, seizure type, the sleep/awake status when seizures occurred, and epileptiform electroencephalogram were not associated with treatment initiation.

At diagnosis, 101 (17%) patients were not offered treatment, and 89 (15%) declined treatment. The most common reasons for patients not being offered treatment were having had only a single seizure (30% of 101), pending further investigations (29%), and presence of seizure precipitants (22%). The most common reasons for patients declining therapy were unconvinced of the necessity of treatment (48% of 89), unconfident of the diagnosis (17%), and presence of seizure precipitants (13%).

Conclusions

More than 30% of adult patients with newly diagnosed epilepsy had delayed or no AED treatment initiation. Decision making in this patient population is complex and influenced by physician-, patient-, and disease-related factors. Further study is needed to understand the variables contributing to the non-treatment of patients with epilepsy when AEDs are available, and the clinical and health economic consequences of this.
Background
Barrett's oesophagus (BO) is a metaplasia of the oesophageal epithelium and has been strongly linked to development of adenocarcinoma. It is a response to epithelial damage from gastro-oesophageal reflux. Barrier defects resulting from this unfavourable environment predispose the oesophagus to inflammation, metaplasia and dysplasia. However, the underlying genetic drivers of this condition remain unclear. As such, there is a lack of diagnostic biomarkers for Barrett's oesophagus. Grainyhead-like 3 (Grhl3) is a transcription factor from an ancient gene family which is crucial for the development of epithelial barriers. Grhl3 loss is associated with defective barriers in utero and predisposition to tumorigenesis in postnatal life. Our study is the first to investigate the role of Grhl3 in postnatal oesophageal epithelium.

Methods
Using conditional knockout mice, \( \text{Grhl3}^{\Delta/\Delta} \text{L}2\text{-cre/+} \), we studied the effect of Grhl3 deletion in mice ranging from 6 to 12 months of age. We developed a novel barrier permeability experimental model, which involved the injection of fluorescent dye into the oesophageal lumen. Oesophagi were later imaged in cross-section to view the depth of barrier penetration. Furthermore, we examined the squamocolumnar junction in these mice with Haematoxylin and Eosin, Alcian Blue and proliferation markers to identify any metaplastic changes. Lastly, we reviewed the regulation of a series of putative barrier genes using immunohistochemistry and qPCR.

Results
Though Grhl3 does not cause an increase in oesophageal paracellular permeability, it likely causes abnormalities in the keratinised layer. Conditional knockout (CKO) mice are more likely to have an expanded gastric cardia region, which may be a precursor to metaplasia. Additionally, several putative barrier genes were significantly downregulated in the oesophageal epithelium of CKO mice, including Hnr, Vstm5, Sprr2k with Krt10 being significantly upregulated.

Conclusion
Despite intact barrier function, Grhl3 loss likely causes abnormalities of the stratum corneum, consistent with other literature. Grhl3 also may lead to impaired wound-healing in the adult oesophagus and increased metaplastic potential. Future research with similar experiments should be conducted in a reflux model to instigate barrier defects and see if there is impaired tissue repair in CKO mice. This will enable us to further understand the role that Grhl3 has in this tissue and increase knowledge of the pathogenesis of oesophageal metaplasia. One day, Grhl3 may serve as a diagnostic biomarker to improve diagnostic certainty in the context of Barrett’s oesophagus.
Control of respiration in children with sleep disordered breathing

Leon Siriwardhana

Background
Sleep disordered breathing (SDB) is a common sleep disorder in children. It represents a spectrum of severity from primary snoring to obstructive sleep apnoea (OSA) and has been associated with a number of long-term cardiovascular and neurocognitive sequela. SDB in children is caused by an anatomically compromised airway, usually as a result of adenotonsillar hypertrophy. However, there is significant variance in the degree of anatomical susceptibility to airway collapse among children with SDB, suggesting non-anatomical factors may contribute to its development. Instability of the ventilatory control system (high loop gain (LG)) has been postulated as a possible pathophysiological mechanism in adults with OSA. This study aimed to explore the role of ventilatory control instability in children with SDB.

Methods
One hundred and ten children (3-18 years) with SBD and 36 non-snoring controls were studied retrospectively. All children had undergone polysomnography at the Melbourne Children’s Sleep Centre and the scored polysomnography data were obtained for the selected children. Ventilatory control instability was assessed using LG, a measure of the sensitivity of the negative feedback loop that controls ventilation. LG was calculated using standard polysomnography data by first identifying spontaneous sighs that occurred in periods of non-rapid eye movement (NREM) sleep using the nasal pressure trace. A standard model of ventilatory control (gain, time-constant, delay) was then fitted to the post-sigh ventilatory pattern to calculate LG. SDB children were grouped according their obstructive apnoea-hypopnoea index (OAHI): primary snoring (<1 event/h), mild OSA (1-5 events/h) and moderate/severe OSA (>5 events/h). Control children all had an OAHI <1 event/h and no history of snoring.

Results
Groups were matched for age, sex and BMI Z-score. There was no significant difference in LG between the control and SDB severity groups. LG showed no significant relationship to the severity of SDB, although an unexpected downward trend in LG was observed across the groups. A large variance in LG was also observed in all groups. Demographic characteristics and anthropometric measures including age, sex, BMI Z-score, neck circumference, waist circumference, neck-to-waist ratio all showed no significant correlations with LG. However, LG was significantly higher in children with a Mallampati score (estimate of oropharyngeal patency) of class I compared with classes III/IV (median LG [range]: 0.37[0.27, 0.44] vs. 0.28[0.24, 0.33]; p=0.028). LG was also higher in children with smaller tonsil size (tonsil grade 0/1) compared with children with larger tonsils (tonsil grade 4) (0.32[0.25, 0.44] vs. 0.25[0.20, 0.42]; p=0.009).

Conclusion
This study found no direct relationship between ventilatory control instability measured using LG and SDB in children. This suggests that different mechanisms of ventilatory control are involved in the pathophysiology of SDB in children compared with adults. LG as a tool to conceptualize the stability of the ventilatory control system is still evolving. Further research is needed obtain a more comprehensive understanding of the role of ventilatory control in the pathophysiology of SDB in children and its therapeutic implications.

I chose to undertake a BMedSc(Hons) after completing my fourth year of medicine. I have always been intrigued by sleep and decided to combine this with my interest in paediatrics to undertake my honours year at The Ritchie Centre. This year offered me an incredible opportunity to gain valuable insight into the world of research and I thoroughly enjoyed my project, especially attending overnight sleep studies and learning about sleep in children.

I was privileged to benefit from the guidance and mentorship of two highly experienced supervisors; Professor Rosemary Horne and Dr Lisa Walter. Under their patient and dedicated tutelage, I was able to develop a range of highly transferrable skills that will no doubt benefit in my future career. I would highly encourage anyone with an interest in research to consider a BMedSc(Hons).
The serine protease tissue-type plasminogen activator (tPA) is known for its classical role as a clot busting enzyme in the bloodstream. This role has extended to the brain where tPA is the only thrombolytic agent approved for use in humans, during ischaemic stroke. Many further functions of tPA in the brain — both beneficial and detrimental — have been discovered in recent years, including a role in synaptic plasticity. tPA is suspected to facilitate synaptic plasticity through plasminogen-dependent (plasmin-mediated brain-derived neurotrophic factor activation) and independently through its actions on N-methyl-D-aspartate receptor and low-density lipoprotein-receptor related protein — exact mechanisms are unknown. The influence on tPA on synaptic plasticity has been demonstrated in vitro in the hippocampus, and in vivo in the visual cortex. Here we investigated its role in synaptic plasticity in the mouse auditory cortex. Synaptic plasticity is lifelong in the auditory cortex and experience-dependent plasticity has been evoked by the application of other synaptic modulators, such as noradrenaline and acetylcholine in the past. These studies have demonstrated changes in the best frequency of neurons, the frequency that elicits the biggest response, and neuronal bandwidth, the range of frequencies to which the neurons respond.

Aim
To determine if exogenous tPA can influence the tuning of neurons in the auditory cortex, when paired with an auditory stimulus.

Methods
Intracranial injection of exogenous tPA or control substance into the auditory cortex under anaesthesia was paired with the presentation of a single-frequency auditory stimulus — conditioned frequency — in awake mice, to assess if tPA or choice of conditioned frequency being higher (higher pairing) or lower (lower pairing) than the neurons best frequency could influence the tuning of neurons, which would be indicative of synaptic plasticity. Electrophysiological recordings were used to determine the tuning of neurons before and after conditioning, to demonstrate changes in neuronal response, including best frequency and neuronal bandwidth.

Results
tPA application under higher pairing significantly influenced the tuning of neurons, causing a best frequency shift away from the conditioned frequency (p<0.001), whilst the inverse effect of a shift towards the conditioned frequency was produced in the tPA lower pairing condition (p=0.024). tPA also significantly influenced the strength of the response to the post-conditioning best frequency, relative to the pre-conditioning best frequency, but only in the higher pairing condition (p=0.002). Changes in the tuning of neurons were also attributed to pairing choice in control conditions, namely when higher pairing was employed. However, these results showed the opposite pattern as the tPA condition, with significant best frequency shifts towards the conditioned frequency.

Conclusions
The known synaptic modulator tPA is capable of producing changes in the tuning of neurons of the auditory cortex, indicative of synaptic plasticity that have not previously been described. These changes appear to be stimulus-dependent, as tPA application produced opposite effects dependent on whether the frequency chosen for conditioning was higher or lower than the best frequency of the neurons. This effect has not been previously described, and the mechanism by which tPA produced these effects is unclear.

I was on 3rd year placement in Mildura, when I first contacted my soon-to-be supervisor, Rob, about an interesting project in Melbourne. The project seemed like a good fit, until I learnt of a similar project, this time in the brain, at Newcastle University in the UK.

Of course, my interest in the complexity of the brain, as well as my love of travel and leaving my comfort zone meant that by the end of 2017, my bags were packed, and I was off to the heart of Geordie-land, Newcastle upon Tyne in the North East of England (with a stop in Uganda and Spain along the way).

From the moment I set foot in England everything was new, I’d never lived in a place where snow was more common than sunshine, I’d never done any research in my life, I hadn’t even held a mouse before, let alone collected data from its brain.

Hence, 2018 has been a huge year of personal and professional growth, I learnt an incredible amount, not only about my project, but about research and academia, and of course the UK! I had a wonderful year, and I would do it again in a heartbeat!
Background
The use of in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) has increased significantly over the last decade in Australia and worldwide and its indications have expanded to include nearly all types of subfertility. We aim to determine whether patients’ diagnostic categories and a simple prognostic algorithm could be used to discriminate between couples that would benefit from immediate ART and couples in whom ART could be delayed.

Methods
We performed a retrospective cohort study of couples consulting an Adelaide fertility clinic in the year 2012. We included heterosexual couples seeking conception with their own gametes. Couples who returned for treatment after a previously successful treatment, couples who were referred for treatment following diagnostic testing at another fertility clinic and couples seeking preimplantation screening and diagnosis were excluded.

 Couples were classified into groups according to diagnosis and their likelihood of natural conception based on female age, duration of infertility, previous pregnancies, semen motility and whether they were referred to the clinic by a gynaecologist or a general practitioner. Kaplan Meier Survival Curves were constructed for each group showing the cumulative pregnancy and live birth rates with treatment effect as well as after censored at the start of fertility treatment.

Results
We studied 513 couples. There were 60 couples with an absolute indication for In Vitro Fertilisation (IVF)/intracytoplasmic sperm injection (ICSI). There were 117 couples with anovulation, for whom assisted reproductive treatment (ART) is likely to be required but treatments less invasive than IVF/ICSI may suffice. In 59 couples, the woman was aged 39 years and above. Out of the remaining couples, 33 were excluded, as their prognosis could not be calculated due to missing data. Out of the couples for whom prognosis of spontaneous pregnancy was calculated, 87 had a good prognosis (more than 40% chance of achieving a spontaneous pregnancy leading to live birth within the next 12 months), 70 had moderate prognosis (30-40% inclusively) and 87 had poor prognosis (below 30%). Fertility treatments were highly beneficial for couples with an absolute indication for IVF, couples where the woman was older and couples with a poor prognosis. However, the value of fertility treatments was limited in couples with a good prognosis. The value of IVF/ICSI was similar to that of less invasive treatments, such as ovulation induction, for couples with anovulation.

Conclusion
Individual diagnostic and demographic characteristics of couples could be used to personalise fertility treatment decisions and optimise the use of assisted reproductive treatment without compromising pregnancy chances.
Background

Menstrual blood is an untapped, naturally occurring resource that may reflect female reproductive health and be a potential source of adult stem cells. In this project, I aimed to characterise the baseline variation of endometrial stem/progenitor cell shedding in menstrual blood across menstrual cycles and between regularly menstruating women. Novel endometrial stem/progenitor cell surface markers, SUSD2 and N-cadherin, were used to identify endometrial mesenchymal stem cells and endometrial epithelial progenitor cells, respectively.

Method

Seven menstrual blood samples were collected from three women with regular menstrual cycles. Samples were processed through a combination of mechanical shearing and enzymatic digestion. Red blood cells were removed via Ficoll Paque density gradient separation and application of a red blood cell lysis buffer. Both fluorescence activated cell sorting and CD45 magnetic bead sorting were trialed to enriched samples for CD45$^-$ endometrial cells before samples were analysed by flow cytometry and cultured to assess clonogenicity. Menstrual blood processing was optimised to generate a reproducible protocol, including performing mechanical shearing and enzymatic digestion to break down blood clots, mucus, and tissue fragments, red blood cell removal via an ammonium chloride-based lysis buffer, and CD45 magnetic bead sorting to remove leukocytes before culturing and flow cytometry.

Results

Performing either CD45 magnetic bead sorting or FACS yielded a higher cloning efficiency of the single cell suspension than culturing all menstrual blood-derived cells (3.87% vs. 0.60% and 17.8% vs. 1.27%, respectively), however CD45 magnetic bead sorting proved more practical than FACS. Between 1.0% and 7.1% of CD45$^-$ cells in each menstrual blood sample were SUSD2$^+$ cells with a median value of 5.4%. The percentage of SUSD2$^+$ cells appears to vary between cycles and women, although this was not statistically significant. N-cadherin$^+$ cells were detected in 5 of 7 samples with varying degrees of certainty. The median percentage of N-cadherin$^+$ cells was 0.06% (range of 0% - 3.0%) with no significant variation between cycles or participants (p=0.4).

While the clonogenicity of menstrual blood-derived cells was inversely associated with the percentage of SUSD2$^+$ cells found in each sample ($R^2=0.3427$, $p=0.4146$), more samples are required to draw this conclusion.

Conclusions

SUSD2$^+$ cells are detectible in menstrual blood and may vary between participants and cycles. Identifying SUSD2$^+$ cells may aid in the detection and isolation of endometrial mesenchymal stem cells in menstrual blood. This research could lead to the development of non-invasive prognostic tests, using menstrual blood to assess for obstetric and gynaecological conditions like endometriosis and female infertility.
Does sildenafil citrate reduce damage to the developing fetal grey matter and hippocampus in fetal growth restriction

Supervisor: Dr Beth Allison
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ABSTRACT

Background
Fetal growth restriction (FGR) is when the growing fetus fails to meet its genetically predetermined growth potential. Of the plethora of FGR-related perinatal and postnatal complications, postnatal neurocognitive deficits may extend well into long term. Abnormal fetal neurodevelopment has been identified as the potential cause of these deficits in FGR infants. A serious global health problem with no definitive treatment and a varied aetiology, placental insufficiency has been singled out as one of the most common causes and a target for treatment. Thus over the past decade, much focus has turned to sildenafil citrate (SC) to alleviate placental insufficiency, thereby attenuating the deleterious effects of FGR.

Method
This study aimed to assess if SC improves neuronal and cerebrovascular development in an ovine model of FGR. I assessed the effects of FGR on neuronal and cerebrovascular development within key regions of the brain identified as vulnerable to FGR-related damage. The abnormalities in the hippocampus, PVWM and CGM are associated with poor postnatal neurocognitive outcomes. I assessed the effects of FGR and SC on fetal weight, brain weight and 'brain sparing'. I assessed gross histopathology using H&E staining, and neuronal development by quantifying the density of NeuN+ neurons. I then assessed markers of cellular damage through quantifying amounts of 8OHdG, GFAP and caspase-3. I assessed cerebrovasculature by investigating blood-brain barrier (BBB) integrity (albumin) and endothelial cells (GLUT1). Lastly I cross-referenced alterations in GLUT1 expressions, with fetal glucose delivery to isolate the cause.

Results
SC reduced fetal weight and brain weight, and increased brain:body ratio. In hippocampal subregion CA3, there was significantly (p=0.02) reduced neuronal number (NeuN) in FGR lambs (27.4 ± 0.7 cells) compared to AG controls (41.5 ± 3.5 cells) which were not attenuated by SC. Increased percentage area of oxidative stress (8OHdG+ cells) caused by growth restriction was tended to be attenuated by SC in the CGM. In the PVWM, FGR had significant increments on the number of cells demonstrating apoptotic cell death (caspase-3) (p=0.0157), total area (p=0.002) and percentage area (p=0.0019). Although attenuated by SC, this did not reach significance. In the PVWM and CGM, FGR caused increased albumin extravasation compared to AG controls. Albumin extravasation in FGRSC was notably more severe compared to FGR lambs. No significant differences were noted in GLUT1 and GFAP across groups.

Conclusions
Based on fetal weights, FGR and ‘brain sparing’ may be exacerbated, not alleviated by SC. SC is associated with compromised BBB integrity and abnormal neuronal development which were not rescued by SC therapy. Although the mechanisms are unclear, my findings suggest that SC may modulate mechanisms in neuronal and cerebrovascular development, leading to regional differences between the hippocampus, PVWM and CGM. Given the recent updates in the STRIDER trial, future research into the mechanisms underlying the SC-related effects on neurodevelopment may help steer future investigations into the treatment of FGR-related neuropathology.

I decided to undertake a lab-based BMedSc(Hons) in feto-maternal medicine after my fourth year. Our women’s health rotation kindled my interest in this field and prompted me to pursue a project with The Ritchie Centre. The successful undertaking of my project would not have been possible without my amazing supervisors and lab group who patiently guided me throughout the year. Naturally a lab-based BMedSc(Hons) project is not an easy task. The steep learning curves and self-directed learning by trial-and-error are some of the main challenges I faced. My word of advice is to first, find a well-established project and supervisors that are willing to guide you. Secondly, although there are times when you encounter obstacles and self-doubt, you are not alone! Never give up and don’t be afraid to seek help from your colleagues. Lastly, one year flies by really quickly so take initiative and work hard, but always remember to take a break!

I really enjoyed my Honours. I believe it’s definitely character building and prepares you well for the future. Should you do a BMedSc? Yes. Absolutely!

I’m more than happy to talk about my project or lab-based research in general on wjtan31@student.monash.edu.
Background
According to recent data from the World Health Organization (WHO), smoking was responsible for 7.2 million deaths in 2017 and high-risk drinking has caused 3.3 million deaths up to 2015. These behaviours can produce physical and mental health disorder, including depression. In Australia, 50% of younger adults (aged 18-24 years old) are associated with high-risk drinking and there is an association between smoking, high-risk drinking, and depression. This pattern has not been described in older populations and there is no adequate research in this area, despite the proportion of older adults within the Australian population increasing over time.

Aims
The main aim is to examine the cross-sectional relationship between tobacco smoking, high-risk drinking, and high depressive symptoms among a cohort of healthy older Australians.

Methods
From the ASPREE Study, 19,114 participants aged 65 years and older, have met the inclusion and exclusion criteria were recruited. In this study, they were required to fill in the questions regarding their smoking status, drinking status, and mental health status (screened by CES-D 10). Univariate and multinomial logistic regression were stratified by sex, adjusted for age (years) and conducted in SPSS software (Version 20). Given multiple testing within the ASPREE cohort for secondary aims, the threshold of significance is p<0.001.

Results
Male participants were more likely to smoke tobacco (Males: 4.6% versus Females: 3.3%, p<0.001) and drink alcohol at high-risk levels (Males: 17.8% versus Females: 3.2%, p<0.001), compared to females, they were more likely to be indicated as depressed (Males: 7.6% versus Females: 11.6%, p<0.001). Among both males and females, being a current smoker increased the likelihood of being a high-risk drinker (Males: 19% and Females: 7%, p<0.001) and the combination of either being a high-risk drinker or indicated as depressed was associated with being a current smoker (Males: 3% and Females: 2%, p<0.001). And being either a current smoker or high-risk drinker was associated with high depressive symptoms (Males: 55% and Females: 69%, p<0.001). For males, having one risk factor (either smoking or high depressive symptoms) increased the chance of being a high-risk drinker by 5% (OR: 1.05, p<0.001).

Conclusion
Among a large cohort of healthy older adults, smoking, high-risk drinking, and high depressive symptoms were associated cross-sectionally. These findings have significant implications for understanding of how older adults deal with challenging life events (losing family members, retirement, and illnesses) that may contribute to smoking, high-risk drinking and high depressive symptoms. These findings highlight that interventions should address these health concerns in combination.
Background
Antibiotic exposure in early childhood has been linked to childhood obesity. It is unknown whether antibiotic exposure in pregnancy is associated with higher birth weight and whether this relationship differs by exposure timing, mode of delivery, child sex, maternal body-mass-index (BMI) and postnatal antibiotic exposure. We therefore investigated the association between caesarean section and antibiotic exposure during pregnancy and postnatally to 18 months of age with birth weight and childhood BMI.

Method
This longitudinal cohort study of 48 025 and 30 542 mother-child dyads used data from the Danish Birth Registry and Danish National Birth Cohort. Exposures were caesarean section and antibiotic use from conception to 18 months of age. Primary outcomes were birth weight and BMI z-score at 5 months, 12 months and 7-years of age. We controlled for maternal parity, age, smoking, BMI, socio-economic status (parental education or job title), and child gestational age and breastfeeding. We conducted linear regression for analysis, and stratified analyses by maternal BMI, mode of delivery and sex. Data analyses were conducted with STATA (StataCorp version 13., College Station, TX, USA).

Results
Prenatal antibiotic use was associated with a 19.31g higher birth weight in boys (95%CI: 5.16–28.48g). The effect size was largest when comparing trimester 1 or 2 exposure in boys with overweight mothers to unexposed boys in this subgroup (+58.85g, 95%CI: 22.05–95.65g). The relationship between postnatal antibiotic exposure from 0-6 months and childhood BMI z-score was less clear and differences between sexes were minor and inconsistent. Additive prenatal and postnatal antibiotic exposure from 0-18 months was associated with higher BMI z-score in girls at 7 years of age (adjusted +0.061, 95%CI: 0.00–0.12). Caesarean section was not associated with a consistent pattern or direction of BMI difference from infancy to mid-childhood.

Conclusions
Prenatal antibiotics were associated with higher birth weight in boys, especially in those born to overweight mothers exposed to antibiotics earlier in pregnancy. The relationship between postnatal or prenatal antibiotics and childhood BMI was small and less consistent. Mechanisms for the association may relate to epigenetics or the gut microbiome, while sex-differences could be explained by placental differences in female versus male fetuses. Judicious use of antibiotics in pregnancy and early childhood, particularly in high-risk groups may reduce the risk of high birth weight, which is predictive of later obesity.
Prevalence, Epidemiology and Clinical Characteristics of Non-Alcoholic Fatty Liver Disease in Rural Victoria

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ABSTRACT

Background
Non-alcoholic fatty liver disease (NAFLD) is a major health issue expected to rise in parallel with obesity and the metabolic syndrome. Epidemiological data regarding NAFLD mostly comes from the United States and Europe, with prevalence estimated at 20-30%; no significant Australian data has been recorded. A possible diagnostic approach to suspected NAFLD includes ultrasonography, vibration-controlled transient elastography (FibroScan®), and liver biopsy. Major complications of NAFLD include liver cirrhosis and cardiovascular disease.

Treatment may include lifestyle changes and medications such as vitamin E. This research aimed to determine the prevalence of NAFLD in the Goulburn Valley region of Victoria, to measure severity of disease in NAFLD cases using liver stiffness measurement (LSM) on FibroScan, and to determine any association between NAFLD and metabolic factors. Additionally, it aimed to assess the utility of FibroScan as a screening tool in the general population to identify those at risk of liver disease.

Method
This research was conducted through the Crossroads study on undiagnosed chronic disease in rural Victoria. It involved reviewing the literature on the area (which I have been lucky enough to be published for in an international journal), data collection and analysis, and result interpretation, which showed a high prevalence of non-alcoholic fatty liver in our community. This year has been by far the best year I’ve had at university and I would highly recommend for anyone considering it to pursue a BMedSc. The year has given me fundamental skills in research and communication and has helped me see the field of medicine from a different and broader perspective, which will certainly be beneficial going into internship and working as a clinician.

Results
The overall cohort was found to have a high prevalence of metabolic risk factors including obesity, diabetes and dyslipidaemia, with 25.6% of the total group being affected by metabolic syndrome. The prevalence of NAFLD was found to be 19% on the basis of ALT levels, and 63.3% using controlled attenuation parameter through FibroScan. NAFLD was associated with metabolic risk factors including obesity and diabetes, and a significant relationship was found between NAFLD and metabolic syndrome (p < 0.001). Significant associations (p < 0.05) were also found between NAFLD and weight, BMI, liver enzymes (ALT, AST, GGT), lipids (total cholesterol, triglycerides, HDL- and LDL-cholesterol) and markers of diabetes (fasting and 2-hour glucose, HbA1c). Those with NAFLD had significantly higher liver stiffness on FibroScan compared to those with normal ALT (p < 0.001).

Conclusions
This study provided the first insight into the issue of NAFLD in the Australian domain, and the results closely resemble similar international studies, indicating a substantial burden of disease. It confirmed the significance of metabolic syndrome as a risk factor for NAFLD, and as a major issue in the rural Australian community. Greater severity of liver disease was found in those with NAFLD, and the feasibility of large-scale screening for liver disease using FibroScan was demonstrated. There is potential for a follow-up study across major metropolitan Australian cities to further explore the issue of NAFLD and study the effects of rural living status on NAFLD and metabolic disease.
Aimy Tran

Epidemiology of adenotonsillectomy in Victoria and risk factors for postoperative complications

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ABSTRACT

Background
Tonsillectomy, adenoidectomy and adenotonsillectomy (collectively referred to as adenotonsillectomy) are the most common paediatric procedures performed in Australia. Factors driving differences in adenotonsillectomy procedural volume and postoperative complications across Victoria are unclear. We aimed to describe the epidemiology of adenotonsillectomy in Victoria and identify predictors for haemorrhage, respiratory compromise, dehydration and length of hospital stay.

Method
The Department of Health and Human Services provided administrative data of people aged 0-19 years having tonsillectomy, adenoidectomy or adenotonsillectomy between 1 June 2010 and 30 June 2015 in Victoria. A linked dataset contained readmission data within 30 days of surgery. We conducted a cross sectional study to describe the epidemiology of adenotonsillectomy, and a retrospective cohort study, using stepwise multivariable regression, to identify risk factors for haemorrhage, respiratory compromise, dehydration and length of hospital stay.

Results
Over the 5-year period, 59,008 patients had 61,281 procedures. Most procedures involved children aged under 10 years (0-4y 38%; 5-9y 36%; 10-14y 14%; 15-19y 12%), the two least socioeconomically disadvantaged quintiles (48%), and were for the indications of obstructive sleep apnoea (47%) and tonsillitis (47%). Rates of adenotonsillectomy by geographical area were highest in regional Victoria and lowest in metropolitan areas. The strongest driver for procedure rate were rural hospitals, compared to metropolitan (coefficient 187.87; 95% CI 185.28-190.47; p<0.001). Other risk factors included tonsillitis diagnosis, decreasing age, and tonsillectomy or adenotonsillectomy procedures compared to adenoidectomy alone.

Of the procedures, 1,660 resulted in haemorrhage (3% total procedures; 50% readmissions), 479 in dehydration (0.78% procedures; 14% readmissions) and 93 in respiratory compromise (0.15% procedures; 3% readmissions). Increasing age was the strongest predictor for haemorrhage (adjusted odds ratio [OR], 1.90; 95% CI, 1.81-2.00, p<0.001). In contrast, youngest age was the strongest predictor for respiratory compromise (OR, 1.37; 95% CI, 1.09-1.72; p=0.008). Having a tonsillectomy/adenotonsillectomy (compared to adenoidectomy alone) was the strongest driver for dehydration (OR 1.60; 95% CI, 1.38-1.86; p<0.001) and longer length of hospital stay (OR 4.40; 95% CI, 4.20-4.61; p<0.001).

Conclusions
This study described the contemporary epidemiology of paediatric tonsillectomy, adenoidectomy and adenotonsillectomy in Victoria, as well as investigated predictors for complications and length of hospital stay. There are demographic and geographic variations in adenotonsillectomy and in postoperative complications for children across the state. These findings will inform evidence-based state-wide recommendations for service provision, access to healthcare and peri- and post-operative care.

I undertook my BMedSci(Hons) following fourth year in the Department of Paediatrics at Monash Children’s Hospital. After having learnt the fundamentals of medicine, I wanted to explore the science that underpins clinical practice. I have an interest in paediatrics and respiratory medicine, and decided to undergo a paediatric quality improvement project involving adenotonsillectomy.

Under the supervision of my very supportive supervisors, I had the opportunity to develop my research skills in creating good methodology, scientific writing, public speaking, manipulating datasets and analysing data. As well as improving skills, this Honours year allowed me to be involved in many events and create professional networks. I had the chance to attend a conference and was invited to be a member of the Victorian Government’s Expert Working Group towards improving adenotonsillectomy provision in Victoria.

I would highly recommend the BMedSci(Hons) to any prospective student seeking to learn new skills and meet experts in medical fields. I’m more than happy to be contacted for any questions: atra44@student.monash.edu
Luke Chenkan Wang

Preventing postoperative middle ear ventilation tube complications in children with topical ciprofloxacin: a randomised controlled trial

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(Department of ENT – Head and Neck Surgery Monash Health)

ABSTRACT

Background
The insertion of middle ear ventilation tubes is one of the most common surgeries performed in the paediatric population in Australia. The main indications for ventilation tube insertion are recurrent acute otitis media and chronic otitis media with effusion. Insertion of the ventilation tube usually leads to prompt quality of life improvements and resolution of symptoms. However, these benefits can be hindered by the presence of postoperative complications such as ventilation tube otorrhoea and blockage. The use of ciprofloxacin antibiotic ear drops to prevent these outcomes is commonplace despite a lack high quality evidence supporting its use. Studies which investigate the quality of life benefit of using antibiotic ear drops are also lacking.

Method
An assessor-blinded randomised controlled trial of 360 paediatric patients undergoing bilateral grommet surgery was designed. Patients were randomised in a 1:1 ratio to receive either ciprofloxacin ear drops during surgery and for 5 days postoperatively or to receive no drops. Baseline and intraoperative characteristics were recorded for each patient. Patients were assessed at 6 weeks postoperatively for ventilation tube otorrhoea and blockage. A validated parent-reported disease-specific outcome measure Otitis Media Outcome 22 (OMO-22) score was used to assess disease severity preoperatively and at 6 weeks postoperatively.

Results
To date, 81 patients were recruited with 35 patients completing follow-up. 19 patients were allocated to treatment while 16 patients were allocated to control.

There was no statistically significant difference in the incidence of ventilation tube otorrhoea between the two groups. The incidence of the treatment group was 18.4% while the incidence of the control group was 6.3% (OR=3.387, 95% CI 0.651 – 17.631, p=0.166).

There was no statistically significant difference in the incidence of ventilation tube blockage between the two groups. The incidence of the treatment group was 13.2% while the incidence of the control group was 9.4% (OR=1.464, 95% CI 0.322 – 6.669, p=0.719).

There was no statistically significant difference in preoperative OMO-22 scores between the two groups (Mann-Whitney U, p=0.528). The median preoperative OMO-22 score for the treatment group was 45 and for the control group was 48.

There was no statistically significant difference in postoperative OMO-22 scores between the two groups (Mann-Whitney U, p=0.057). The median postoperative score was 14 for the treatment group and 14.5 in the control group. The median score improvement was 51.1% for the treatment group and 66.6% in the control group. This difference was statistically insignificant (Mann-Whitney U, p=0.057).

Conclusions
Our current findings suggest that the use of ciprofloxacin ear drops does not decrease the incidence of ventilation tube otorrhoea and blockage compared to control. Furthermore, the use of ciprofloxacin ear drops does not increase the quality of life benefit compared to control. At this preliminary stage, we lack the statistical power to detect small differences between treatment and control groups in the primary outcomes of ventilation tube otorrhoea and blockage, nor the secondary outcome of quality of life improvement. Further recruitment is required for this study to make definitive recommendations regarding the use of ciprofloxacin ear drops in the prevention of postoperative complications.
The Impact of Preoperative Factors on Knee Pain and Function After Total Knee Arthroplasty For Osteoarthritis.

ABSTRACT

Background
The growing prevalence of knee osteoarthritis places a large burden on the healthcare system. Correspondingly, the rates of total knee arthroplasty (TKA) have risen substantially, offered as an effective management option in advanced osteoarthritis. Despite the suggested effectiveness of joint replacement, 10-34% of recipients remain in a painful and functionally limiting state postoperatively. Thus it is important to determine preoperative factors that may identify those at increased risk of poor outcome.

Aims
To examine the association between preoperative factors and poor postoperative outcome at 12 months following TKA, and to determine the associations between preoperative factors and knee pain and function at 12 months following TKA in a public hospital population.

Method
A retrospective cohort study assessed all patients undergoing primary TKA for a primary diagnosis of osteoarthritis, referred into the Alfred Hospital Osteoarthritis Hip and Knee Service between 1st January 2013 and 31st December 2015. Data was collected prospectively. Parametric and non-parametric descriptive methods were used to describe differences in preoperative characteristics between groups in primary and secondary outcome measures. Binary logistic regression was then performed to determine the likelihood of a poor outcome based on preoperative factors, with appropriate adjustment for important confounding variables.

Results
A total of 158 participants met the inclusion criteria. Regarding primary outcome measures, 133 participants had a good postoperative outcome following TKA (84.2%) and 21 had a poor outcome (13.3%). There were no significant differences in preoperative baseline characteristics between patients of good compared to poor outcome; none of the examined preoperative factors were associated with a significant increase in odds of a poor outcome. However, there was a tendency for female gender to be associated with an increased odds of poor outcome (OR=1.82 [0.66-4.98]).

Secondary outcome measures found older age at surgery was a predictor of postoperative gait aid use (OR=1.08 [1.02-1.14], p=0.01). Female gender increased the likelihood of postoperative pain on movement (OR=3.44 [1.48-8.00], p=0.004). Poorer fitness for surgery increased the odds of postoperative pain at rest (OR=3.42 [1.20-9.77], p=0.02) and postoperative pain on movement (OR=2.19 [1.01-4.75], p=0.047). And presence of preoperative pain at rest increased the likelihood of postoperative pain on movement (OR=5.09 [1.80-14.43], p=0.02).

Conclusions
No preoperative variables were predictive of overall poor TKA outcome on primary outcome measures. However, there was a tendency for female gender to be associated with an increased odds of poor outcome. The size of the study had limited power to identify any but the strongest associations thus a small to moderate effect on outcome cannot be excluded. Secondary outcome measures found female gender, poorer fitness for surgery and the presence of preoperative pain at rest to be associated with increased likelihood of poorer postoperative pain after knee replacement. The findings in this study suggested that patients undergoing knee replacement in public hospital settings have similar outcomes to the general population, including those in private health, despite having greater disease severity at time of surgery.
Identifying lipidomic changes associated with cold exposure and brown adipose tissue activity

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ABSTRACT

Background
Brown adipose tissue (BAT) has been of particular interest as a potential therapeutic target for obesity and associated metabolic disorders. BAT normally functions to undergo compensatory non-shivering thermogenesis in response to cold exposure, which is mediated via sympathetic activation of \( \alpha \)-adrenoceptors. It is theorised that maximal pharmacological BAT activation can increase whole-body energy expenditure by 25%, and has been shown to greatly improve markers of glucose and lipid homeostasis. Recent studies have revealed novel interactions between BAT and circulating lipid species, and highlight the potential to develop clinically relevant BAT activators and biomarkers. The aim of the present study was to measure the plasma lipidome before and after mild cold exposure in healthy individuals to identify lipid biomarkers of cold-stimulated sympathetic activity and BAT thermogenesis.

Method
Fourteen healthy male volunteers (age 22 ± 2 years; mean ± SD) were recruited and subjected to 90 minutes of mild cold exposure, after which their BAT activity was measured via 18F-fluorodeoxyglucose ([18F]FDG) positron emission tomography/computed tomography (PET/CT). Blood samples taken before and after cold exposure underwent mass-spectrometry-based lipidomic analysis which assessed the plasma concentrations of 729 individual lipid species. Additionally, blood samples were taken at 30-minute intervals throughout the trial to quantify plasma noradrenaline (NA) concentration as a surrogate marker of sympathetic activity.

Results
In summary, cold exposure did not alter total lipid concentration, but led to a significant change in non-esterified fatty acid (NEFA) lipid class concentration, as well as the concentrations of 40 individual lipid species from other classes. No changes in lipid species concentrations, either individually or combined in class/subclass groups, were significantly associated with BAT activity after Benjamini-Hochberg correction. However, the total lipid concentration change, along with the cold-induced concentration changes of 28 lipid classes and 434 lipid species, were significantly correlated with sympathetic activity post-Benjamini-Hochberg correction. Furthermore, the study identified 84 lipid species that underwent greater cold-induced changes than the established BAT-associated lipid, 12,13dihydroxy-9Z-octadecenoic acid (12,13diHOME), and 58 lipid species which had stronger correlations between cold-induced concentration change and BAT activity.

Conclusions
This study revealed novel lipid associations with BAT activity, NA concentration change and cold exposure for further exploration. The lipids which performed better than 12,13diHOME, in particular, represent promising targets for future BAT-directed interventions. Interestingly, many more significant correlations were identified between lipids and NA concentration change than between lipids and BAT activity. Taken together with the existing literature, this suggests that the effects of sympathetic BAT activity may be masked by other sympathetically stimulated tissues, and that future BAT studies should employ methods that allow assessment of BAT in greater isolation.
Background
Retinopathy of prematurity (ROP) is currently one of the leading causes of childhood blindness in well-developed countries. This disease happens in low birth weight pre-term infants with the administration of supplemental oxygen in the neonatal intensive care unit (NICU) one of the main causes of ROP. This causes a decrease of oxygen mediated angiogenic factors in the developing retinal vasculature which leads to the destruction of the developing retinal vasculature, this is known as phase 1 of ROP. In phase 2 as the supplemental oxygen is removed, an influx of angiogenic factors causes an excessive growth of the retinal vasculature and leads to neovascularization. These vessels are inadequate to support the retina and may lead to retinal detachment which can cause blindness. Inflammation has emerged as one of the key factors in ROP with recent studies showing that it may contribute to the development of ROP. It was previously thought that the retina is immuno-privileged but recent studies have demonstrated that immune cells indeed migrate to the retina due to the leakage of the blood retinal barrier (BRB). Studies now explore to ways in which to dampen the inflammation, one of which is through Foxp3+ Tregs which can enact suppressive capabilities on the immune cells on the retina such as microglia. The administration of low dose IL-2 may be a candidate to increase Tregs due to the high affinity of Tregs to bind with IL-2 and the ability of this cytokine to promote the survivability and functionality of Tregs.

Method
We sought to determine this by using a well-established model of ROP in mice named oxygen-induced retinopathy (OIR) where newborn mice at post-natal day (P) 7 are put into an oxygen chamber with 75% oxygen to mimic the events in the NICU. They are then taken out at P12 and are culled at P18. Low dose IL-2 is injected at P6, 7, 8, 11, 13 and 16. The mice were then examined for vascular pathology using wholemounts stained with isolectin. Flow cytometry was used to examine if low dose IL-2 increased the number of Tregs without influencing the abundance of other immune cells that may be responsive to IL-2.

Results and Conclusions
Our results showed that low dose IL-2 indeed reduced the vascular pathology as well as increase the number of Tregs in the lymphoid organs and the blood of mice with OIR. Low dose IL-2 also minimally influenced the abundance of other immune cells such as CD8+ T cells, NK and NKT cells which may contribute to the vascular pathology and shows promise as a future treatment in ROP. Future studies measuring the effect of low dose IL-2 on the retinal immune cells as well as its effects on the angiogenic factors may help in understanding the factors causing vascular pathology improvements as well as future clinical trials may be in consideration in the future.
Patterns of antibiotic prescribing in the paediatric community

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ABSTRACT

Aim and Background
Antibiotics are the most commonly prescribed medication in pediatrics. We analysed antibacterial prescribing trends in two distinct primary care settings; a retrospective analysis of paediatric community care in Victoria from 2013-2017 and prescribing patterns in a single outpatient clinic within a tertiary Chinese metropolitan paediatric hospital.

Method
Antibiotic prescribing data from de-identified, digital records on children (age<18 years) were retrieved from 231 anonymised general practices in southeastern Melbourne, Victoria from 2013-2017. Sex, age, antibiotic characteristics and repeat prescriptions were analysed. Rates of broad-spectrum antibiotic usage and reasons for prescribing were also evaluated.

For the second study, antibiotic prescription data from paediatric (<18 years) computerised records were retrieved from the infectious diseases outpatient services at Shenzhen Children’s Hospital in 2017; sex, age, diagnosis, and antibiotic characteristics were analysed.

Results
788,711 antibiotic prescriptions were captured, from a total of four million paediatric presentations to Victorian general practices. Antibiotic prescribing rates reduced by 31% over the 5-year period. The most commonly prescribed antibiotics were amoxycillin (43% of total) followed by cephalexin, amoxycillin-clavulanate, phenoxymethylpenicillin and cefaclor.

Prescription of broader spectrum antibiotics, such as cefaclor and amoxycillin-clavulanate, decreased over the five-year period, whilst cephalexin and phenoxymethylpenicillin usage increased. Diagnoses most associated with cefaclor and amoxycillin-clavulanate prescriptions included otitis media other upper respiratory tract infections. 28.8% of antibiotic prescriptions included a corresponding repeat script.

In China, a total of 1040 antibiotic prescriptions were captured with an overall antibiotic prescription rate per presentation of 20%. Cephalosporins were the most commonly used antibiotic class, in particular second and third-generation cephalosporins. Antibiotic prescribing rates remained stable throughout the 2017 period. Diagnoses classed under the respiratory, gastrointestinal and skin & soft tissue system accounted for the majority of diagnoses (93%).

Conclusions
From 2013-2017, there was a marked decline in antibiotic prescription rates in the paediatric population in Victorian general practices. Encouragingly, prescribing of broad spectrum antibiotics reduced at a swifter rate, consistent with prescribing guidelines. This study provides the largest targeted examination of antibiotic prescribing patterns for Australian children to date.

In China, antibiotic prescribing rates remained stable in the paediatric infectious diseases outpatient population throughout 2017. This study provides a targeted examination of antibiotic prescribing patterns for children within a major Chinese metropolitan tertiary paediatric hospital.
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Prevalence and determinants of antibiotic use among women in early pregnancy living in rural Vietnam

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ABSTRACT

Background
Antibiotics are one of the most commonly used medications in pregnancy. However, antibiotics in pregnancy are associated with foetal malformations, low birth weight and asthma in infancy. Antibiotic use in low-and-middle-income countries (LMIC) is affected by structural determinants and prescriber, dispenser and patient factors in a setting where the infectious disease burden is high. This has led to the use of antibiotics inappropriately, either incorrectly or at suboptimal therapies. In addition, non-prescription use, which is the use of prescription medications without obtaining a prescription, is common in LMICs. However, to date, no studies have examined the prevalence and determinants of antibiotic use in early pregnancy in LMICs.

Aim
The aim of the project was to describe the prevalence and determinants of antibiotic use among women in early pregnancy living in rural Vietnam.

Method
This study was nested within the competitively funded NHMRC study located in the Ha Nam province, Vietnam: Learning Clubs to improve women’s health and infant’s health and development in Vietnam: a cluster randomised control trial. Our study analysed a component of the baseline data, collected at 20 weeks gestation or less of the cluster randomised control trial. Our study analysed a component of the baseline data, collected at 20 weeks gestation or less of the cluster randomised control trial. Through a structured individual interview schedule, 1245 women were asked about sociodemographic characteristics, health and pregnancy characteristics, health service usage and knowledge, attitudes and behaviours in pregnancy were described. The primary outcome was antibiotic use and its characteristics of use.

Results
This study found that 162 women (13%) had taken antibiotics in their current pregnancy. The median duration of use was 3 days. The most common indication for antibiotic use was respiratory condition (n=95, 55.5%). Just under half of antibiotic users had used antibiotics without a medical prescription.

Women who were older (P=0.05), more advanced in gestational age (P=0.016) and used other medications in pregnancy (P=0.001), were more likely to use antibiotics. In logistic regression analysis, women with a chronic condition were more likely to use antibiotics (OR 1.8, P=0.03, 95% CI 1.1-3.0). Women with higher DASS21 scores were also more likely to use antibiotics (OR 1.1, P=0.007, 95% CI 1.0-1.2). Women who believed that they would seek professional advice around medication use in pregnancy were more likely to take antibiotics (OR 2.0, P=0.02, 95% CI 1.1-3.6)

Conclusions
Our study is the first to identify significant associations between poorer physical and emotional wellbeing and antibiotic use. In addition, it was noted that self-medication of antibiotic tended to be for respiratory conditions, including for viral infections, and non-serious symptoms. Our research points to the need for targeted health promotion activities educating women around the risks and benefits of antibiotic use, especially self-medication, in pregnancy.
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