Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) – COVID-19 Virus

This illustration, created at the Centers for Disease Control and Prevention (CDC), reveals ultrastructural morphology exhibited by coronaviruses. Note the spikes that adorn the outer surface of the virus, which impart the look of a corona surrounding the virion, when viewed electron microscopically. A novel coronavirus, named Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), was identified as the cause of an outbreak of respiratory illness first detected in Wuhan, China in 2019. The illness caused by this virus has been named coronavirus disease 2019 (COVID-19).

https://commons.wikimedia.org/wiki/File:SARS-CoV-2_without_background.png

Charlotte O’Callaghan – The Difficulty of Working from Home

Due to the COVID-19 pandemic I spent most of the year working from home, which meant sharing my workspace with Boudica (the family cat). After many days of her sitting on my laptop, walking across the keyboard or otherwise being a nuisance, we eventually compromised.
Message from the BMedSc(Hons) Convenor and Course Management Committee

Dear BMedSc(Hons) students, congratulations on completing your BMedSc(Hons) degree! Well done, it is a very significant achievement, particularly in such a challenging year. You should all feel very proud of what you have achieved.

The Course Management Committee and I would like to thank you for choosing to undertake a formal year of research in BMedSc(Hons). We have no doubt that this year has challenged you personally. We also hope that it has challenged you academically and given you an appreciation of: how new knowledge is created, how medical research is translated into changes in clinical practice, how important evidence-based medicine is for ensuring that changes to practice are justified, and an appreciation of how much more there still is to learn about medical practice and how our bodies function in health and disease! We are sure that you will have much more confidence in your ability to critically evaluate new research findings and hope that you also have more confidence in your ability to develop into a practitioner of evidence-based medicine.

We would also like to express our thanks to your supervisors and to the very large number of unsung heroes who have devoted their time to help you learn during the year. 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 Literature Reviews, Theses, Departmental Oral Seminars and the Faculty Presentations and to our BMedSc(Hons) support staff. Thank you also to the MRSS committee, particularly your BMedSc(Hons) Student Representative Michael Dong. Michael has been wonderful, providing suggestions and passing on your questions and comments, helping to improve your own experience as well as that of future cohorts. I would also like to thank Michael Dong, Gayatri Bimal and William Barbis for organising the inaugural BMedSc(Hons) conference! I am sure that everyone agrees that it was a terrific success and a really wonderful way to end your BMedSc(Hons) year.

The BMedSc(Hons) Course Management Committee and I, wish you all the very best for your future.

Kind regards,

A/Professor Megan Wallace,
Director of Medical Student Research,
Faculty of Medicine, Nursing and Health Sciences

Message from MRSS

Congratulations on completing the BMedSc(Hons) course for 2020! This has certainly not been the year we were expecting. However, despite the surprises and challenges of 2020, we have all achieved so much. It is true of every honours year that it is a year full of personal and professional development, in the year of COVID, I think this is more apparent than ever. We embarked the year with very little experience in research, let alone experience living and working amidst a global pandemic. I have no doubt that there were significant challenges along the way yet it was incredible to see the breadth and depth of research our cohort conducted. It’s surreal to think that our efforts this year have made meaningful contributions to medical research. We have managed to adapt, learn and apply ourselves in the most difficult of times. Armed with new skills, more knowledge and greater confidence, I hope that this is only the beginning of our research careers. I would like to extend my gratitude on behalf of the cohort to all those who made this year possible. Thank you to A/Prof Megan Wallace, Cathy Nolan-Shaw, the heads of schools, the Course Management Committee and all the supervisors for their generous support. It has been a privilege serving as your student representative and I am honoured to graduate and work alongside you in the near future.

Michael Dong, BMedSc(Hons) student representative.
ABSTRACT

Background

Obesity is strongly associated with the risk of cardiovascular diseases as well as cardiovascular diseases-related mortality. However, in the context of cardiac surgery, some studies have reported about an obesity paradox, in which obese patients undergoing cardiac surgery had better postoperative outcomes compared to non-obese patients. Although, the causal factor underpinning the obesity paradox is still unclear. Furthermore, the obesity paradox has not been extensively studied in Australian patients undergoing cardiac surgery. This study looked into the relationship between body mass index (BMI) and post-cardiac surgery outcomes and also explored the relationship between age, sex, and BMI in relation to post-cardiac surgery outcomes.

Method

Data from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons Database for isolated Coronary Artery Bypass Graft (CABG) surgery performed between July 2001 and December 2018 were included in the analysis. The longer-term mortality data were provided by linkage with the Australian National Death Index. The cohort was categorised into six BMI groups according to the World Health Organization BMI categories. Descriptive analyses were done to examine the differences in patient risk factors and postoperative outcomes by BMI, age, and sex with chi-square test and ANOVA for categorical and continuous variables, respectively. Multiple logistic regression modelling was performed to assess the association between the preoperative risk factors and primary outcomes. Primary outcomes analysed included short-term mortality, longer-term mortality, reoperation for bleeding, new renal failure (NRF), deep sternal wound infection (DSWI), and permanent stroke.

Results

From a total of 74,295 cases of adult CABG surgery, 41.2% was classified as overweight, 24.7% obese class I, 22% normal BMI, 8.2% obese class II, 3.2% obese class III, and 0.6% underweight. After adjusting for risk factors, the underweight group had increased short-term mortality while the longer-term mortality was reduced in the overweight to obese class II groups. Reoperation for bleeding was also decreased in the overweight to obese class III groups. In contrast, rates of NRF and DSWI significantly increased with obesity. The logistic regression models showed that older age was associated with increased short-term mortality, longer-term mortality, reoperation for bleeding, NRF, and permanent stroke. Compared to male patients, females had increased short-term mortality, longer-term mortality, and DSWI, but had reduced reoperation for bleeding and NRF.

Conclusion

The obesity paradox presents in Australian patients undergoing isolated CABG surgery, particularly for longer-term mortality and reoperation for bleeding. Being underweight was associated with increased short-term mortality, whereas NRF and DSWI were strongly linked with obesity. No relationship was found between permanent stroke and obesity. Older age was an independent predictor for short-term mortality, longer-term mortality, reoperation for bleeding, NRF, and permanent stroke. Between the sexes, females were associated with increased short-term mortality, longer-term mortality, and DSWI, while reoperation for bleeding and NRF were higher in males. As each of the post-cardiac surgery outcomes had different predictors, this study highlights the need for each patient undergoing cardiac surgery to be treated appropriately by considering their respective risk factors prior to surgery.
Ms Madison Andrew

The Association between Intrapartum Interventions and Breastfeeding Outcomes

Supervisor Names and Institute Affiliations:
Dr Mary-Ann Davey
The Hudson Institute, Department of Obstetrics and Gynaecology
School of Clinical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University

Dr Miranda Davies-Tuck
The Hudson Institute, Department of Obstetrics and Gynaecology
School of Clinical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University

Hi, my name is Maddy and I had the pleasure of undertaking my BMedSc(Hons) year with the School of Clinical Sciences at the Hudson Institute. I have always had an interest in women's health and this project allowed me to further develop this interest. It was an incredibly enjoyable year and I learnt so much about the world of research. I obtained many skills about working with large datasets and scientific writing. Although it was a shame to be unable to interact with my fellow students and other staff members face-to-face this year, I was extremely grateful for the virtual support and friendships I have created from this program.

ABSTRACT

Background
The promotion of breastfeeding is an important public health priority due to the numerous health benefits it has for mothers and babies. Despite high rates of breastfeeding initiation in Victoria, early discontinuation and supplementation with infant formula is common. Emerging evidence suggests that intrapartum interventions may interfere with optimal breastfeeding success. This is important because interventions are becoming increasingly popular in Australian obstetric practice. Existing studies examining associations between intervention use and breastfeeding outcomes show mixed results, and evidence in the Australian setting is limited. Identifying women at risk of less favourable breastfeeding outcomes is essential for enabling the provision of breastfeeding support, where it is the desired feeding method.

Aim
To assess the association between intrapartum interventions (caesarean section, epidural analgesia and oxytocin infusion) and breastfeeding outcomes.

Method
This project is made of two retrospective cohort studies. The first used the Victorian Perinatal Data Collection (VPDC) from 2010 to 2018. The second used a linked dataset of the VPDC and the Child Development Information System (CDIS) from 2015 to 2017. The study population included singleton livebirths delivered at term (≥37 weeks gestation) in hospital whose mother initiated breastfeeding. The exposures of interest were pre-labour caesarean section (CS), in-labour CS, epidural analgesia and oxytocin infusion. The outcomes were formula supplementation in hospital, last feed before hospital discharge exclusively at the breast and breastfeeding status at 3-months and 6-months post-partum (any or exclusive). We performed descriptive statistics to analyse data and Pearson's chi-square test to determine significance. We undertook binomial logistic regression to obtain associations between each intervention and each breastfeeding outcome, adjusting for confounders and reporting adjusted Odds Ratios (AdjORs) and their 95% confidence intervals (CI).

Results
After adjustment for confounders, all intrapartum interventions were significantly associated with less favourable breastfeeding outcomes. Pre-labour CS, in-labour CS, epidural analgesia and oxytocin infusion increased the odds of using formula in hospital (AdjOR 1.92 (95% CI 1.85-1.95), AdjOR 1.98 (95% CI 1.94-2.02), AdjOR 1.35 (95% CI 1.33-1.37), AdjOR 1.22 (95% CI 1.20-1.23), respectively). Each intervention was associated with decreased odds of any and exclusive breastfeeding at 3-months and 6-months post-partum. For example, pre-labour CS, in-labour CS, epidural analgesia and oxytocin infusion each decreased the odds of exclusive breastfeeding at 3-months (AdjOR 0.73 (95% CI 0.71-0.76), AdjOR 0.79 (95% CI 0.76-0.83), AdjOR 0.77 (95% CI 0.75-0.80), AdjOR 0.89 (95% CI 0.86-0.92), respectively). Additionally, feeding methods in hospital were associated with breastfeeding status at 3-months and 6-months post-partum (P<0.001). Finally, increasing numbers of interventions received had an additive effect on less favourable breastfeeding outcomes.

Conclusion
Women who have intrapartum interventions have increased odds of less favourable breastfeeding outcomes, both in hospital and in the months after birth. The effect is stronger with increasing numbers of interventions received, particularly when one in CS. Feeding methods in hospital significantly predict long-term breastfeeding outcomes. These findings confirm the importance of providing additional breastfeeding support to women who have intrapartum interventions, when this is the preferred feeding method.
ABSTRACT

Background
Coronary heart disease (CHD) is the main cause of death and one of the leading causes of disease burden in the world. While there is a declining trend in CHD mortality in high income countries due to improved public measures, CHD remains one of the most burdensome disease in Australia. With the outbreak of COVID-19, there are significant indirect effects of the strategies used to control the pandemic. In terms of CHD, the lockdown and major restructing of the healthcare system are impacting adversely on cardiovascular risk factors, preventive care and even acute care. The present study sought to estimate the potential indirect effects of the COVID-19 pandemic on CHD.

Aim
To estimate the indirect impact of COVID-19 on coronary heart disease (CHD) in the Australian population in terms of years of life lost, quality-adjusted life years (QALYs) lost, healthcare costs, and societal cost.

Method
Life-table modelling of Australian population of all ages, with projected modelling up to ten years (2020-2029). Contemporary data on population demographic, mortality, incidence, and prevalence of CHD were derived from the Australian Bureau of Statistics (ABS) and the Australian Institute of Health and Welfare (AIHW). The health-attributable quality of life decrements and information on the impact of COVID-19 on cardiovascular risk factors were obtained from published sources. The model will estimate the burden of CHD assuming no change in the expected epidemiology of CHD, and the analysis will be re-simulated in scenario analysis assuming that the incidence of CHD will increase as a consequence of the indirect effects of COVID-19. The differences in the two model outputs will represent the indirect CHD effects of the COVID-19 pandemic in Australia. All outcomes following the first year were discounted by 5% per year.

Results
The projected prevalence of CHD among Australians of all ages in 2020 in males and females were 3.02% and 1.67%, respectively. Upon scenario analysis, over the next ten years, projected increases in CHD incidence by 0.5%, 1%, 1.5%, and 2% were estimated to lead to: 760, 1519, 2279, 3037 excess deaths, respectively; 457, 915, 1372, and 1829 excess years of life lost, respectively; 1,244, 2,487, 3,731, and 4,975 QALYs lost, respectively; and AUD $86 million, AUD $173 million, AUD $260 million, and AUD $347 million in excess costs, respectively. These findings illustrate that a slight increase in CHD incidence can lead to substantially greater burden in the future. In the context of COVID-19, many growing evidences has suggested that the pandemic has negatively affected the risk-factors of CHD, especially in smoking, physical activity, and mental health. With the current evidence surrounding cardiovascular risk factors as the indirect impact of COVID-19 pandemic, it is likely that the risk of developing CHD as well as worsening of CHD are heightened in Australian population.

Conclusion
CHD will continue to cause a substantial burden in Australia. The secondary impact of COVID-19 pandemic in Australia will likely indirectly lead to an increase in CHD cases in Australia. The findings of this study highlight the importance of developing awareness in pandemic management impacts on chronic diseases, which can be implemented in future practice and policy.
Ms Lilly May Backshell

Investigating the role of a putative transcriptional regulator of the Glucocorticoid Induced Leucine Zipper (GILZ) in CD4+ T helper cells

Supervisor Names and Institute Affiliations:
Dr. Wendy Dankers, Dr. Sarah Jones & Professor Eric Morand.
Rheumatology Research Group, Centre for Inflammatory Diseases, Department of Medicine, School of Clinical Sciences, Monash University

I completed my honours year in the Rheumatology Research Group investigating the role of an immunomodulatory protein known as the Glucocorticoid-Induced Leucine Zipper (GILZ).

I previously studied a Bachelor of Science at Monash majoring in Immunology and Human pathology, and completed an undergraduate research project unit with the Rheumatology Research Group. I decided to return to this group for my BMEdSci(Hons) year following the Year 4C exams, to take a break from medicine and increase my research experience.

I have thoroughly enjoyed the honours year, despite all the disruption from the pandemic. Completing the BMEdSci(Hons) year has improved my laboratory and communication skills, particularly presenting and writing.

In the future, I hope to pursue a career as a clinician-scientist in a field involving immunity, such as Rheumatology, Dermatology or Infectious Diseases. I would also like my career to encompass Paediatrics and Indigenous Health.

Please feel free to contact me if you wish to learn more about my experience as an Honours student in the Rheumatology Research Group.

Email: lmbac1@student.monash.edu

ABSTRACT

Background
Glucocorticoids (GC) are a widely used therapy, however use over long periods or at high doses results in metabolic adverse effects, and so replacement therapies are required. Glucocorticoid-Induced Leucine Zipper (GILZ) is a GC-induced immunomodulator which plays a significant role in the regulation of inflammation with implications in autoimmune diseases. Unlike GC, GILZ function is not mediated via glucocorticoid receptor binding, suggesting it may avoid the adverse effects of GC.

Little is known about the mechanisms responsible for regulation of GILZ expression, and it is paramount that we understand this to enable development of GILZ as a steroid-sparing target. This may yield targetable pathways to therapeutically increase GILZ abundance. A putative enhancer region, known as the GILZ 12-Del region, was previously identified as a potential area of importance in the regulation of GILZ in CD8+ T cells. This project investigated in what immune cell types the GILZ 12-Del region is active, what transcription factors bind the GILZ 12-Del region, and the consequence of GILZ 12-Del region deletion on GILZ expression, activation and effector function in CD4+ T cells.

Method
ATAC-sequencing and RNA-sequencing data from publicly available datasets were utilised to determine GILZ 12-Del chromatin accessibility and GILZ expression across immune cell subsets. Analysis of Transcription Factor Binding Site predictions and ChIP-sequencing were used to determine what transcription factors interact with the GILZ 12-Del region. Using a GILZ 12-Del deletion mouse, naïve CD4+ T cells were polarised toward T helper cell subsets. Proliferation and GILZ expression were assessed by flow cytometry. GILZ mRNA, lineage-determining transcription factors and cytokines were quantified using qPCR and ELISA.

Results
The GILZ 12-Del region is accessible in CD4+ T cells during development and naïve states, and inaccessible during effector states. This accessibility profile correlates with GILZ expression. The region is not active in B cells, dendritic cells, monocytes or macrophages. Transcription Factor Binding Site prediction analysis and ChIP-sequencing revealed that the GILZ 12-Del region is highly active with many transcription factors capable of interaction. Many of these transcription factors are involved in T cell development and differentiation. Despite this, in vitro polarisation of Th2 and Th17 cells from WT and GILZ 12-Del deficient naïve CD4+ T cells revealed no effect of GILZ 12-Del deletion on GILZ expression, activation and effector function.

Conclusion
This study provided insights into the molecular mechanisms that control immunity, by exploring the transcriptional regulation of the immunomodulatory protein GILZ. It established the potential role of a putative transcription enhancer, known as the GILZ 12-Del region, in the regulation of GILZ expression in CD4+ T cells that may be responsible for regulating the gatekeeper effect GILZ asserts on T cell activation.

However, preliminary in vitro analysis did not establish this region is responsible for the regulation of GILZ expression in CD4+ T cells. Further studies exploring regulation of GILZ expression at earlier time points are required. In the future this research could provide strategies for transcriptionally enhancing GILZ expression, with positive consequences in replacing GC and treating autoimmune conditions.
Hi all! I completed a BMedSci(Hons) in 2020 and delved into the research side that underpins clinical practice. Having completed Year 4C I was eager to explore anaesthetics and critical care in more depth. I set out to conduct a critical care related clinical trial however was soon sent back to the drawing board by COVID-19. Instead, I elected to tackle the instigator of the problem and, like many researchers worldwide, pivoted my attention towards COVID. This represented uncharted territory as, along with my supervisors, I planned a systematic review and meta-analysis for studies which had not even been published yet, needing to anticipate the direction of the literature. My experience encapsulates an important element of research – that much of it is unexpected and does not always take the direction we expect. Despite the disruption I’ve enjoyed a year of delving into the most topical subject of the moment, honing time-management skills and taking ownership of my own project. Regardless of whether you feel your year goes to plan, you will be able to navigate a path forward and learn immensely from your experiences. All the best!

C-reactive protein and procalcitonin for the prediction of mortality in COVID-19 patients: A systematic review and meta-analysis

Supervisor Names and Institute Affiliations:
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Critical Care and Perioperative Medicine, School of Clinical Sciences, Monash University
Dr Amie Hayley
Centre for Human Psychopharmacology, Swinburne University of Technology

ABSTRACT

Background
COVID-19 is a serious and ongoing global health issue with a respiratory origin and important inflammatory pathogenesis. The rapid voluminous publication on the condition necessitates timely synthesis into clinically meaningful conclusions that may assist prognostication.

Objectives
A meta-analysis was performed to assess the evidence on the potential role of C-reactive protein (CRP) and procalcitonin (PCT) as predictive biomarkers of COVID-19 clinical outcomes, primarily mortality. The review also sought to determine the optimal cut-off for admission CRP and PCT as predictors of mortality.

Method
The electronic databases MEDLINE, EMBASE, Cochrane Library, Scopus and Web of Science were systematically searched up to 19th June 2020. Articles were sought on adult COVID-19 patients reporting CRP and PCT as continuous data in direct relationship to mortality, intensive care unit (ICU) admission, need for supplemental oxygen, invasive mechanical ventilation (IMV), renal replacement therapy (RRT) or development of acute kidney injury (AKI). All studies were assessed through random effects meta-analysis to estimate the pooled mean difference (MD) with 95% confidence interval (95%CI). Receiver operator characteristic (ROC) curves were constructed to define optimal cut-off values for admission CRP and PCT and assessed by calculating the area under the curve (AUC). A modified Newcastle-Ottawa scale was utilised to assess study quality, and the I2 statistic and funnel plot for heterogeneity and publication bias respectively.

Results
Fifty-one eligible studies were included, constituting 16236 patients. Compared with survivors, CRP was 62.37mg/L (95%CI 41.19-83.55, p <0.00001, I2 = 99%) greater and PCT 0.32ng/mL (95%CI 0.24-0.40, p <0.00001, I2 = 93%) greater in deceased hospitalised COVID-19 patients. Subgroup analysis by age and publication date was not significant and reinforced the significant predictive association when the biomarkers are sampled on hospital admission. CRP, but not PCT, was also significantly raised in hospitalised COVID-19 patients who progressed to need ICU admission (MD = 62.92mg/L, 95%CI 41.15-84.68) and IMV (MD = 36.96mg/L, 95%CI 9.10-64.82). There was a paucity of evidence for the remaining secondary outcomes. High variability was evident between studies, mitigated on occasion by sensitivity analysis, whilst minimal evidence of publication bias was observed. Most studies were of low risk of bias, however frequently constrained by incomplete outcome follow-up and lack of detail. The optimal cut-offs for mortality were CRP >87.79mg/L (AUC = 0.821, 95%CI 0.698-0.943, p < 0.0001) and PCT >0.175ng/mL (AUC = 0.810, 95%CI 0.654-0.967, p < 0.001).

Conclusion
This analysis identified both CRP and PCT of adult COVID-19 patients on hospital admission to be predictive of mortality and provided cut-offs with good predictive utility. CRP, but not PCT, was also predictive of need for ICU admission and IMV, whereas there was insufficient evidence to derive meaningful conclusions on the need for supplementary oxygen, RRT and development of AKI. An international cohort provides good generalisability. These findings constitute simple conclusions to aid, but not substitute, clinical judgement and resource allocation in COVID-19 patient care.
Ms Gayathri Bimal

Identifying influencing factors for perinatal mortality in women of African origin

Supervisor Names and Institute Affiliations:
Dr Kirsten Palmer (Department of Obstetrics and Gynaecology, Monash Health)
Dr Miranda Davies-Tuck (Hudson Institute)
Professor Ben Mol (Department of Obstetrics and Gynaecology, Monash Health)

ABSTRACT

Background

Perinatal mortality is a devastating outcome affecting eight women in Australia every day. Women born in Africa face significantly higher perinatal mortality rates than Australian-born mothers but known feto-maternal and social risk factors for perinatal death fails to account for their disparate outcomes. Accelerated placental ageing, resulting in poorer outcomes at term gestations, may contribute to perinatal inequities in African women. Decrease engagement in maternity care or declined obstetric interventions owing to culturally unsafe care may also play a role.

Aims

Our overarching aim was to identify modifiable factors for perinatal death in African women and offer these mothers tailored and culturally sensitive strategies to reduce perinatal inequities. We sought to compare rates of perinatal mortality between African and Australian-born women and assess the influence of gestation on perinatal death. We also aimed to assess differences in healthcare engagement and declined obstetric care between African women with livebirth and perinatal death. Finally, we strived to understand reasons for declined care in African women and compare this to Australian-born mothers.

Methods

This was a retrospective cohort study of all African and Australian-born women delivering at Monash Health between 2012 and 2018. Feto-maternal demographics, gestation length and measures of healthcare engagement were extracted from routinely collected hospital data. Rates of perinatal mortality and perinatal mortality per ongoing gestation at term were compared between African and Australian-born women. African-born women with livebirth and perinatal death were contrasted to identify influencing healthcare factors for perinatal death.

Results

26,033 pregnancies were included in the study, of which 23,499 were to Australian-born women and 2,533 were to African women. Perinatal mortality rates were significantly higher for African women (OR 1.5, 95%CI 1.1 – 2.0) compared to Australian-born mothers. The risk of stillbirth per advancing gestation increased earlier (37 weeks vs 38 weeks gestation) and faster for African mothers compared to Australian-born mothers. African women with perinatal death were less likely to have aneuploidy screening and more likely to use less accurate screening techniques than those with perinatal deaths. There were no other differences in healthcare engagement between African women with livebirth and perinatal death, including overall rates of declined obstetric care. Reasons for declined care varied for African women with livebirth and perinatal death and Australian-born women with perinatal death. Unexplained antepartum fetal death was disproportionately high in African women with lower uptake of perinatal autopsy compared to Australian-born mothers.

Conclusion

Healthcare engagement is not significantly associated with disparate perinatal outcomes in African mothers. Higher rates of unexplained antepartum death in African women may be related to decreased uptake of post-mortem. Further research is needed to understand driving forces for perinatal death among African-born women in Australia.

During my fourth year of medical school, I developed a strong passion for obstetric medicine and interest in improving pregnancy care experiences for culturally and linguistically diverse women. My project was a wonderful opportunity to tangibly improve perinatal outcomes of culturally and diverse women while developing a better understanding of research and medical science. I have had an incredible experience in my BMedSc(Hons) year, gaining valuable critical thinking skills and getting several opportunities to deeply explore my chosen field. I am deeply grateful for the support of my supervisors, faculty and fellow colleagues and would be more than happy to be contacted by any future BMedSc(Hons) students.
Ms Melissa Jane Bruerton

Genome-based typing of Shigella flexneri

Supervisor Names and Institute Affiliations:
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Host-Pathogen Interaction Lab, Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research
Dr Jane Hawkey
Department of Infectious Diseases, Monash Central Clinical School, The Burnet Institute

ABSTRACT

Background
Shigella flexneri is one of four species of Shigella that causes the highly infectious disease shigellosis. S. flexneri invades and colonises the colon, with the help of a large virulence plasmid to induce shigellosis characterised by fever, abdominal cramps and bloody diarrhoea. Shigellosis places a large burden of disease on the global community and is responsible for over 160,000 deaths every year. S. flexneri is common in developing regions but has recently caused outbreaks in the men who have sex with men community in developed countries including Australia.

The S. flexneri species is divided into serotypes based on the variation in the O-lipopolysaccharide antigen. However, the classification is not phylogenetically informative and limited by serotype switching facilitated by transfer of the genes that transcribe the O-lipopolysaccharide antigen. Serotype switching also limits vaccine development as current prototypes are based on the O-lipopolysaccharide antigen. Other molecular classification tools are limited by time, cost, technical difficulties and low precision differentiation. Recently, whole genome sequencing has identified the population structure of S. flexneri species but due to computational difficulties it is not yet optimised as a classification scheme.

The development of a high definition and phylogenetically informative typing scheme will help the current surveillance and management of S. flexneri.

Method
This project collated a global representation of publicly available S. flexneri genomes. The genome data was mapped to a reference genome (S. flexneri 2a 301) to identify genetic differences that formed the basis of a maximum-likelihood phylogenetic tree. Distance-based analysis was performed to subdivide the phylogeny into genetically distinct clusters and to create a genotype nomenclature. Associated metadata was used to assess temporal and geographical distribution of S. flexneri species. The presence of antimicrobial resistance genes and serotype were also investigated. In conjugation, a wet-lab plaque assay was performed on clinical and reference S. flexneri isolates to investigate intercellular spread.

Results
A total of 2,461 genomes were collated, to create a maximum likelihood phylogeny made up of 446 genotypes across 9 lineages. Europe was overrepresented in the data (78%) due to routine whole genome sequencing in the region. In the last five years, lineage 3 was most commonly isolated followed by lineage 1 and 2. The global distribution was limited by testing location that overlooked the true isolate origin. There was no distinct clustering of antimicrobial resistance, however, the presence of azithromycin resistance was confirmed in men who have sex with men defined groups previously identified in the literature. The project also represented the spread of serotypes across the lineages. The plaque assay was optimised in the HT-29 cell line and confirmed the importance of S. flexneri virulence plasmid in intercellular spread.

Conclusion
The genotypes identified in this project will form the foundations of a high-resolution genome-based typing scheme. The typing scheme will create a global classification system that will allow researchers and clinicians to identify the evolutionary relationships and clinical importance of S. flexneri stains, therefore providing a universal framework for epidemiological surveillance, specific antimicrobial guidelines and vaccine development.
Mr Kenny Budiman

Associations between Bariatric Surgery, Barrett’s Oesophagus, and Oesophageal Cancer

Supervisor Names and Institute Affiliations:
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Professor Wendy Brown¹,²
1. Department of Surgery, Central Clinical School, Monash University, Melbourne, Victoria, Australia
2. The Alfred Hospital, Melbourne, Victoria, Australia

ABSTRACT

Background

Bariatric surgery has become an effective solution to treat obesity and prevent its inflicting comorbidities. However, bariatric surgery may cause complications which are still unknown. Several current studies have shown associations between bariatric surgery and an increased oesophageal cancer incidence and its precursor, Barrett’s oesophagus. Other challenges remain as endoscopic appearance of the oesophago-gastric junction following sleeve gastrectomy is not fully elucidated.

The overarching aim of this project is to identify the complex interactions of obesity and bariatric surgery, with the development of Barrett’s oesophagus and oesophageal cancer. The interactions include bariatric surgical cancer outcomes, relative risk, and endoscopic appearance following sleeve gastrectomy, the most commonly performed bariatric surgery.

Method

This project is a retrospective study taken from a prospectively maintained database. The project consists of three related studies. The first study, a case-control study, looked for oesophageal cancer outcomes in bariatric patients (n=15) and non-bariatric patients (n=95). The second study was a population-based cohort study to measure the relative risk of oesophageal cancer among bariatric patients. Bariatric patients (n=11595) were compared with Australian population’s rate obtained from AIHW using indirect standardisation. Finally, the third study was a retrospective cohort study from endoscopic synoptic reports, to describe the newly endoscopic appearance and changes following sleeve gastrectomy, with a validation study using histology and manometry.

Results

In the first study, it was observed that bariatric patients were younger (62.20 ± 10.16 vs 68.52 ± 9.10, p=0.0191) and higher in weight (127.0 (95.50 – 147.3) vs 73.00 (61.30 – 90.00), p<0.0001). In management, bariatric patients were also unexpectedly less likely to obtain curative management (66.67% vs 87.37%, p=0.0393). Moreover, following oesophageal reconstruction surgery, bariatric patients had higher complication rates (100% vs 53.73%, p=0.0438). The second, population-based cohort study showed an increased risk of oesophageal cancer following bariatric surgery (SIR = 2.42, 95% CI 1.17 – 3.22).

Conclusion

This study demonstrates that the risk for oesophageal cancer is associated with obesity and bariatric surgery and is more challenging to treat in bariatric patients. There is also an association of bariatric surgery with oesophageal cancer, but it requires further study as the cancer is multifactorial. And lastly, following sleeve gastrectomy, an effaced OGJ appearance may be expected, and should be differentiated with Barrett’s appearance endoscopically.

My name is Kenny, a fourth-year medical student from Indonesia. I decided to do an honours year mid 2019 since I’ve always been interested in conducting research and observe new perspectives from different countries. I took this project since I have always been interested in metabolic diseases, including obesity. It is an interesting aspect since surgery is a viable option of obesity care in Australia, which is uncommon back in my country. I learned so many new things from this honours year, starting from how to design a research to perfecting academic writing. I also managed to obtain several clinical aspects from surgery and understand how surgical setting works.

If there are advice that I would give, it is to always focus on the solution of the problem, instead of focusing on the problem itself. There will be many challenges during your honours year, but there are also plenty opportunities to pursue during the honours year. Also, don’t hesitate to ask for help!
Ms Sarah Elizabeth Butler

The relationship between induction of labour and caesarean section – Do we really have all the answers?

Supervisor Names and Institute Affiliations:
Dr Mary-Ann Davey, Prof Euan Wallace, The Ritchie Centre, Monash University

ABSTRACT

Background

The rising rates of induction of labour (IOL) continue to concern health professionals, particularly in the absence of clear evidence for its benefit. In Australia, the rate of IOL continues to rise, from 31% in 2004 to 43.1% in 2017 among low-risk nulliparous women. Is it credible that nearly half of all pregnancies require active delivery to improve outcomes? Currently, research into the impact of IOL on maternal and neonatal outcomes has yielded conflicting results and is commonly hindered by flaws in study design and analysis protocols. The potential increased risk of caesarean section is a particular concern. With IOL becoming an increasingly common intervention, we need robust evidence to both provide clinicians and expectant women a better understanding of the relevant risks and benefits of IOL and allow women to make informed decisions about their birth. Given continued uncertainty and the possibility of harm, I sought to further explore the relationships between IOL and potential outcomes, learning from some of the flaws of previous approaches. Specifically, I sought to explore whether IOL influences the rate of caesarean birth.

Method

I undertook a retrospective cohort study of all singleton births delivered at ≥37 weeks’ gestation in Victoria from 2010-2018. The primary outcome was caesarean birth. I also examined perinatal mortality, peripartum haemorrhage, anal sphincter injury, shoulder dystocia, uterine rupture and special care nursery (SCN) or neonatal intensive care (NICU) admission. I performed descriptive analyses and logistic regressions to assess these outcomes in women undergoing IOL compared to women who deliver beyond the given week (primary analysis), or at or beyond the given week (secondary analysis). After replicating the Stock 2012 methodology, I repeated my analyses with several modifications in place, to improve the study design, and re-examine the outcomes observed.

Results

The proportion of singleton women who underwent IOL ≥37 weeks’ gestation in Victoria has increased from 24.5% in 2010 to 36.8% in 2018 (p-value <0.001). IOL in nulliparous women was associated with an increase in the odds of caesarean birth ≥38 weeks’ gestation (p-value <0.001). IOL was also associated with an increase in the odds of assisted vaginal birth from 38 weeks (p-value ≤0.001), postpartum haemorrhage from 37 weeks (p-value ≤0.003) and SCN/NICU admissions at 37-39 weeks’ gestation (p-value <0.001). There was an association between IOL and an increase in the odds of shoulder dystocia (p-value <0.001). We also demonstrated an association between IOL at 37-40 weeks and a reduced odds of anal sphincter injury (p-value =0.013) and at 41 weeks with reduced odds of SCN/NICU admissions (p-value <0.001).

Conclusion

IOL is an increasingly common intervention which is associated with an increase in the odds of caesarean section among nulliparous, term, singleton pregnancies in Victoria from 38 weeks’ gestation. This emphasises the importance of examining the specific risks and benefits of IOL for the low-risk nulliparous, pregnant woman to permit informed recommendations and decisions about labour.

I chose to undertake a BMedSc(Hons) after completing year 4C in 2019, hoping to develop my skills in research and data analysis, and further my interest in the O&G field. After looking at a number of different projects in the O&G department, I decided that this topic, exploring one of the most commonly asked questions in obstetrics, with a wide variety of conflicting research already completed, was a fascinating and complex topic that I was excited to delve into. Whilst not the year I had anticipated, completing a BMedSc(Hons) in 2020 was a wonderful change from clinical medicine, and a great experience overall, especially thanks to my incredible supervisors and BMedSc(Hons) colleagues.
Ms Lara Ines Calligaro

The effects of corticosteroid and progesterone therapy on brain structure and function in growth restricted fetal sheep

Supervisor Names and Institute Affiliations:
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Both:
- The Richie Centre, Hudson Institute of Medical Research, Melbourne, VIC
- Department of Obstetrics and Gynaecology, Monash University, Melbourne, VIC

ABSTRACT

Background

Fetal growth restriction (FGR) is a common complication of pregnancy predominantly caused by suboptimal placental function causing chronic hypoxia, and conferring poor physical health and neurodevelopmental outcomes. The majority of growth restricted infants are born preterm, and thus are more likely to be exposed to antenatal glucocorticoid therapy to rapidly mature the fetal lungs and improve neonatal survival. However, the extra-pulmonary effects of glucocorticoids are unclear and there are concerns antenatal glucocorticoids may have adverse effects on fetal neurodevelopment and exacerbate growth restriction.

Levels of placental-derived neurosteroids, such as allopregnanolone, which are essential for normal fetal brain development, are altered in FGR fetuses, and prematurely lost with preterm birth. Furthermore, antenatal glucocorticoid therapy significantly reduces fetal levels of allopregnanolone, which may adversely impact brain development. Therapeutic intervention to increase fetal levels of allopregnanolone (i.e. Progesterone) may promote normal brain development in FGR fetuses exposed to antenatal glucocorticoids.

Aims

Our study aimed to investigate the differential effects of betamethasone and progesterone on hippocampal injury and fetal brain function, in FGR and normally grown fetal sheep.

Method

Single umbilical artery ligation surgery was performed on fetal sheep at 105 days gestation (term = ~145 days), to induce placental insufficiency and FGR. During the surgery, arterial catheters and electrocorticogram (ECoG) probes were implanted in the fetus. At 112 days gestation a three-day course of progesterone began (400mg IM BD), whilst betamethasone was given in line with current clinical guidelines for preterm fetal lung maturation on days 113 and 114 (11.4mg betamethasone, 24 hours apart). Fetal arterial blood gases and ECoG recordings were taken throughout the experimental period. At 124 days gestation, the fetuses were euthanised and brain tissue collected. Brain tissue was fixed in 10% formalin, cut and stained using immunohistochemistry to investigate neuropathology. Neuronal wellbeing (NeuN +ve cells) and inflammation (Iba-1 +ve cells) were assessed within the hippocampus (dentate gyrus, CA3 and CA1). Seizure burden and abnormal brain activity were assessed from ECoG recordings.

Results

FGR fetuses were significantly more hypoxic and hypoglycaemic than control fetuses, and betamethasone administration resulted in hyperglycaemia and increased lactate. Progesterone did not alter fetal blood gas parameters. FGR fetuses had higher seizure burden, with increased seizure number, duration and amplitude compared to control fetuses. Betamethasone treatment did not alter seizure activity, and progesterone administration did not reduce seizure activity in FGR fetuses, but increased seizures in controls. Neuronal count (NeuN) and microglial activation (Iba-1) were not altered by FGR, BM or progesterone.

Conclusions

FGR fetuses develop in a hypoxic and hypoglycaemic environment, which may alter brain development. The FGR brain appears hyper-excitabile, with increased seizure activity compared to controls, which may underlie or reflect the neuropathology and functional deficits seen in FGR children. Progesterone did not improve seizure burden in FGR or control fetuses, which may be due to a lack of allopregnanolone synthesis. In this study, neuronal wellbeing and microglial activation was not altered at the level of the hippocampus within FGR and/or betamethasone treatment compared to controls, which may be due to regional variations within the model.
Mr Nathan Samuel Dalton

Short- and Long-Term Outcomes of Medical Emergency Team Calls at an Australian Regional Hospital

Supervisor Names and Institute Affiliations:
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Mr Zakary Doherty, School of Rural Health, Monash University

ABSTRACT

Background

A medical emergency team (MET) is a group of clinicians in a hospital setting with specific training, skills and resources which enable them to respond in a timely and appropriate fashion to clinical deterioration occurring in patients outside of the intensive care unit. METs have been implemented and studied in hospitals worldwide, but little research has been conducted on METs in regional Australian settings. Further, the long-term survival outcomes of patients reviewed by the MET are unknown.

Aims

To investigate the short- and long-term mortality outcomes of patients who had a MET call at a regional Victorian hospital, and to describe the associated patient and MET call characteristics.

Method

This retrospective cohort study analysed data of adult patients’ MET calls occurring at Bendigo Health, a regional Victorian hospital, from July 2012 to March 2020. Details of each Bendigo Health MET call are recorded in a local on-site database. Data linkage to local hospital data and the Victorian Death Registry was performed. Date of death data were retrieved from the Victorian Death Registry to allow for long-term mortality analysis. Binary logistic regression was performed to determine patient and MET call factors associated with 30-day mortality (after a patient’s first MET call). Cox proportional hazards (PH) regression was performed to determine patient and MET call factors associated with long-term mortality (measured from 30 days after a patient’s first MET call). A Kaplan-Meier curve was created describing the survival probability for the patient cohort, stratified by age <75 and >75 years.

Results

Our study included 6499 eligible patients. The cohort median age was 71.5 years. Female patients accounted for 52.4% of the cohort. Surgical patients (43.5%) and medical (43.0%) comprised the majority of the patient cohort. In-hospital mortality was 6.9%; 30-day mortality was 13.5% and one-year mortality was 27.5%. Factors significantly associated with higher 30-day mortality after the MET call included increasing age (odds ratio [OR] 75-84 years = 2.44, OR 85+ years = 2.61, compared with 18-54 years), male sex (OR females = 0.75), medical admission (OR surgical admission = 0.58), presence of limitation of medical treatment (LOMT) before first MET call (OR = 4.56) and LOMT instituted by the MET (OR = 3.76). Factors significantly associated with higher long-term mortality included increasing age (hazard ratio [HR] 85+ years = 1.44, compared with 75-84 years), male sex (HR females = 0.75), medical admission (HR surgical admission = 0.88) LOMT present before the patient’s first MET call (HR = 1.89), and LOMT instituted by the MET (HR = 1.64).

Conclusions

To our knowledge, this is the first study to document the characteristics associated with long-term mortality risk in MET patients. As with short-term mortality outcomes, factors such as age, male sex and presence of LOMT (both before and instituted by the MET) were associated with increased mortality risk.
ABSTRACT

Background

Multiple Sclerosis (MS) is an inflammatory condition that affects the central nervous system. While the pathophysiology is not fully understood, a shift from acute inflammatory to neurodegenerative processes occurs at later stages of the disease. It is thought that this shift relates to iron uptake by microglia in the rim of MS lesions that perpetuate ongoing chronic inflammation. The presence of iron affects the local magnetic susceptibility of brain tissue, a factor that is fundamental to MRI imaging. Phase contrast imaging is sensitive to shifts in magnetic susceptibility and has therefore been suggested as a potential method of identifying these chronic inflammatory processes through the presence of phase-contrast enhancement of paramagnetic lesion rims.

Aims

The primary aim of this study was to evaluate the relationship between MS lesion enhancement on phase-contrast imaging and lesion progression over time. A secondary aim was to analyse changes to the distribution of phase-contrast MRI signal and measures of diffusion within MS lesions.

Method

This was a retrospective cohort study of 110 MS patients from the Royal Melbourne Hospital. Clinical MRI scans were collected across a 6 year period and included the following MRI modalities performed at 3T: 3D FLAIR, T2*-weighted magnitude, phase-contrast, apparent diffusion coefficient (ADC), and magnetisation-prepared rapid gradient echo. MRI images were co-registered and processed to create image masks identifying the lesions, lesion rims and normal appearing white matter. Lesion volumes, phase-contrast and apparent diffusion coefficient values were calculated from these masks for use in the statistical analysis. The effect of phase-contrast measures and time on lesion progression was analysed using two mixed linear models with lesion volume and ADC as dependent variables. Comparison of the NAWM and lesions was performed through a histogram analysis and bootstrapped ANOVA.

Results

43 patients who displayed 515 lesions were included in the analysis. Lesions when compared to NAWM displayed a phase signal distribution that was shifted with an increased mean (-5.65 vs 8.98; p<0.001) and smaller standard deviation (125.40 vs 103.04; p<0.001). The ADC distribution for lesions was drastically shifted compared to the NAWM with the mean (776.15 vs 1220.81; p<0.001) and standard deviation (184.31 vs 352.06; p<0.001) almost doubling. An enhancing phase-contrast rim produced a 0.17 unit (p<0.001) increase in lesion log volume, while an increase of 1 unit in log maximum phase value related to a 0.86 unit (p<0.001) increase in log volume. The effect of a phase rim and maximum phase signal reduced over time. Only maximum phase signal significant related to lesion ADC value, with a 1 unit increase in log maximum phase signal corresponding to a 0.11(p<0.001) unit increase in log mean ADC value.

Conclusions

Phase-contrast imaging is able to detect features that relate to the lesion volume and diffusivity. Whether these features reflect the chronic inflammatory processes responsible for neurodegenerative MS is not yet clear. While these relationships indicate phase-contrast imaging is a viable method for obtaining further information about lesion composition, accurate interpretation and the predictive value of these relationships require further study.

Following fourth year I undertook this BMedSc(Hons) to have a break from clinical placement and gain some broader experience in research. While I expected this year to be challenging, I came into it looking forward to acquiring new skills and knowledge that I could apply in future. As I’m sure is common in many honours projects, the initial task of more thoroughly understanding my topic area of Multiple Sclerosis and MRI was daunting. There was a significant amount of learning required that involved complicated concepts. However, after clearing this first hurdle I felt much more comfortable with the data processing and interpretation in my study. Overall, the year was very rewarding and I would highly recommend an honours year for anyone who wants a break from clinical or would like to better understand research.
Ms Tara Dev

Women’s perspectives of over-the-counter access to oral contraception

Supervisor Names and Institute Affiliations:
Primary supervisor: Professor Danielle Mazza
Secondary supervisor: Doctor Natalie Amos
SPHERE (NHMRC Centre of Research Excellence in Sexual and Reproductive Health for Women in Primary Care)

ABSTRACT

Background

Over 100 countries around the world provide contraceptive pills over-the-counter (OTC). Majority of the oral contraceptive (OC) options still require doctor’s prescription in Australia. While many studies conducted internationally have suggested that patients are in favour of over-the-counter access, there is limited research on Australian women’s perspectives. There are many models of OTC access that have been trialled internationally however, there is limited research on which model is most preferable for women. The aim of this study is to explore Australian women’s perspectives of over-the-counter access to oral contraception and to explore whether they have a preferred model of OTC access.

Method

A qualitative-descriptive method was used. Women participants (N=20) aged 18-44 were recruited through a post to a relevant Facebook group. They participated in a semi-structured, telephone interview and the interviews were transcribed verbatim. Data was then coded in NVivo 12 and analysed using Braun and Clarke thematic analysis with two coders to develop themes and subthemes.

Results

Four main themes were identified surrounding confidence and trust in pharmacists; the importance of autonomy and access for women; health and safety concerns regarding OTC access and models of pharmacy provision of OCs. The data from our study demonstrates that women in Australia feel comfortable seeking information and guidance from pharmacists. Many women felt that pharmacists possessed adequate knowledge around OCs from a medication perspective, however, they expressed concerns regarding their knowledge surrounding a patient’s medical history and their ability to screen for contraindications. Women described greater access and autonomy and lessened stigma when obtaining contraception as benefits to OTC access to OCs. Some concerns were also highlighted by women regarding decreased safety and the lack of comprehensive contraceptive counselling. Women were asked to appraise different models of OTC and the findings suggest that women might like a model that involves an interaction with a pharmacist for first-time users of OCs. This interaction should include screening for contraindications to OCs, contraceptive counselling and encouragement to complete preventive screening. These interactions with a pharmacist should be regular as well as private and comfortable for women. However, women would like for more experienced users of OCs to be able to access OCs directly off-the-shelf with guidance available from pharmacists should they need it.

Conclusions

This study produced new knowledge detailing women’s perceptions of OTC access to OCs in addition to describing their preferred attributes of each OTC model. The results from this study detailing women’s concerns and how these concerns can be addressed should be used if trialling pharmacy provision of OCs was to be pursued. The findings of this study will be particularly useful when designing a model of OTC access.
Ms Supipi Devadittiya
Development of a prototype for a novel, steroid-eluting dressing for benign vocal fold lesions

Supervisor Names and Institute Affiliations:
A/Prof Deb Phyland - Department of Surgery (School of Clinical Sciences at Monash Health), Monash University
Dr Paul Paddle - Department of Surgery (School of Clinical Sciences at Monash Health), Monash University

ABSTRACT

Background
There is an unmet clinical need for a non-invasive arm therapy that achieves quick-onset, prolonged therapeutic relief in the management of benign vocal fold lesions. This project hypothesized that this need could be met through developing an adherent, thin film dressing that could reliably elute steroid particles directly onto the epithelial surface of the lesion over a prolonged period of time. The challenge lies in that such a dressing must withstand the mechanical stresses of vocal fold collision and the turbulent aerodynamics of the larynx. Therefore, metal-phenolic networks (MPN) were hypothesized to be an appropriate biomaterial for the dressing due to their unique, universal adherence properties and established drug-elution capacity.

Method
Gyeongwon’s protocol was modified to develop an MPN-based prototype. Atomic Force Microscopy and Dynamic Mechanical Analysis were used to characterise the thickness and elasticity of the films, respectively. Film adhesion was then tested using a benchtop epithelial surface. Film degradation within laryngeal pH ranges was also studied. Finally, the morphology and elution profiles of fluorescent-Dexamethasone and -Poly-lactic-co-glycolic acid loaded films were examined.

Results
The theoretical phases of this study formulated a detailed characterisation of a novel steroid-eluting dressing that can be successfully assembled in a lab-based setting. The MPN-based films were fashioned into an ultrathin (<7.665 μm) that demonstrated greater elasticity than the vocal fold epithelium. The films exhibited promising adherence to epithelial surfaces and were resilient to persistent aerodynamic stress. Furthermore, they showed mechanically stability when immersed in a pH 6.8 environment. We were also able to confirm, for the very first time, the successful chemical impregnation of Dexamethasone-fluorescein and PLGA-fluorescein into MPN films. The physicochemical properties of MPN, as characterised by our experiments, support our hypothesis that MPN is a suitable biomaterial for use within this clinical context.

Conclusions
Although a clinically viable dressing remains in its nascent stages of development, our prototypical design and experimental findings serve as an important proof of concept. The development of such a dressing could revolutionize the current paradigm of treatment for BVFL. In conjunction with our promising findings, the potential of such an exciting innovation underpins the rationale for further advancement in this area.

Prior to my BMedSc(Hons) year, I had very shallow insight into the world of medical research. I decided to opt in to BMedSc(Hons) after my fourth year because I was drawn to the freedom of developing expertise within a specialised area. My project centres around engineering a novel dressing that could ideally be translated into standard ENT practice in the future. Therefore, my research question lies at the interface between two fields; ENT surgery and chemical engineering. This granted me the opportunity to engage in medical-technology development from two fascinating vantage points. These made for some of the most satisfying learning curves of my entire university experience. The themes of my project helped me to actualise new non-clinical interests that I would like to infuse into my medical career in the future. It has also sharpened my creative and strategic thinking in a way that I believe will shape the lens through which I view clinical practice. I am lucky to be able to report having had a deeply enriching experience with this project in spite of the COVID19. Please don’t hesitate to contact me if you have any questions! Best of luck!
Ms Suwandi Dewapura

Perinatal Mortality: Identifying Targets for Improvement

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Safer Care Victoria, Department of Health and Human Services

ABSTRACT

Background

The five-year gestation standardised perinatal mortality ratio (GSPMR) is an expression of perinatal mortality that is used as a crude performance indicator of Victorian maternity services. It has shown significant variation between hospitals. Most recently for 2014-18, in comparison to the state-wide average which is by definition 1.0, the three Victorian Level 6 maternity services, Mercy Hospital for Women, Monash Medical Centre and Royal Women’s Hospital, recorded GSPMR values of 0.61, 0.87 and 0.95. It was proposed that exploring the underlying reasons for this variation may identify useful insights into opportunities for a reduction in the perinatal mortality rate. In this project I sought to describe and compare the profile of perinatal deaths across the three Victorian Level 6 hospitals, to identify any differences in populations and care between the hospitals that might explain differences in GSPMR, and to derive potential targets for improvement accordingly.

Method

A retrospective study using whole-of-population perinatal mortality data from the three Victorian Level 6 maternity services from 2010 to 2018. I sourced data from the Victorian Perinatal Data Collection, extracting information related to patient demographics, type of death (stillbirth or neonatal death), gestational age and cause of death, as per the Perinatal Society of Australia and New Zealand (PSANZ) Perinatal Death Classification (PDC) and Neonatal Death Classification (NDC). The analysis was subdivided to identify whether differences in perinatal mortality may be attributable to stillbirths, neonatal deaths, or both.

Results

The results are presented in a de-identified form, with each hospital randomly allocated a letter (Hospital A, Hospital B and Hospital C) to protect confidentiality. Overall, the highest stillbirth and neonatal mortality rates were observed at Hospital B and the lowest rates at Hospital A. There were significant differences between the hospitals in the stillbirth rates across gestation (p=0.031). Similarly, there were significant differences in the proportions of stillbirths due to different causes between the hospitals (p<0.001). The largest differences between hospitals were seen prior to 25 weeks and from 37 weeks onwards. There were no significant differences in neonatal mortality between the hospitals. The most prevalent PDC classification of neonatal death was spontaneous preterm and the most prevalent NDC classification was extreme prematurity.

Conclusions

There was significant variation in the perinatal mortality profiles between the three hospitals, both with regard to gestation and causes. This inter-hospital variation offers opportunities to identify where pregnancy care may be improved to reduce perinatal mortality across all hospitals. In particular, there were major differences between the three hospitals in relation to stillbirths prior to 25 weeks and after 37 weeks, and those classified as spontaneous preterm, specific perinatal conditions or fetal growth restriction. These should be the priority targets for improvement.

Having been inspired by my O&G rotation in fourth year, in 2020 I wanted to further explore my interest in the field and develop a deeper understanding of research. When Professor Wallace mentioned a project at the Department of Health and Human Services focussing on reducing perinatal deaths in Victoria, I was beyond excited to be involved. My supervisors have worked to give me a well-rounded research experience, from taking me along to research meetings and sending me thought-provoking literature, to actively engaging me in numerous research opportunities. I’m amazed at and proud of my transformation from a rather green research student daydreaming in meetings that made no sense, to now being able to actively participate in those discussions and research somewhat independently.

In overcoming the challenges of the BMedSci(Hons) year, I have developed greater resilience and skills I’ll use time and time again. Shoutout to the staff and students of Prof Wallace’s research group for your support and encouragement!

Doing a BMedSci(Hons) has sparked my passion for research and given me important skills that will serve me well in the future. I couldn’t recommend the experience more highly!

Happy to be contacted with questions: skdew4@student.monash.edu
Ms Anasya Diandra

Cryopreservation of Primary Human Placental (Cytotrophoblast) Cells

Professor Wendy Brown — Department of Surgery, Central Clinical School
Dr Sarah Marshall, Prof Euan Wallace. Department of Obstetrics and Gynaecology, Ritchie Centre, Hudson Institute of Medical Research

Hello, there! I’m Anasya, a fourth-year medical student of Universitas Indonesia. I completed my honours year in 2020, and if I only had one word to describe it, it would be “spectacular”! I came to Australia with no experience in doing laboratory work, but with the help of my amazing supervisors, I am proud to say that I could now perform trophoblast isolation from a fresh placenta! Being a thousand miles away from home during a pandemic was definitely out of my comfort zone, but it was rewarding at the same time. I also learnt to cope with and overcome the challenges I faced. The honours years had also provided me with the opportunity to improve my research skill that will be very useful as an aspiring doctor. I also met many scientists who are experts in their own fields and got to learn from them! With that being said, I was beyond fortunate to undertake a research project that could hopefully pave the road toward improving the maternal and fetal health, and this is an invaluable experience that I will forever treasure.

ABSTRACT

Background

Placental abnormalities, which underlie various pregnancy disorders, are often thought to arise at the cellular level. Amongst the types of cells that contribute to the pathogenesis of these disorders are cytotrophoblasts. These cells are commonly used as in vitro models to enable researchers to gain a better understanding of pregnancy disorders. Due to their nature, cytotrophoblasts must be used as soon as they are isolated from the placenta. Unfortunately, not all scientific researchers have access to fresh samples. To overcome this obstacle, the technique of cryopreservation is often employed to preserve cells for later use. However, no cryopreservation protocol has been established for cytotrophoblasts. Successfully cryopreserved cytotrophoblasts could hopefully be the answer for those who wish to work with cytotrophoblasts but lack access to them.

Method

Primary cytotrophoblasts were isolated from a total of ten placentae from pregnant women who had elective caesarean after >37 weeks gestation. Cytotrophoblasts were supplemented with 0.1mol/L sucrose, 10% human serum albumin and 1,2-propanediol as a cryoprotectant before overnight dehydration and slow-cooling in one of these three temperatures; (1) 4°C, (2) -20°C, or (3) -80°C. To store these cells, they were plunged in liquid nitrogen (-196°C) until they were revived. Thawing was done by rapidly warming the cell suspension at 37°C until ice crystal dissipated. Then, cytotrophoblasts were resuspended in either regular culture media or a concentration gradient of sucrose. Their viability was assessed using MTS assay, cytokeratin 7 (CK7) staining, and measurements of human chorionic gonadotropin (hCG), oestradiol (E2), and lactate dehydrogenase (LDH) after 48 or 72 hours culture.

Results

Cell viability were shown to be the highest in cytotrophoblasts that were cooled in -80°C and thawed in regular trophoblast culture media (MTS 0.203 ± 0.014). Thawing cytotrophoblasts in regular culture media also yielded significantly higher viability compared to a sucrose gradient (p < 0.05). Visualisation using CK7 revealed that the initial cell counts of living cytotrophoblasts were higher in those dehydrated in -80°C, and the number of cells survived remained the highest throughout 72 hours in culture. Hormone measurements after 72 hours showed a significantly higher level of hCG in cells thawed in a sucrose gradient and cooled in -80°C than cells cooled in -20°C (26,133 ± 5,194 vs. 9,167 ± 6,092 IU/L, p < 0.05). The level of E2 was also significantly higher in cells cooled in -80°C than the cells cooled in -20°C (8597 ± 1433 vs. 6346 ± 1508 pmol/L, p < 0.05) and thawed in regular media. LDH level after 72 hours were the highest in cells cooled in -80°C (17 ± 8.505 IU/L).

Conclusions

The initial temperature of -80°C was the most suitable to slow cool and dehydrate cytotrophoblasts. Thawing them with a gradient sucrose supplementation, however, was shown to decrease their viability. Unfortunately, the different protocols tested in this work were unsuccessful in cryopreserving cytotrophoblasts. Lower concentration of sucrose could be opted to thaw primary cytotrophoblasts in future research, while also assessing different cryoprotectant medias.
ABSTRACT

Background

Cataract surgery in patients with uveitis presents a challenge and is associated with higher rates of complications compared to non-uveitic cataract surgery. There are technical difficulties caused by the altered anatomy in a uveitic eye that often necessitates additional surgical trauma. These eyes have a significant risk of postoperative inflammation that may lead to complications including cystoid macular oedema (CMO). Intracameral triamcinolone is used at the time of uveitic cataract surgery to reduce postoperative complications; however, its efficacy and safety have not yet been fully evaluated.

Method

A retrospective cohort study from 2005 to 2020 was conducted at The Royal Victorian Eye and Ear Hospital. Consecutive adult patients with significant iris manipulation, defined as the use of iris hooks or a Malyugin Ring, were included in the study. Cataract surgery cases prior to 2009 where intracameral TA was not available (the control group) were compared with cases after 2009 where intracameral TA was administered (the study group). Data collection was performed using digital and paper health records with a follow-up period of 12 months. The main outcome measures were central macular thickness, incidence of cystoid macular oedema, visual acuity, intraocular pressure, anterior chamber cells grading and oral prednisolone usage.

Results

54 eyes from 46 patients were included in the study group and 19 eyes from 16 patients were included in the control group. Significantly fewer eyes in the study group developed CMO during the follow-up period (22% vs 53%, RR 0.42 (95% CI 0.22 to 0.83), p=0.020). At one month, eyes that received intracameral TA had only ¼ the risk of having CMO compared to the control group (9% vs 35%, RR 0.26, (95% CI 0.10 to 0.75), p=0.019). There was no significant difference in visual acuity between the two groups at baseline. However, the study group achieved a median visual acuity that was 3 Snellen lines better than the control group at one month (p=0.013) and three months (p=0.009). Mean intraocular pressure (IOP) was statistically significantly lower in the study group at one week (p=0.004) and three months (0.015) but not significantly different at all other time points. There were more cases of IOP-rise ≥10mmHg in the study group (50% vs 37%, p=0.425); however, this was not statistically significant. Patterns of inflammation control were not significantly different at any time point. There were no significant differences in rates of adverse events.

Conclusion

Our findings support the use of intracameral TA as a safe and effective method of postoperative inflammation prophylaxis for uveitic cataract surgery. It appears to be particularly effective for prevention of early CMO which may confer a visual acuity benefit.
Mr Husharn Duggan


Supervisor Names and Institute Affiliations:
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ABSTRACT

Background

Early-onset sepsis (EOS) is a lethal condition, especially among premature infants. The highly variable presentation of EOS, compounded by limited diagnostic information provided by investigations, hinders accurate diagnosis. Clinicians therefore rely on intrapartum antibiotics administered to the mother, and empirical antibiotics administered to neonates in the initial hours after birth, to prevent invasive microbial disease. Although this strategy leads to an effective reduction in mortality, some neonates are still unnecessarily exposed to antibiotic treatment, resulting in an increased risk of other serious comorbidities. The identification of the predictive factors for EOS among premature infants will assist clinicians to determine the necessity for antibiotics on a case-by-case basis and reduce unnecessary exposure.

Method

The Australian and New Zealand Neonatal Network provided data for neonates born at less than 32 weeks’ gestation who were admitted to a neonatal intensive care unit (NICU) in Australia or New Zealand between 1 January 2007 and 31 December 2018. We conducted a retrospective cohort study, using linear regression analysis to determine the trends of EOS and its causative microorganisms, and backwards stepwise multivariate logistic regression analysis to identify the predictive factors for EOS. We used SPSS software to analyse the data.

Results

Over the 12-year period, 43,178 extremely premature neonates were admitted to an Australian or New Zealand NICU. Of these, 614 were diagnosed with EOS. Higher rates of mortality, other serious conditions, treatment for respiratory support and ventilation, and lower rates of nasal continuous positive airway pressure use were observed in neonates diagnosed with EOS compared to those that were not.

The leading causative organisms of EOS were E. coli (33.7%) followed by GBS (16.1%). Neonates diagnosed with E. coli-specific EOS had higher rates of mortality and lower rates of intraventricular haemorrhage and retinopathy of prematurity compared to those diagnosed with GBS-specific EOS. The incidence of E. coli-specific EOS increased between 2007 and 2018. Mortality due to GBS-specific EOS decreased over the same period.

The strongest predictor for EOS was fetal distress on antenatal visit (Model 1 - adjusted odds ratio 1.935; 95% CI, 1.601 – 2.338, p-value < 0.001). Other risk factors included a previous premature delivery, preterm labour, maternal antibiotics and maternal age of more than 30 years. Protective factors included hypertension in pregnancy, non-singleton pregnancy and intrauterine growth restriction. The risk of EOS increased when gestational age and birth weight decreased. Certain time periods between membrane rupture and delivery were also associated with an increased risk of EOS (4 – 12, 19 – 336 and ≥ 673 hours).

Conclusions

This study analysed the contemporary trends in extremely premature EOS in Australia and New Zealand between 2007 and 2018, and identified risk and protective factors in this population. There are complex multifactorial issues that influence the risk of EOS in this cohort. These findings will inform evidence-based optimisation of national guidelines and form the foundation for a preterm neonatal sepsis calculator.
Ms Ellen Forster

Viscoelastic Testing During Resuscitations of Adult Trauma Patients

Supervisor Names and Institute Affiliations:
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ABSTRACT

Background

Haemorrhage is a leading cause of early death in trauma patients. A proportion of critically bleeding patients develop acute traumatic coagulopathy (ATC) and have eight times the risk of dying within the first 24 hours compared to patients without coagulopathy. Point-of-care Viscoelastic Haemostatic Assays (VHA) offer a more rapid diagnosis of ATC and may expedite targeted blood product transfusion following this functional bedside coagulation assessment.

Aim

The aim of this research project is to investigate if VHA are able to detect ATC as comparable to our current standard of care: the standard laboratory tests (SLT).

Method

A systematic review was performed to investigate the differences in diagnostic capacity of VHAs. Six databases were search alongside secondary searching to identify eligible manuscripts. Additionally, a prospective cohort study was conducted, to compare VHAs with SLTs in the detection of ATC after major trauma. VHA testing was used as a research tool only and results were blinded to treating clinicians.

Results

For the systematic review, fourteen observational studies satisfied inclusion criteria, but consisted of significant heterogeneity in definitions of ATC, setting and study design, with varied numbers of participants. A meta-analysis of manuscripts that compared VHAs to SLTs, in studies that included trauma patients injured by all mechanisms, concluded that VHAs were associated with a trend downward in blood product usage and mortality rates. The results of the prospective study concluded that VHA was able to differentiate and diagnose patient with coagulopathy as defined by SLTs. Time to SLTs was 47.4 (16.0 mins, while VHAs, by definition produced initial results within 10 minutes.

Conclusions

There is promising evidence to suggest that VHA are able to identify ATC in a faster capacity, however further research is required to identify the clinical benefit of its application in trauma.
ABSTRACT

Background
Osteoarthritis is a common and debilitating degenerative joint disease. Joint replacement is the only treatment for severe cases and has been shown to be an effective treatment by improving quality of life and reducing pain and function 6-12 months postoperatively.

Aim
To investigate the change in quality of life, physical function and gait speed after hip or knee replacement over four years in a population of community-dwelling older people, and compare these changes to those who do not receive a joint replacement over the same period.

Design
A community based observational retrospective cohort study.

Method
843 participants who had a joint replacement and 8879 controls were included in this study. All participants were healthy, community-dwelling Australian adults aged 70 and over. Joint replacements were identified from hospital records. Participants were measured pre-operatively at baseline and up to four years post-operatively, with 79% of participants possessing a follow-up of 12 months of greater. Results were analysed using ANCOVA models after adjusting for confounders.

Results
Women who had a hip or knee replacement continued to report worse SF-12 PCS to the control population (TKA: 42.27 (SE 0.53) vs 46.55 (SE 0.49), p<0.01. THA: 41.58 (SE 0.68) vs 46.60 (SE 0.14), p<0.01) and slower gait speed (TKA: 0.88 m/s (SE 0.01) vs 0.95 m/s (SE 0.01), p<0.01. THA: 0.86 m/s (SE 0.01) vs 0.97 m/s (SE0.01), p<0.01), and experienced a greater decline compared to the control population. (p<0.01). Men who had a knee replacement had similar SF-12 PCS and gait speed and experienced a similar rate of decline to men without a joint replacement. Men who had a hip replacement also experienced a similar rate of decline but reported significantly lower SF-12 PCS (47.01 (SE 0.67) vs 49.09 (SE0.13), p<0.01) and slower gait speed compared to the control population(1.01 ms (SE 0.02) vs 1.04 m/s (SE0.01), p=0.04). Mental health was found to remain stable and was not affected by joint replacement.

Conclusion
In a cohort of older independently living Australians, hip and knee replacements were shown to reduce the disparity in quality of life and functional status between those with a joint replacement and their peers for men, while women continued to report significantly worse quality of life and slower gait speed. More research needs to be done in older age groups and over longer periods of time to assess the lasting impact of joint replacement.
Ms Jessica Garzarella
The effect of a novel Nox inhibitor (GKT137831) on Nox5 mediated renal injury in a mouse model of diabetic kidney disease

Supervisor Names and Institute Affiliations:
Prof Karin Jandeleit-Dahm and Dr Jay Jha
Department of Diabetes, Central Clinical School

ABSTRACT

Background
Diabetic kidney disease (DKD) represents the leading cause of end-stage renal disease worldwide, with no curative pharmacological strategies currently available. Oxidative stress is a promising target in DKD, with the NADPH oxidase (Nox) enzymes increasingly examined. The isoform, Nox4, has been primarily implicated preclinically however Nox5, an isoform not expressed in conventional mouse and rat models, warrants further characterisation. The dual Nox1/Nox4 inhibitor, GKT137831, is the most clinically advanced agent in this area, however little is known about its effect toward Nox5. Given that Nox5 is being increasingly recognised as pathological in the human diabetic kidney, it is of clinical relevance to assess the effect of GKT137831 toward Nox5 in DKD.

Hence, we aimed to assess if the Nox1/Nox4 inhibitor GKT137831 is renoprotective in diabetic mice expressing Nox5 compared to diabetic mice without Nox5, and hence to evaluate the role of Nox5 in DKD in the context of Nox4 inhibition with GKT137831.

Method
The effect of GKT137831 on Nox5 and DKD was examined with the use of transgenic mice expressing Nox5 selectively in vascular smooth muscle cells (renal mesangial cells). GKT137831 was administered to diabetic and control mice, in the absence or presence of Nox5 expression. Renal structural injury, including mesangial expansion, glomerulosclerosis, and extracellular matrix protein accumulation, as well as renal inflammation, oxidative stress and albuminuria, were examined.

Results
It was found that GKT137831 did not effectively inhibit Nox5 in DKD. This was evidenced by increased intrarenal oxidative stress, inflammation, albuminuria, renal structural injury (increased mesangial expansion, collagen IV accumulation and glomerulosclerosis) in association with elevated expression of the inflammatory and fibrotic markers EGR1 and PKC-α in diabetic mice expressing Nox5 compared to diabetic mice without Nox5, despite treatment with GKT137831.

Conclusions
Collectively, these findings establish that the only clinically examined Nox inhibitor, GKT137831, does not effectively inhibit Nox5 in vivo. This study further supports the key role of Nox5 in the promotion of diabetes induced renal injury in the context of human diabetes and provides an impetus for the development of a Nox5-specific inhibitor as a therapeutic agent for the future prevention and treatment of diabetic kidney disease.
Clinician Perspectives on A Smartphone Safety Planning App for the Management of Suicidal Patients

Supervisor Names and Institute Affiliations:
A/Professor Glenn Melvin & A/Professor Michael Gordon
School of Clinical Sciences at Monash Health, Monash Medical Centre
School of Psychology, Deakin University

ABSTRACT

Background
Suicide accounts for approximately 800,000 deaths per year globally and is one of the leading causes of death both worldwide and in Australia. Among existing suicide prevention strategies, safety planning is a relatively new, brief intervention that is simple, cost-effective and accessible. A safety plan provides patients with suicide prevention strategies to use in a crisis and currently has preliminary evidence to support its use in practice. More recently, suicide prevention has been expanding into digital means, including adapting existing tools into digital forms like smartphone apps. The literature in this field is limited however, and more so for the use of these tools in practice. Understanding clinician views on these novel digital interventions is critical to both enhancing their implementation in practice and supporting effective suicide prevention management.

Aims
This study aims to evaluate clinician perceived usefulness and ease of use of BeyondNow, a successfully implemented Australian safety planning smartphone app. It also aims to investigate the demographics of clinicians who use BeyondNow and ascertain what modifications and improvements can be made to enhance its implementation and use in practice.

Method
A cross-sectional study was conducted with 124 Australian clinicians and professionals who used the BeyondNow app. Participant recruitment occurred through a self-elected survey that was available within the app across seven months in 2017. Data was analysed using Microsoft Excel and SPSS Software and predominantly underwent descriptive statistical analysis.

Results
The majority of clinicians found BeyondNow useful and easy to use in practice.

Conclusions
This is the first study on a successfully implemented safety planning app in Australia and the largest to date globally. It suggests that clinicians have generally positive attitudes towards using a safety planning smartphone app in practice and supports the transferability of a pen-and-paper safety plan to a digital app form. These findings also have wider implications in encouraging and supporting the use of digital mental health and suicide prevention tools – particularly relevant given the widespread and unprecedented effects of the COVID-19 pandemic.
ABSTRACT

Background

Conflicting evidence surrounds the effect of dietary macronutrient intake (carbohydrate, fat and protein) and cardiovascular disease (CVD). We investigated the association between carbohydrate and saturated fat intake with CVD and death in women.

Method

Middle-aged women (50-55 years) free of CVD at baseline were recruited into the Australian Longitudinal Study on Women’s Health (ALSWH). Surveys were performed at baseline and 3-4 yearly (1996-2016) assessing sociodemographic factors, health behaviours and health outcomes. Women were analysed in quintiles according to baseline carbohydrate/saturated fat intake as a percentage of total energy intake (TEI) with Quintile 1 representing the lowest carbohydrate intake, and Quintile 5 the highest. The primary endpoint was new onset CVD (heart disease/stroke). Secondary endpoints included all-cause mortality, incident hypertension, obesity and/or diabetes mellitus. Multivariate logistic regression models assessed for associations with the endpoints.

Results

Total 10,511 Australian women (mean age 52.6 ± 1.5 years) were followed for 15-years with 1,709 (16.3%) new CVD events and 526 (5.0%) deaths. On multivariate analysis, increasing carbohydrate intake was inversely associated with risk of incident CVD. Women in Quintile 3 with a moderate carbohydrate intake (41-44% TEI) had the most significant CVD-odds reduction compared to Quintile 1 (Quintile 3 versus Quintile 1, Odds Ratio (OR) 0.58 95% confidence interval (CI) 0.42-0.81, p=0.001, Quintile 5 versus Quintile 1 OR 0.67 95%CI 0.45-0.99, p=0.046). Increasing carbohydrate intake was also found to markedly reduce odds of hypertension, diabetes mellitus (DM) and obesity in women (Quintile 5 versus Quintile 1 for hypertension: OR 0.28 95%CI 0.20-0.39, p<0.001, Quintile 5 versus Quintile 1 for DM: OR 0.13 95%CI 0.07-0.24, p<0.001, Quintile 5 versus Quintile 1 for obesity: OR 0.02, 95%CI 0.01-0.04, p<0.001). No significant correlation was seen between carbohydrate intake and all-cause mortality (Quintile 5 versus Quintile 1 OR 0.36 95%CI 0.28-1.12, p=0.100). Increasing saturated fat intake had no significant effect on CVD or total mortality (Quintile 5 versus Quintile 1 for CVD: OR 0.90 95% CI 0.62-1.30 p=0.573, Quintile 5 versus Quintile 1 for mortality: OR 0.60, 95% CI 0.35-1.35 p=0.273). Increasing saturated fat intake had a significant inverse relationship with CVD risk factors (Quintile 5 versus Quintile 1 for hypertension: OR 0.64 95%CI 0.48-0.86, p=0.003, Quintile 5 versus Quintile 1 for DM: OR 0.36 95%CI 0.26-0.63, p<0.001, Quintile 5 versus Quintile 1 for obesity: OR 0.31 95%CI 0.21-0.45, p<0.001).

Conclusions

In a large Australian cohort of middle-aged women, increasing intake of dietary carbohydrate was associated with lower odds of CVD, hypertension, DM and obesity but had no effect on mortality. Increasing intake of saturated fat was not associated with either CVD or total mortality and instead correlated with beneficial effects on CVD risk factors.
Dr Fabien Vincent, Prof Eric Morand, Dr James Harris. Centre for Inflammatory Diseases, School of Clinical Sciences, Monash University.

Supervisor Names and Institute Affiliations:
Dr Fabien Vincent, Prof Eric Morand, Dr James Harris. Centre for Inflammatory Diseases, School of Clinical Sciences, Monash University.

I chose to do a BMedSc(Hons) after an academically challenging 4th year, where I was left feeling burnt out after 6 years of non-stop studying since VCE. I was interested in completing my BMedSc(Hons) with the Rheumatology Research Group after my positive experiences on rheumatology placement, and found the unknowns of inflammatory diseases intriguing. Although I’m not sure where I’d like to specialise in the future, I thought that I could learn a lot from the people involved in this team. Despite the difficult circumstances of this year, my BMedSc(Hons) experience has been everything I hoped for and more. It gave me the space I needed to breathe and spend time with myself, and to learn more about what’s important to me. Additionally, it allowed me to build relationships with some of the kindest and most helpful clinician-scientists I’ve had the pleasure of knowing, where I felt supported every step of the way by my supervisors and their confidence in me.

For anyone considering a BMedSc(Hons), I highly encourage you to take that leap of faith! If you would like to further discuss my project, supervisors, or BMedSc(Hons) experience, please feel free to do so at:

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ABSTRACT

Background
Systemic lupus erythematosus (SLE) is a heterogeneous multisystem autoimmune disease, where cytokines significantly influence disease pathogenesis. Macrophage migration inhibitory factor (MIF) and D-dopachrome tautomerase (D-DT) are potentially two such cytokines, hypothesised to interact with other disease-modifying cytokines, with possible roles in glucocorticoid-resistance. I investigated the difference in serum MIF and serum D-DT concentrations between healthy controls (HC) and SLE patients, and the relationships between serum MIF and serum D-DT concentrations and clinical parameters in SLE. Additionally, I investigated associations between serum MIF and serum concentrations of other cytokines implicated in SLE pathogenesis.

Method
Prior to this study’s commencement, 211 serum protein concentrations were measured in samples from 202 SLE patients and 38 HC. Quantibody assays were used to measure 209 serum proteins, including MIF. Serum D-DT concentration was measured by myself in the same samples in a subset of SLE patients (N=155) and HC (N=21), using ELISA. SLE disease activity and organ damage were assessed using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the Systemic Lupus International Collaborating Clinics Damage Index (SDI).

Results
Serum MIF was detectable in 97.4% (37/38) HC and 97.5% (197/202) SLE patients. Contrastingly, serum D-DT was detectable in 14.3% (3/21) HC and 19.9% (31/155) SLE patients. Median serum MIF concentration was significantly higher in SLE compared to HC, and serum MIF concentration was higher in patients over 40 years of age. This was demonstrated using chi-squared testing, Mann-Whitney U test, and univariable logistic regression analysis.

No significant relationships were observed between serum MIF concentration and patient demographics, disease activity, flare, organ damage, or treatments. No additional significant relationships were observed when the above analyses were repeated in a subset of only female SLE patients. No difference was observed in median D-DT concentration between SLE and HC. Serum D-DT was dichotomised into detectable or undetectable, due to its low detection rate. Detectable D-DT occurred more frequently in patients with low C4, and less frequently in patients with high CRP. No significant relationships were observed between detectable serum D-DT and patient demographics, disease activity, flare, organ damage, or treatments. Many positive correlations were observed between serum MIF concentration and the concentration of analytes of interest in SLE pathogenesis, including IL-16, IL-18, IFN-γ, and LIGHT, and numerous chemokines, including CCL17, CXCL1, and CCL18. No significant relationship was observed between serum MIF concentration and IFN-CK score—a surrogate marker of Type I IFN activity, calculated using normalised scores of Type I IFN-inducible chemokines (CCL2, CXCL10, and CCL15).

Conclusion
Serum MIF is significantly higher in SLE compared to HC, and higher in patients over 40 years. In contrast, serum D-DT is not significantly higher in SLE than HC, but higher in patients with low C4, and lower in patients with high CRP. No other relationships were observed between serum MIF or D-DT and patient demographics, disease activity, flare, organ damage, or treatments. Serum MIF is positively associated with several serum cytokines involved in SLE pathogenesis. Further investigation is required to evaluate these relationships’ causality, to better understand SLE’s complex pathology.
Ms Alissa Lin Qi Heng

Assessment of Risk Factors and Oxygen Treatment Strategies for Delivery Room Hypoxia in Infants ≥32 Weeks’ Gestation

Supervisor Names and Institute Affiliations:
Douglas Blank1,2,3
Calum Roberts2,3
Shiraz Badurdeen1,4

ABSTRACT

Background

Approximately ten percent of infants worldwide receive respiratory support for neonatal distress at birth. Hypoxia is both a driver and outcome of neonatal distress, which contributes to significant respiratory morbidity. However, the risk factors for delivery room hypoxia are not well-documented. Identifying the risk factors for delivery room hypoxia may lead to improved detection of neonatal distress, leading to early implementation of respiratory support by the clinician. Furthermore, the management of hypoxia at birth may include supplemental oxygen. However, oxygen treatment strategies are poorly defined in clinical guidelines. This may lead to variability in amongst clinicians in the management of delivery room hypoxia, resulting in inconsistent neonatal outcomes. We aimed to assess the risk factors and oxygen treatment strategies for delivery room hypoxia in infants ≥32 weeks’ gestation.

Method

This was an observational study of 398 infants from two tertiary hospitals in Victoria, Australia. Hypoxia was defined using a widely-used centile chart representing the oxygen saturation levels of infants who did not require interventions at birth. We defined hypoxia as an SpO2 below the 10th centile in the first ten minutes after birth. To assess the risk factors for hypoxia, univariate comparisons were made between cases and controls for 51 perinatal risk factors. Significant risk factors from the univariate analyses were used to construct decision trees. To assess the treatment strategies for infants who received oxygen, we described the percentage of time spent within targets, the amount of oxygen given to infants by clinicians, and the relationship between oxygen exposure and time spent within targets.

Results

We identified 106 (27%) of 398 infants who developed hypoxia in the first ten minutes after birth. The decision tree algorithm identified that the strongest predictor of hypoxia was a heart rate ≤130bpm, where 59% of these infants developed hypoxia. There was no variability in the initial level of supplemental oxygen given to infants based on the infant’s degree of hypoxia (p=0.06). Finally, a higher initial oxygen exposure was associated with more time spent within targets for the most severely hypoxic infants (adjusted R2=0.304, p=0.019).

Conclusions

Our findings have two main implications for practice. Firstly, we should consider routine auscultation of heart rate at birth, with a lower threshold for the application of a pulse oximeter in infants with heart rate ≤130bpm, as these infants may have a higher risk of developing hypoxia. Secondly, we should consider using a higher initial FiO2 for the most severely hypoxic infants to increase their time spent within SpO2 target ranges. As hypoxia is a significant cause of respiratory morbidity in the delivery room and potentially beyond, improving our detection and management of delivery room hypoxia may lead to improved neonatal outcomes at birth.

My decision to take BMedSci(Hons) was a rather last minute one. I’ve always been interested in research, but never thought I’d take the full year off to do it. Thanks to finding the perfect project and encouragement from passionate past-year honours students, I decided to take an honours year after completing fourth year. It’s been the best year of my medical school experience! I took a project in neonatal resuscitation, which allowed me to somewhat combine my interests for paediatrics and O&G. As my project utilised data from the Baby-DUCC RCT, it was meant to be a clinical project, heavily based in birth-suites and assisting with recruitment for the RCT. Due to COVID-19, I ended up spending the year at home, which was a blessing in disguise as it allowed me time to figure out everything from searching the literature to statistics. It is a challenging but extremely rewarding year, and I highly recommend combining two fields you are interested in for an honours project, if you’re able to do so.

Feel free to contact me at alhen9@student.monash.edu if you’re interested in a project in neonatology, or if you’re still on the fence about taking an honours year!
Mr Joshua Alward Herdiman

Patients’ and Caregivers’ Perception of Informed Consent and Identifiable Data, Telehealth and Quality of Life in Cystic Fibrosis

Supervisor Names and Institute Affiliations:
Dr Rasa Ruseckaite, School of Public Health and Preventive Medicine (SPHPM)

ABSTRACT

Background
In the last few decades, demographics, treatments, clinical outcomes of Cystic Fibrosis (CF) have changed drastically. However, there is a growing need to address the quality of life (QoL) of patients with CF. QoL can be measured using patient-reported outcome measures (PROMs). The Australian Cystic Fibrosis Data Registry (ACFDR) is considering to incorporate PROMs as it might bring advantages for the registry to improve healthcare services for patients with CF. Also, the ACFDR have not collected identifiable data, such as names and surnames. Furthermore, the ACFDR want to identify the clinical data collected during telehealth (e.g. lung function and height and weight measurements).

Aim
To 1) assess ethical considerations of identifiable data collection from patients with CF or their caregivers; 2) assess the feasibility and possible barriers of incorporating PROMs into ACFDR from the views and perceptions of patients with CF and their caregivers including the frequency, preferred modes and methods of administration, and dissemination of the results; and 3) evaluate experiences on telehealth services, benefits, and data collection from the views and perceptions of patients with CF or their caregivers.

Method
A qualitative descriptive study was conducted with patients with CF or their caregivers. Student-researcher (JAH) organised semi-structured interviews using a topic guide. Data were audio-recorded and transcribed using paid transcription service. Data analysis utilise convenient content analysis method in NVivo 11.

Results
Total of 15 participants, six patients and nine parent-caregivers, were interviewed. Four themes emerged from confidentiality and identifiable data; 1) confidentiality and identifiable data collection in the ACFDR; 2) commencement of identifiable data collection; 3) distribution and utilisation of identifiable data; 4) views on mandatory enrolment to the ACFDR. Four themes emerged from PROMs incorporation into the ACFDR; 1) participants’ knowledge and experiences regarding QoL and PROMs; 2) PROMs collection in the registry; 3) possible challenges during PROMs collection in the registry; 4) PROMs reporting and feedback. Five themes emerged from telehealth services; 1) participants’ knowledge and experiences on telehealth; 2) clinical data collection during telehealth; 3) how telehealth services compare to the clinic/hospital visits; 4) advantage of telehealth services; 5) long-term use of telehealth services.

Conclusions
Participants from both groups supported collection of identifiable data in the registry and support PROMs inclusion in the registry with electronic/online administration quarterly in a year. Telehealth services are great for quick check-ups, but face-to-face meeting with clinicians are essential.
Ms Nicola Ivec

Rural paramedicine: what are the indicators of paramedicine graduates entering the rural workforce?

Supervisor Names and Institute Affiliations:
Dr Alison Beauchamp, Dr Keith Sutton, Dr Eleanor Mitchell; Monash School of Rural Health Warragul and Bairnsdale.

ABSTRACT

Background

Limited Australian paramedicine literature exists relating to the paramedic workforce in rural areas. Of the research available, little to none discuss influences to rural practice from the perspective of both a paramedicine student and a graduate paramedic, or interactions between potential influencing factors. In addition, minimal knowledge exists regarding work locations of paramedicine graduates and hence, accurate workforce numbers are unknown.

Objectives

This study aims to explore the relationship between background, placements during tertiary studies, and principal place of practice after graduation, amongst paramedicine students and graduate paramedics. It also examines the practice intentions of paramedicine students, and the factors which influence principal place of practice after graduation. In addition, this study seeks to identify how the findings of this study reflect the factors known to influence practice location decision making in other health professions.

Method

This data linkage study utilises de-identified university administrative data, university placement data, graduate Australian Health Practitioner Regulation Agency (Ahpra) information, and survey data from cohorts of Monash students undertaking a paramedicine-related degree; as a part of the larger Nursing and Allied Health Graduate Outcomes Tracking (NAHGOT) study. This present study utilises, in part, a retrospective cohort study design and a cross-sectional study design. Pearson’s Chi2 or Fisher’s exact tests and Wilcoxon Rank Sum Tests are used to determine significant associations between variables. To test the relationship between student background and number of rural placements during their degree, linear regression analysis was utilised. Ordinal regression was used for investigating the association between student background and number of rural placement days. Lastly, logistic regression was utilised to test how graduate place of practice was influenced by either student background or number of rural placements.

Results

Rural originating paramedicine students undertaking a single-degree were less likely than their metropolitan counterparts to have rural placements during their degree. It was demonstrated, in line with literature in other health disciplines, that rural background significantly predicts practice in a rural location as a graduate, however, the number of rural placements during study does not. Practice intentions of students do not fluctuate significantly during their studies, with a majority preferring to practice in major urban centres regardless of their year level or place of origin. Graduates, when asked, believe that they are more skilled and knowledgeable than their current job requires. Furthermore, over half of participants were working in their current location for an ‘opportunity for career advancement’.

Conclusions

This study provides important insight into the factors which predict rural practice location amongst paramedicine students, and links student university data to that of graduates. The longitudinal aspect of the data allows adequate follow-up of participants. The results of this study aim to both illustrate these influences and to promote further research into the working locations of paramedicine graduates.
Miss Sarah Jaboury

The role of interferon epsilon in the immunopathology of gynaecological cancers

Supervisor Names and Institute Affiliations:
Supervisors: Professor Paul Hertzog & Dr Sophia Frentzas
Institute: Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research

ABSTRACT

Background
Gynaecological cancers comprise of ovarian, cervical, endometrial, vulvar and vaginal cancers. As it is typically diagnosed at an advanced stage, ovarian cancer has the poorest prognosis, with a 5-year survival rate of 45%.

The link between immunology and carcinogenesis is becoming increasingly clear, with the advent of immunotherapy, a treatment which primes the body’s immune defence to attack a cancer. Type I interferons are cytokines which form an integral role in the anti-tumour response and are being researched as therapies in several cancers. This study hopes to explore the role of the novel type I interferon, interferon epsilon (IFN-ε), in the immunopathology of gynaecological cancers, by examining its expression patterns and relation to prognosis in these patients.

Method
IFN-ε was investigated at two levels. The first involved analysis of publicly available genomic data from The Cancer Genome Atlas, comparing the levels of IFNE, the gene corresponding to IFN-ε expression, in RNA transcripts for ovarian, cervical, endometrial and breast cancer cohorts – the last group acting as a control. Survival analysis was performed comparing overall survival between low and high IFNE expression groups. This was then controlled for age, molecular and histological subtype, and stage. The related genes of IFNAR1, IFNAR2, and ELF3, were also studied.

The second branch involved immunohistochemistry staining of 58 ovarian cancer samples and 39 healthy ovary controls, against both IFN-ε and its receptor, IFNAR1. Staining intensity was quantititated using Aperio software. Clinical data from the patients was also analysed for patterns corresponding to IFN-ε expression levels.

Results

Genomics
Across the studied cancers, IFNE was expressed highest in cervical cancer. In cervical and breast cancers, expression was lower in the over 55-year-old age group.

Higher IFNE expression, defined as the top quartile, was correlated with significantly improved overall survival (OS) in ovarian cancer, when compared to low IFNE expression (bottom quartile). The Hazard Ratio (HR) of high compared to low expression was 0.69 (p = 0.0496). This effect was limited to Stage III cancers, disappearing in Stage IV patients.

In endometrial cancer, higher IFNE expression correlated to poorer OS (HR = 2.4, p = 0.0026). This effect was strongest in the Microsatellite Instability molecular subtype and limited to the endometrioid endometrial cancer histological subtype.

Breast cancer also demonstrated a protective effect of higher IFNE expression (HR = 0.51, p = 0.0028).

Immunohistochemistry
Normalised values of IFN-ε expression were significantly lower in the stroma of ovary tumour samples when compared to healthy tissue controls (difference of means of 1.205 ± 0.1850, p < 0.0001). Staining was strongest in epithelium but also present in stroma and follicles.

Conclusions
Higher IFN-ε expression at the genomic level is correlated with better prognoses for ovarian and breast cancers, and poorer outcomes in endometrial cancer. Any protective benefit in ovarian cancer is likely to be specific to preventing metastasis, as survival benefit is lost in Stage IV patients.

IFN-ε expression is lower in ovarian cancer tissues than in healthy normals, indicating a possible role of IFN-ε downregulation in the pathogenesis of the cancer.
ABSTRACT

Background

Convolutional Neural Networks (CNNs) have been successfully used in many areas of ophthalmology, such as diabetic retinopathy, AMD, glaucoma and retinal detachment. Prediction of spectacle refraction was not attempted until 2018, when a collaboration between Google and Moorfield’s Eye Hospital demonstrated successful prediction of spherical equivalent refractive error from retinal images. Ocular axial length has not been predicted in any published study on retinal image-based neural network techniques, but the successful prediction of spherical equivalent refraction suggests that detectable information associated with axial length exists within retinal image data. Our aim is to use a convolutional neural network to predict axial length from widefield fundus photographs.

Method

Data was collected dating from start of January 2001 to the end of July 2020 of patients who had undergone ocular biometry and had widefield retinal imaging. Participants were recruited through convenience sampling and consent was gained via in person consent forms and telephone consent. Data was then processed to ensure high quality images were used for training the neural network. A total of 864 images were used; 691 for the training set, 86 for the validation set and 87 for the testing set. The neural network was evaluated using mean absolute error (MAE) of axial length prediction, as well as percentage of predictions within 0.33mm and 1.0mm of the gold standard measurement. Data with a higher representation of long and short eyes, a broader patient age range and ethnicity would enable this technology to produce more reliable results for use in the general population. For now, this technology is of academic interest, but there is strong potential for the usefulness of this technology to grow with more data.

Results

The CNN design employing transfer learning scored the highest prediction accuracy, with a MAE of 0.74mm. 37.9% of predictions were within 0.33 mm and 79.3% were within 1.0 mm. Higher error rates were recorded for very short and very long eyes. IOL power calculations were within one dioptre for 41.4% of eyes, and an exact match in 9.2%.

Conclusions

Our work demonstrates for the first time that ocular axial length can be predicted from a retinal image by a CNN, with moderate accuracy in most eyes and high accuracy in some eyes. There is potential for this technology to aid ophthalmologists as a cross check mechanism for axial lengths before cataract surgery. Furthermore, countries with underdeveloped medical resources may use this inexpensive technology in satellite clinics to measure eyes for cataract surgery if gold-standard techniques are not accessible, or possibly to screen for axial-length related pathology such as nanophthalmos and high myopia.
Mr Edmund Wai Chi Khong

Determining the effect of pregnancy and the postpartum on diabetic retinopathy in patients with type 1 and type 2 diabetes mellitus

Supervisor Names and Institute Affiliations:
Associate Professor Lyndell Lim, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne
Associate Professor Anthony Hall, Department of Surgery, Alfred Hospital

I decided to undertake a BMedSc(Hons) after completing 4th year in 2019 as I felt that it would be a great opportunity to not only take a bit of a break from the intensity of medicine, but also to gain an insight into the world of research. I chose a project in ophthalmology, a specialty I was interested to learn more about but had little opportunity to do so in my clinical years so far. Despite the chaos of 2020, it was a great year and I have learnt a lot about the process of research as well as gained an appreciation of just how much we still don’t know! A big thank you to my supervisors for helping me make the most of the year (and to future students, your choice of supervisor is probably the most important decision you’ll make) and I would recommend an Honours year to anyone considering it.

I’m very happy to be contacted, feel free to reach me on:
ewkho2@student.monash.edu

ABSTRACT

Background

Diabetic retinopathy (DR) is a leading cause of blindness worldwide. Many risk factors have been associated with the development and progression of DR, including pregnancy. Much controversy remains around the effect of pregnancy and the postpartum period on DR. The paucity of data in these areas has led to a lack of management guidelines for sight-threatening diabetic retinopathy (STDR), and DR in general, in the postpartum. Management of STDR in pregnancy is complicated due to the risk and teratogenicity of available treatments. Understanding the postpartum course of DR and identifying risk factors that can predict the disease trajectory in this time will enable the development of clear guidelines that minimise the risks to the mother’s vision and the growing foetus. This study aims to determine the prevalence and typical course of DR during pregnancy and the postpartum.

Method

This study is a subgroup analysis of a pre-existing longitudinal project of pregnant T1DM and T2DM women at the Royal Women’s Hospital and Mercy Hospital for Women. Baseline demographics and medical information were obtained via a questionnaire at recruitment and from their hospital records. A total of 6 eye examinations were scheduled throughout pregnancy and the postpartum. Adaptations due to COVID-19 restrictions were made to the follow-up and examination procedures. DR severity was graded using the modified Airlie House classification system by an external DR grader. STATA was used to analyse the DR trajectory during pregnancy and the postpartum.

Results

A total of 87 pregnancies from 87 women were included in this analysis. The prevalence of DR per eye at ≥27 weeks postpartum was 33%. Of the eyes that experienced DR progression during pregnancy, 38% subsequently regressed in the postpartum. Postpartum regression was seen in 80% of eyes with no DR, 20% of eyes with NPDR and 0% of eyes with PDR. In eyes with DMO at their latest exam in pregnancy, 53% had resolution of their DMO by their latest postpartum follow-up. The likelihood of DR progression in the postpartum was higher than the likelihood of regression. Progression in the postpartum was more commonly seen in the late postpartum compared to the early postpartum.

Conclusion

The postpartum prevalence of DR in T1DM and T2DM women is similar to the prevalence in the non-pregnant diabetic population. In eyes that progressed during pregnancy, the majority did not regress in the postpartum, especially eyes with PDR. Treatment of STDR in pregnancy cannot be based on an expectation of spontaneous improvement in the postpartum. Treatment should therefore not be delayed in pregnancy. The risk of DR progression in the postpartum highlights the need for adequate postpartum eye screening. Our recommendations aim to minimise unnecessary examinations whilst still allowing timely diagnosis of DR changes.
Ms Eve Lardner

Sleep in children with developmental and epileptic encephalopathies, and the impact of the COVID-19 pandemic

Supervisor Names and Institute Affiliations:
A/Prof Margot Davey, The Ritchie Centre, Hudson Institute of Medical Research and Department of Paediatrics, Monash University; Melbourne Children’s Sleep Centre, Monash Children’s Hospital
Prof Ingrid Scheffer, Epilepsy Research Centre, Department of Medicine, Austin Hospital, The University of Melbourne
Ms Amy Schneider, Epilepsy Research Centre, Department of Medicine, Austin Hospital, The University of Melbourne

ABSTRACT

Background
People with developmental and epileptic encephalopathies (DEEs) are a complex cohort with severe seizures, associated with cognitive, behavioural and medical comorbidities, which may include sleep problems. Sleep has a complex bidirectional relationship with seizures, and may impact on development and wellbeing, however, has not been adequately investigated in people with DEEs. This study characterises the sleep habits and sleep problems of people with DEEs, and their associations with participant characteristics. Additionally, we describe the impact of the COVID-19 pandemic on this vulnerable cohort, focusing on the impact on routine, mood, health, access to healthcare, and sleep.

Method
A four-part online survey was distributed to families of participants with DEEs within the Genetic Basis of Epilepsy research program during Australia’s second ‘coronavirus wave’. The questionnaire collected data on patient health, sleep (using the Sleep Disturbance Scale for Children questionnaire), the impact of the pandemic, and the impact of the patient’s condition and the pandemic on families of people with DEEs. This cross-sectional study was combined with prospective analysis of sleep problems using baseline sleep data collected in 2019 using the Sleep Disorder Scale for Children in a select group of participants. All sleep findings and changes during the COVID-19 pandemic were analysed for association with patient factors, including DEE syndrome, seizure characteristics, comorbidities and treatments, using comparative statistics, correlation and regression analysis. Data analysis was performed using SPSS software.

Results
A total of 55 respondents participated in the survey, comprising patients with Dravet syndrome, Lennox-Gastaut syndrome, West syndrome and other solved and unclassified DEE syndromes. Total nightly sleep time was 8:42 hours (SD 1:52 hours) and did not significantly differ across the range of ages represented (2.35-37.8 years, mean 13.15 years), or different DEE syndromes. Pathological sleep problems occurred in 77% of children with DEEs. The most common sleep problems included disorders of initiation and maintenance of sleep (49%), sleep-wake transition disorders (36%), sleep breathing disorders (26%), and disorders of excessive daytime somnolence (19%). The COVID-19 pandemic had a significant impact upon seizure frequency and worsening of comorbidities in children with DEEs. Despite considerable changes to daily routine among children with DEEs and their family members, sleep and mood did not differ significantly from baseline in 2019. Telehealth was widely implemented and accepted by patients.

Conclusions
This study highlighted that sleep problems were a common comorbidity in children with DEEs and remained consistent throughout the pandemic. We suggest that sleep problems may be intrinsically linked to the underlying disease mechanism of the genetic conditions or their comorbidities, rather than reactive to environmental factors.
Ms Samantha Leng

Does Peritoneal Lavage Influence the Rate of Complications in Paediatric Laparoscopic Appendicectomy? A Prospective Multisite Randomised Controlled Trial

Supervisor Names and Institute Affiliations:
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Department of Paediatric Surgery, Monash Children’s Hospital
School of Clinical Sciences, Monash University

ABSTRACT

Background
Appendicitis is the most common cause for emergency abdominal surgery in children. Approximately 30% of these children have complex appendicitis (CA), in which the risks of post-operative complication rates are high. Despite being common, some aspects of the management of appendicitis are not evidenced-based. One such aspect is the use of peritoneal lavage (PL) intraoperatively to minimise abdominal contamination and hence complications.

Aim
We aim to investigate post-operative outcomes with the use of PL as compared to suction only (SO) without irrigation in children undergoing laparoscopic surgery for CA. The primary outcome was the incidence of intra-abdominal abscess (IAA) in these two cohorts. The secondary outcomes include surgical wound infections (WI), small bowel obstruction (SBO), length of stay (LoS) in hospital and analgesia requirement.

Method
We are conducting a multisite prospective randomised controlled trial (RCT) that compares the use of PL and SO in paediatric CA. Our patient population is children (4-16 years old) who have CA. We aim to recruit 1232 patients to our non-inferiority trial across six paediatric tertiary centres in Australia, over a three-year period. Each patient will be randomized to either the PL or SO trial arm. Data collection will include: patient demographics, incidence of IAA, surgical WI, SBO, LoS and post-operative analgesia requirements. To quantify analgesia requirement, data collected will include type of medication, as well as dose and number of doses for any opioid analgesia. Follow-up will occur whilst the patient remains in hospital, as well as at a routine outpatient appointment four to eight weeks later.

Results
At this interim time point 12 participants were analysed; 10 were randomised to receive PL, and two to receive SO. All participants included in this analysis had completed the four to eight-week follow-up. No significant differences were found between baseline demographic variables for the two groups. No IAA were detected in either group. No WI, or SBO were detected in either group. The average LoS in both groups was five days. Fewer children in the PL group required intravenous (IV, 40%) and oral (70%) opioids, than in the SO group where 50% required IV and 100% required oral opioids. However, children in the PL group used more doses of oral opioids on average compared to the SO group (p=0.3324). Hence, there were no significant differences detected for IAA, WI, SBO or analgesia use. An additional 12 eligible children were treated at our centre but not recruited to the trial, the IAA rate in this group was 25% (3/12) and the WI rate was 8% (1/12).

Conclusion
No statistically significant differences were detected for our study outcomes. Although this indicates support of the null hypothesis, the results at present are not sufficiently powered to draw definitive conclusions. Recruitment should continue for this trial, at both the primary and additional tertiary paediatric centres, to the proposed sample of 1232 participants.

I chose to do my BMedSc(Hons) between my fourth and fifth years of medicine, and had the great privilege of doing it under the supervision of Ram and Maurizio in the Department of Paediatric Surgery.

I decided to do an honours year to further explore research, and my interest in surgery, as well as gain a different experience of medicine to that which we received in the regular MD degree. For me, the Department of Paediatric Surgery was the best place to do so, as I had the opportunity and support to coordinate a nation-wide randomised controlled trial.

Although we have faced some unexpected disruptions in 2020, I have learnt much more from the SWAP trial and my honours year than I could have ever anticipated and would highly recommend a BMedSc(Hons) (particularly with Ram and Maurizio!) to any student who is considering it.

If you would like to contact me, please feel free to do so at:
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Ms Olivia Leyden

Premenstrual Dysphoric Disorder (PMDD) and early life trauma

Supervisor Names and Institute Affiliations:
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Monash Alfred Psychiatry research centre (MAPrc)

ABSTRACT

Background
Premenstrual Dysphoric Disorder (PMDD) is a severe, cyclical depression that profoundly affects the lives of numerous women of reproductive age. Early life trauma is well established as a risk factor for the development of various mental disorders, and particular types and ages of trauma appear to confer risk for particular conditions. While some studies suggest an association between early life trauma and PMDD, the literature is currently insufficient to definitively determine whether early life trauma confers risk for PMDD, and which, if any, specific types or ages of trauma are particularly common among women with this condition.

Aim
Firstly, our study aimed to determine the prevalence of early life trauma in women with PMDD. Secondly, to characterise type and age of early life trauma experience in women with PMDD.

Method
The Monash Alfred Psychiatry research centre Women’s Mental Health Clinic Database was searched, identifying 323 women, 100 of which had a diagnosis of PMDD. Of these women with PMDD, the presence or absence of a history of early life trauma was identified. If trauma was present, type was classified as childhood physical abuse, sexual abuse, emotional abuse and/or neglect, and age was classified as 0-5, 6-10, 11-14 and/or 15-18. Frequencies were calculated to determine the overall prevalence of early life trauma in the sample, and the prevalence of each type and age of trauma, which was statistically compared with published estimates for the Australian and worldwide populations using chi-square goodness of fit tests. Two case reports were collected, detailing histories of women with PMDD and early life trauma.

Results
In our sample of women with PMDD, 83% had a history of early life trauma. Childhood emotional abuse was the most common type of early life trauma, experienced by 71% of women, but no one age of trauma was significantly more or less common than others. Instead we found that the majority (51.8%) of women with early life trauma histories experienced trauma in all four age groups throughout early life. All types of early life trauma were significantly more common in our sample of women with PMDD compared with the Australian population, while only childhood emotional abuse and neglect were significantly more common compared with the worldwide population.

Conclusion
Our results suggest a strong association between experiencing early life trauma and developing PMDD. Given the especially high prevalence of childhood emotional abuse, and of experiencing trauma at all ages throughout early life, it is possible that emotional abuse and chronic trauma (as opposed to a single age of trauma) confer the greatest risk of PMDD development. Further research is warranted to improve our understanding of the association between early life trauma and development of PMDD, and the mechanisms underlying this association.
Ms Hannah Boya Li

Fairness of Artificial Intelligence in Healthcare: an exploration at the intersection of philosophy, medicine, computer science and criminal justice

Supervisor Names and Institute Affiliations:
Professor Julian Savulescu1, Professor Catherine Mills2, Dr Alberto Giubilini1, Abhishek Mishra1

1Oxford Uehiro Centre for Practical Ethics, University of Oxford
2Monash Bioethics Centre, Monash University

ABSTRACT

Background

Advancements in artificial intelligence are increasingly allowing for significant decisions to be informed by algorithmic decision-making processes. This has prompted growing discussion around ethical issues, such as that of fairness. In particular, issues of fairness have arisen in relation to concerns of bias and discrimination on the basis of protected characteristics such as race. I show that existing measures used in computer science to track notions of fairness are often one dimensional and it is mathematically impossible to satisfy multiple measures simultaneously in the vast majority of situations. Drawing on different accounts of fairness in ethical theory, I argue that a sophisticated understanding of fairness is required in order to capture the relevant normative properties that can be contextually specific, particularly for applications in healthcare. I examine various aspects of this problem, including i) the different forms of discrimination; ii) the statistical conflict between two common measures of fairness; iii) the impact of decision thresholds on fairness; and iv) how different theories of justice may evaluate the fairness of potential parameters in machine learning. Existing lessons from applications of artificial intelligence in criminal justice will be drawn on to demonstrate that perceived intuitions of unfairness may not necessarily hold when examined from the point of view of ethical theory. These ideas will be translated to a hypothetical healthcare scenario to illustrate that a model may theoretically be equally predictive across subgroups and still result in seemingly unfair outcomes.

Aim

This project aims to bring together the normative considerations associated with fairness and interpretations of fairness that predominate in computer science in order to address questions around the design of machine learning algorithms in healthcare.

These include:

- When different measures of fairness are mathematically incompatible, how should we navigate trade-offs?

Does violation of a measure of fairness necessarily equate to unfairness?

Conclusions

Fairness in relation to AI in healthcare is an emerging area of research that is interrelated with issues of bias, discrimination and justice. Further interdisciplinary collaboration is required in order to develop formalised regulations that capture a holistic representation of fairness and acknowledges the contextual considerations involved in healthcare. The current statistical approach limits fairness to being operationalised in a one-dimensional manner, and these statistical measures are often based on intuitions of fairness. I have shown that not all existing measures of fairness may represent normatively significant properties, and a theory of justice may be required in navigating the trade-offs involved in deciding between measures. If intuitive notions of fairness are sufficient to justify the evaluation of fairness or unfairness, there may be misleading portrayals of AI-driven systems. However, the lack of formalised requirements around fairness, combined with the black-box and proprietary nature of most AI systems today, remain a challenge to identifying cases of unfairness. A more sophisticated understanding fairness is crucial to allow for the potential benefit of AI in healthcare to be realised whilst preventing truly unfair systems from having a widespread influence upon the many decision-making processes that underpin healthcare.
Ms Rose Kong Liu

Identifying components of an online educational intervention to increase preference for, and uptake of, long acting reversible contraception: perspectives of women from culturally and linguistically diverse backgrounds

Supervisor Names and Institute Affiliations:
Dr Asvini Subasinghe, Prof Danielle Mazza
Department of General Practice

ABSTRACT

Background

Increasing uptake of long-acting reversible contraception (LARC) in women from culturally and linguistically diverse (CALD) backgrounds may help reduce the burden of unintended pregnancy in this priority group. Findings from the PREFER study demonstrated that an online educational video was effective at increasing preference for, and uptake of, LARC in young women. We aimed to describe what factors an online educational intervention need to address in order to increase preference for and uptake of LARC by CALD women.

Method

This qualitative study involved semi-structured interviews with English-speaking women from Chinese, Indian and Middle Eastern cultural backgrounds. Women were recruited through Facebook advertising and snowballing. Demographic information was gathered through a Qualtrics survey. Interviews were informed by Andersen’s Model of Health Service Utilisation examining individual and system factors influencing engagement with health services. Data were entered into NVivo 12 software and transcripts were analysed thematically.

Results

Eighteen interviews were conducted with 6 women from each cultural group. The three major themes identified were culturally tailored messages, delivery of online intervention and target audience. For all women the covertness of each contraceptive method, the cost and options for accessing subsidised LARC were important factors. Culturally tailored messages for each cultural group were also identified such as highlighting the effect of contraceptive methods on the menstrual cycle for Indian women. Delivery modifications include promotion of the video on WeChat and Chinese schools to reach Chinese women and on government websites to reach Indian and Middle Eastern participants. It was also suggested that the video be translated into Chinese, Hindi and Arabic and be delivered by a female doctor from the same cultural group. Finally, given the role of family members in contraceptive decision making, women across all groups indicated the value of making the video accessible to men and women from a wide age range.

Conclusion

Several cultural modifications were identified for improving the reach of an online educational intervention to increase preference for, and uptake of, LARC among women from CALD backgrounds. These modifications related to culturally tailored messages, delivery of online intervention and target audience. Findings of this study will be used to modify the PREFER video for women from Chinese, Indian and Middle Eastern backgrounds in the Australian context. As such, this culturally adapted online intervention will be used to improve reproductive autonomy and reduce the burden of unintended pregnancy in this priority group. Further research on subcultural attitudes towards family planning in these highly heterogenous cultural groups would also be beneficial.

I completed BMedSc(Hons) between the 3rd and 4th years of the medical degree. I chose this project because of an interest in public health and primary care. Valuable lessons learnt include qualitative research skills and an appreciation for the importance of teamwork in conducting research. For future students my advice is to be organised by making a timeline at the beginning of the year and aiming to complete all assessments many weeks before the deadline, giving your supervisor plenty of time for reviewing. I am happy to be contacted by future students.

Identifying components of an online educational intervention to increase preference for, and uptake of, long acting reversible contraception: perspectives of women from culturally and linguistically diverse backgrounds

Supervisor Names and Institute Affiliations:
Dr Asvini Subasinghe, Prof Danielle Mazza
Department of General Practice
ABSTRACT

Introduction/Aims

Malaria is a disease caused by infection of the parasite genus Plasmodium, with the most prevalent species, P. falciparum and P. vivax, responsible for an incredible burden of morbidity and mortality in areas such as Sub-Saharan Africa and Papua New Guinea. The largest burden of disease is in the young, who lack antibodies against the parasite. With many exposures to malaria infection, those living in malaria endemic areas acquire “clinical immunity” by adulthood, with symptomatic infection becoming very rare, but infection not prevented. Many human polymorphisms have been shown to protect against malaria infection, and a possible mechanism of protection is through increasing the immune response to malaria and speeding up the acquisition of clinical immunity. Three such gene polymorphisms, Complement Receptor One (CR1) mutation, Alpha Thalassemia, and Glycophorin C (GLYC) mutation, have shown inconsistent associations with protection from clinical infection. Investigation into how these polymorphisms effect antibody response to specific antigens such as PfRh4, which binds to CR1, could explain these past inconsistencies.

Method

In a retrospective cohort study of children aged 4-14 years old living in a malaria endemic area of Papua New Guinea, associations between RBC genotypes and antibody responses to a number of Plasmodium falciparum antigens were analysed. RBC genotype and antibody assay (ELISA or C1q fixation) data was used in order to measure associations using between the two. Data available was previously attained from a treatment reinfection trial, with all data assessed in this study collected at the initial timepoint of the trial.

Results

Within the cohort CR1 mutation and Alpha Thalassemia were common (85%, 85%). CR1 mutation was associated with an increase in IgG3 response to Rh4 domains Rh4.2 (p = 0.003) and Rh4.9 (p = 0.005). Alpha Thalassemia was associated with an increase in IgG response to invasion antigens including AMA-1 (p = 0.035) and EBA140 (p = 0.025). Analysis of associations between GLYC mutation and antibody response lacked power, but an interesting trend of decreased IgG response to EBA140, which binds to GLYC, was present. The trend of increased IgG3 response to Rh4.9 in children with CR1 mutation appears to be stronger when alpha thalassemia is also present.

Conclusion

In this cohort of young children from Papua New Guinea, CR1 mutation and alpha thalassemia were associated with an increase in antibody response to specific malaria merozoite antigens. The low number of children with GLYC mutation meant that results lacked power, though a trend of decreased antibody responses to EBA140 was seen. These results support the hypothesis that these RBC mutations influence antibody acquisition and highlight the need for further research into this relationship.
Mr Clark Christensen Matheos

Cost-effectiveness of tobacco control strategies in Indonesia

Supervisor Names and Institute Affiliations:
Supervisor: Professor Danny Liew
Co-Supervisors: Associate Professor Zanfina Ademi Delaney, Dr Ella Zomer
Centre of the Cardiovascular Research and Education in Therapeutics (CCRET), School of Public Health and Preventive Medicine, Monash University

ABSTRACT

Background
In Indonesia, tobacco smoking is a public health problem that continues to grow, with prevalence among the highest in the world and with the five leading causes of death being smoking-related. Smoking also causes a significant impact on society though lost productivity. Current tobacco control interventions implemented in Indonesia include health warnings in cigarette packs, limited tobacco taxation and certain smoking bans. However, many more measures can be tailored and adopted. From a broader economic perspective, such strategies need to be considered in the context of a thriving Indonesian tobacco industry.

Aim
To assess the cost-effectiveness of government-funded varenicline, smoking bans in public places and a further 10% tobacco tax in Indonesia.

Method
Markov modelling of the Indonesian population aged 15 to 80 years, with simulated follow up until age 85 years. Data on demographics, the prevalence of smoking and mortality were drawn from the Global Burden of Disease Study 2017, the World Bank, and the World Health Organisation. Inputs regarding efficacy and costs of the three interventions were gathered from published sources and Indonesian local data. Costs and benefits accrued beyond one year were discounted at a 3% annual discount rate.

Results
Government-funded varenicline, smoking bans in public places and a further 10% tobacco tax were predicted to save 5.5 million, 1.6 million and 1.7 million years of life, respectively, as well as 11.9 million, 3.5 million and 3.8 million quality-adjusted life years (QALYs) (all discounted). From the perspective of the healthcare system, all three interventions were cost-saving, due to substantial reductions in smoking-related healthcare costs. Hence from a health economic point of view, all interventions were dominant. Outside of the healthcare system, government-funded varenicline, smoking bans in public places and a further 10% tobacco tax were predicted to also save 1.7 million, 500,000 and 500,000 productivity-adjusted life years (PALYs), respectively, equating to USD $21 billion, $6 billion and $7 billion gains in gross domestic product.

Conclusions
In Indonesia, government-funded varenicline, smoking bans in public places and a further 10% tobacco tax are all likely to be highly cost-effective, and even cost-saving from the perspective of the healthcare system. However, these cost savings need to be balanced against broader economic losses that would result from the impact on the large Indonesian tobacco industry.

Hello there! By the time that you’re reading this, I’m finishing up my fourth year of medical studies, following the three years I’ve spent in Universitas Indonesia.

I learned a ton from my Honours year here at Monash about research, thesis writing, health economics, and unexpectedly, the current tobacco landscape in my home country. I was (and still am) very grateful to be guided and taught by the most wonderful supervisors: Danny, Zanfina and Ella – who are experts in the field of health economics.

It is also the first time I’ve lived overseas for almost a year, independently, on top of an ongoing global pandemic. For better or worse, I will cherish the memories I’ve made with my colleagues and teachers in this special year.

A few advices for future students are to have good communication between your supervisors, to always appreciate every step of the process, and to not take your Honours year for granted. Godspeed!
Ms Hannah Matthiesson

Fertility and pregnancy knowledge and concerns, and
information needs and preferences for men and women with thalassaemia

Supervisor Names and Institute Affiliations:
Supervisor: Associate Professor Esther Briganti, School of Public Health and Preventive Medicine, Monash University
Co-supervisor: Professor Susan Davis, School of Public Health and Preventive Medicine, Monash University

ABSTRACT

Background

The β-thalassaemias are a group of genetically inherited blood disorders which result in a chronic severe anaemia. β-thalassaemia has a significant effect on fertility for men and women and is also associated with significant risks in pregnancy for women. Considering these risks, it is important to understand the experiences, concerns and information needs of people living with thalassaemia with regards to fertility and pregnancy.

Method

A cross sectional study using an online anonymous survey was designed. Two surveys were created for use in this study: one for males and one for females. The investigators used survey tool designed by Charron-Prowchownik et al created for reproductive health issues in chronic disease, as well as a review of the literature and input from medical specialists and consumers, in their design of the surveys. The survey asked questions across six domains (demographics, thalassaemia related questions, contraception and pregnancy experience, contraception knowledge, fertility and pregnancy/testosterone levels knowledge, information preferences) and was delivered on REDCap®, a survey platform licensed by Monash University. The survey was advertised to potential participants via patient support groups and major thalassaemia units across Australia. Descriptive and inferential analysis was conducted using STATA and Microsoft Excel.

Results

Sixty-eight participants were included in the data analysis. Fifty-one (75%) were female and 17 (25%) were male. Two-thirds of sexually active, pre-menopausal women were using contraception. Around half of the participants who were sexually active had children and half of these had required ART to achieve a pregnancy. There was poor knowledge about contraception, with less than half of participants identifying it as very important for people with thalassaemia, and close to half of female participants not knowing if the progesterone only pill, intrauterine device or vaginal ring were safe for women with thalassaemia to use. While the majority of participants understood that thalassaemia was associated with an increased risk of infertility and testosterone issues for males and pregnancy complications for females, there was poor knowledge of the mechanism causing this. The majority of males and females had significant concerns about pregnancy and fertility issues and around half of participants indicated they wanted more information on these topics.

Conclusion

While small, our study indicated that Australian men and women with thalassaemia have significant concerns and knowledge gaps with regards to fertility and pregnancy. It is vital that these are addressed in order to improve patient care and maximise fertility and pregnancy outcomes for Australians living with thalassaemia.

I was lucky enough to undertake a BMedSc(Hons) at the School of Public Health and Preventive Medicine after my fourth year of Medicine. I have always been interested in the research aspect of medicine and thought a BMedSc(Hons) was a perfect opportunity to see how it works. I learnt so much throughout the year, not only about medicine and research but also how to work independently and manage your own project. It was certainly challenging at times, but it was also extremely rewarding and I would recommend it to any students considering it.

I am happy to be contacted at:
hkmat3@student.monash.edu
if anyone had any questions!
ABSTRACT

Background
Advances in cancer treatment and early detection measures, as well as an ever-growing ageing population, has resulted in a steady increase in numbers of cancer survivors. It has been suggested that older cancer survivors may experience ageing at an accelerated rate when compared to their similar-aged, cancer-free counterparts. Ageing is undoubtedly a significant risk factor for cancer. There is evidence to suggest, however, that this relationship may in fact be bidirectional, with cancer and its treatments contributing to the ageing process.

Aim
To investigate whether cancer and anti-cancer treatment are associated with accelerated ageing in older cancer survivors.

Method
A post-hoc analysis of a randomised controlled trial (RCT), namely the ASPirin in Reducing Events in the Elderly (ASPREE) trial, an international, multi-centre, RCT that investigated the benefits and risks of aspirin in healthy older people, was performed. The ASPREE longitudinal dataset contained the majority of data required for analysis, although cancer treatment data was not available and required further data collection from participant records. Multivariate time-dependent Cox regression analysis was used to investigate the time-to-development of ageing events, namely chronic disease, cognitive decline, and functional decline. The impact of both a post-randomisation cancer diagnosis and anti-cancer treatment on ageing events was analysed using time-varying covariates. Subgroup analysis was performed by metastatic status and cancer type.

Conclusions
The findings of this study indicate that both cancer and anti-cancer treatment are associated with an acceleration in the ageing process, although an independent effect of cancer itself cannot be definitively concluded. Given the implications of ageing events for quality of life and mortality, this study may provide a basis for the integration of screening and management of ageing events into routine care for cancer survivors.
ABSTRACT

Background
Current antiplatelet agents approved for clinical use are associated with increased bleeding risk. A safer antiplatelet agent with low bleeding risk but retaining high potency of thrombosis inhibition is needed to improve the treatment outcome. Thrombin, the most platelet activator, activates platelets via PAR1 and PAR4. The first PAR1 antagonist was recently approved for clinical use, but has limited clinical utility due to increased bleeding. PAR4 is an emerging target for new antiplatelet agents given its distinct role in thrombus formation (vs PAR1 and other known targets) that predicts the promise of preventing thrombosis with lower bleeding risk. One approach to block PAR4 is via function-blocking PAR4 antibodies. Toward this goal, three fully human anti-PAR4 (hPAR4) antibodies were recently generated. However, their anti-thrombotic efficacy has not been evaluated.

Method
Aggregation of platelets isolated from healthy donors was performed via light transmission aggregometry. Concentration-inhibition curves for hPAR4 antibodies were performed to determine IC50 values for hPAR4 antibodies and BMS-986120 in response to the physiological PAR4 agonist, thrombin. We then developed a microfluidic thrombosis assay for subsequent assessment of hPAR4 antithrombotic activity. Here, blood was labeled with fluorescent antibodies against platelets and fibrin and the effects of hPAR4 antibodies and BMS-986120 examined in blood flowed through a microfluidic channel coated with type I fibrillar collagen and flowed at a wall shear rate of 600s⁻¹. Platelet and fibrin deposition was detected using confocal microscopy.

Results
All three hPAR4 antibodies showed some level of PAR4 inhibition in a thrombin-induced aggregation assay. However, RGN14 and RGN15 exhibited a wide variation of response. In contrast, RGN16 was uniformly effective and quite potent (IC50 13µg/mL). Given this, RGN16 was taken forward for assessment of antithrombotic efficacy. However, the establishment of a suitable assay was not completed, since none of RGN16, BMS-986120, or any positive control tested showed significant anti-thrombotic effects.

Conclusion
RGN16, a fully human anti-PAR4 antibody, is an effective inhibitor of thrombin-induced PAR4 activation. However the testing of this reagent as an antithrombotic will require the establishment of a suitable ex vivo human whole blood thrombosis assay.

Hi! I'm a fourth year medical student from Universitas Indonesia, took a year off to do research because I want to explore more about 'behind the clinical practice' part of medicine. I read somewhere that your life can change in one year and this was definitely a real proof that I’ve experienced. I've learned and grow not only as a medical student but also as a person. I chose a study on a newly developed antiplatelet drug to prevent thrombosis (aimed for heart attack and stroke prevention) as my project as I was interested in that area. It wasn’t easy when COVID-19 suddenly happened in the middle of the cohort but in the end, doing honours was a total fun ride and bring a lot of new skill and perspective into what I’m aiming to become.
Mr Joseph Nguyen

Responsibility sensitive healthcare policies: lessons from tort law

Supervisor Names and Institute Affiliations:
Prof Julian Savulescu, Dr Thomas Douglas, Dr Gabriel De Marco (Oxford Uehiro Centre for Practical Ethics, University of Oxford)
Prof Justin Oakley (Monash Bioethics Centre, Monash University)

ABSTRACT

Background

Some philosophers argue that personal responsibility for health decisions should be taken into account by policymakers when an individual’s choices leads to that individual developing a disease. Responsibility sensitive healthcare policies (RSHPs) are policies that would hold individuals to account for unhealthy lifestyle choices and would enforce obligations by individuals to take care of their health. Indeed, health authorities throughout the world have used the language of personal responsibility to justify a wide range of policies in order to ration healthcare resources and influence treatment decisions.

Defenders of RSHPs have argued that a healthcare system is fair or just when it holds individuals responsible for their lifestyle choices. Yet, scholarship on responsibility in healthcare has argued that such policies are impractical or unachievable, suggesting that (i) too many resources will be required to implement them, (ii) they do not accurately assess responsibility, and (iii) they unrealistically prohibit a wide range of societal activities. These objections ultimately revolve around the worry that we cannot realistically and efficiently assess responsibility.

Discussion

My thesis proposes that it may be permissible to implement RSHPs, despite these objections. Assuming that people are responsible for their unhealthy lifestyle choices and outcomes, I propose a potential way of assessing responsibility that is practical. I draw from the concept of reasonableness in tort law to approximate responsibility as a model to approximate responsibility that offers an appropriate trade-off between fairness and practicality.

Firstly, this thesis investigates what it means to be responsible in healthcare and explore reasons for and against RSHPs. Assessing responsibility with as much accuracy and efficiency as possible is an important consideration in implementing RSHPs. This means that if we are to hold people responsible in healthcare, we should be careful about stipulating the conditions under which we do so.

Secondly, this thesis explores how attributions of liability in tort law work. I examine similar issues of practicality in tort law where responsibility is difficult to determine. I show that tort law makes important trade-offs to assess responsibility whilst operating efficiently by using the reasonable person standard. I then elaborate on how the reasonable person test is defined, exploring the merits of three approaches of this: welfare maximisation, statistical normalcy and interpersonal duties.

Thirdly, I apply these three views of reasonableness to attribute responsibility in cases in healthcare and show how they come to determinate but occasionally divergent answers. I argue that these accounts of reasonableness can solve the practicality problems of RSHPs by making such policies easier to implement, whilst sacrificing little fairness.

Finally, I suggest that a realistic reasonable person model that incorporates the most plausible features of all three views of reasonableness could be used as the basis of future RSHPs.

I did my BMedSc(Hons) at the Oxford Uehiro Centre for Practical Ethics after Year 4C. I have always been interested in the ethical aspects of medicine as well as moral and political philosophy more generally.

I was fortunate enough to spend two months at Oxford this year. I had the opportunity to attend philosophy and law discussion groups which were very intellectually stimulating experiences. I was also able to take advantage of extracurricular opportunities including a student consulting group and the Oxford Union debating society.

My project looked at the question of personal responsibility in healthcare. For example, when medical resources are scarce, a question arises whether priority should be given to those who are not responsible for their medical condition. It was fascinating to explore the philosophy of moral responsibility, decision science and legal philosophy in my project.

I have learnt a great deal about bioethics, philosophy, and academic writing, as well as how to survive writing a thesis during almost 6 months of lockdown. My supervisors were inspirational and passionate, and I have gained a deeper appreciation for the philosophical issues in medicine.

I am happy to be contacted by students who are interested in the program.
ABSTRACT

Background
Medical therapy with intravenous (IV) acetylcysteine is highly effective at preventing hepatotoxicity following paracetamol overdose. Traditionally, this has been administered using a regimen comprising of three separate infusions (150 mg/kg over 15-60 minutes followed by 50 mg/kg over 4 hours then 100 mg/kg over 16 hours). Multiple studies have shown that this regimen is associated with frequent and long delays during treatment. A newer two-bag regimen (200 mg/kg over 4 hours then 100 mg/kg over 16 hours) is equally effective at preventing hepatotoxicity and has replaced the three-bag regimen as recommended practice in Australia. While there is some evidence to suggest that the two-bag regimen is associated with fewer interruptions and delays to treatment, the extent of this difference is still unclear.

Aim
Our primary aim was to compare the cumulative length of delays during IV acetylcysteine infusion between patients receiving the three-bag regimen and two-bag regimen for the treatment of paracetamol overdose. Secondary aims were to compare the frequency of delays and to identify causes of delay.

Method
Our study was a retrospective cohort study – conducted at Monash Health emergency departments – of patients receiving the three-bag regimen and two-bag regimen for the treatment of paracetamol overdose. Secondary aims were to compare the frequency of delays and to identify causes of delay.

Results
Of 974 patients who received IV acetylcysteine for paracetamol overdose, 313 cases were included in our three-bag cohort and 661 cases were included in our two-bag cohort. The median cumulative length of delay during acetylcysteine infusion was significantly longer in the three-bag cohort, compared to the two-bag cohort: 65 (IQR: 40, 105) minutes vs 35 (IQR: 15, 70) minutes, p<0.01. Additionally, delays longer than one hour were more common in the three-bag cohort: 51% vs 31%, p<0.01. The occurrence of cutaneous NAARs was associated with significantly longer delays in both cohorts and was more frequent in the three-bag cohort. 51% vs 31%, p<0.01. The occurrence of cutaneous NAARs was associated with significantly longer delays in both cohorts and was more frequent in the three-bag cohort. Interruptions to IV access were associated with significantly longer delays in the two-bag cohort only. There were no significant differences in delays associated with smoking status and administration of nicotine replacement therapy (NRT), interruptions to IV access and evidence of adverse drug reactions – gastrointestinal reactions and cutaneous and systemic non-allergic anaphylactoid reactions (NAARs) – were also recorded.

Conclusions
The two-bag IV acetylcysteine regimen was associated with significantly fewer and shorter delays during acetylcysteine infusion, compared to the three-bag regimen. Cutaneous NAARs (in both cohorts) and interruptions to IV access (in the two-bag cohort only) were associated with significantly longer delays and could present a target for reducing frequency and length of treatment delays in the future.
ABSTRACT

Background

Major trauma comprises injuries which are likely to result in disability or death. The management of major trauma is time critical and requires highly specialised care. The goal of modern trauma systems is to rapidly match and transport major trauma patients to an appropriate level of care. A key component of modern trauma systems is the coordination of interhospital transfers, so that injured patients can be safely and efficiently moved from the presenting hospital to a higher level of care. To improve service delivery, a number of trauma systems have established dedicated interhospital transfer services. These services hold several theoretical advantages over more disparate methods, yet evidence about the trends in use and impact of dedicated transfer services on patient outcomes remains limited.

Aims

This study had 3 aims:

i. Identify the rates and patterns of Adult Retrieval Victoria (ARV) use for interhospital transfers within the Victorian State Trauma System (VSTS); and,

ii. Identify case characteristics which are associated with the use of ARV for interhospital transfers; and,

iii. Determine whether the use of ARV for interhospital transfers is associated with improved in-hospital outcomes and patient-reported outcomes at 6 months when compared to other transfer methods.

Methods

A registry-based cohort study was conducted using data from the Victorian State Trauma Registry (VSTR). All adult patients (>16 years of age) who were injured between July 2008 and June 2019, met VSTR inclusion criteria and had an interhospital transfer, were included. Key indicators requested from the VSTR included: patient demographics, injury details, transfer details, key outcomes and clinical indicators. The primary outcomes of interest were in-hospital mortality, the Glasgow Outcome Score Extended (GOS-E) and 3 Level EuroQol 5D (EQ-5D-3L) summary score at 6 months post injury.

Results

A total of 9,125 interhospital transfers occurred within the study period. The transfer was coordinated by ARV in 3,454 (37.9%) cases and ARV coordination rates were higher in rural settings. Sex, injury mechanism, injury severity and rural status were significantly associated with ARV coordination. No significant association between ARV coordination and in-hospital mortality, GOS-E score at 6-months post injury or EQ-5D-3L summary score at 6-months post injury was found.

Conclusion

Less than forty percent of interhospital transfers were coordinated by ARV, and there was a significant difference in case mix between ARV and non-ARV coordinated cases. Rates of ARV coordination differed between metropolitan and rural settings, and further research into the reasons why may allow for barriers to ARV coordination to be addressed. Insight into predictors of ARV coordination may allow patients requiring ARV coordination to be identified earlier and with greater confidence. Further research into the impacts of specialist transfer services is likely needed.
ABSTRACT

Background
Osteoarthritis (OA) is the most prevalent chronic joint disorder which has multifactorial aetiologies. There has been some evidence for the involvement of vascular pathology in the progression and development of knee OA. Popliteal artery wall thickness has been displayed as a surrogate marker of cardiovascular disease and atherosclerosis and associated with knee structural changes. Therefore, the study aims were to investigate (i) the association between popliteal artery wall thickness and knee structural changes; and (ii) the natural history and associated factors of popliteal artery wall thickness in individuals with symptomatic knee OA.

Methods
The design of this study was a prospective cohort study. Data was obtained from Osteoarthritis Knee Statin (OAKS) trial. A total of 176 participants met the clinical criteria for knee OA without a high radiographic score, significant knee pain, and previous knee injury was enrolled. All participants underwent magnetic resonance imaging (MRI) of the knee at baseline and 2-year follow-up. Popliteal artery wall thickness, tibial cartilage volume and bone marrow lesions were measured from baseline and follow-up MRIs using validated methods. Multiple linear regression and binary logistic regression were performed to assess the association between popliteal artery wall thickness and structural changes with adjustment for confounding factors. Change in popliteal artery wall thickness was analysed using paired t-test.

Results
Of 176 participants, 152 (86.4%) completed the two-year follow-up. Greater baseline popliteal artery wall thickness was associated with a lower medial ($b=-12.1, 95\% CI: -23.6, -0.5; p=0.039$) and lateral ($b=-15.2, 95\% CI: -29.2, -1.2; p=0.033$) tibial cartilage volume at baseline, and increased rate of medial tibial cartilage volume loss over two years ($b=-0.11, 95\% CI: -0.22, 0.01; p=0.034$) after adjusting for confounders. A trend was observed for an association between greater popliteal artery wall thickness at baseline and worsening of bone marrow lesions in the lateral knee compartment over two years (OR: 1.08, 95\% CI: 0.99, 1.19; p=0.075). There was a trend for increased popliteal artery wall thickness over two years ($p=0.060$), which was statistically significant in males ($p=0.012$) but not females ($p=0.822$). Atorvastatin intervention was associated with a reduced popliteal artery wall thickness over two years in males.

Conclusion
The findings of this study revealed that greater popliteal artery wall thickness which was a surrogate marker for vascular pathology was associated with detrimental structural changes in knee OA, illustrated by an increased rate of tibial cartilage volume loss and a trend for worsening of bone marrow lesions, both of which are structural indicators of OA progression. These findings offer the involvement of vascular pathology in the progression of knee OA and that targeting vascular pathology may provide strategies for the management of the disease.
The initial neutrophil to lymphocyte ratio as a predictor of mortality and ICU admission after major trauma

ABSTRACT

Background

Early identification of trauma injury severity is important for prognostication. Recent research has proposed the neutrophil to lymphocyte ratio (NLR) as a marker of systemic inflammation in major trauma patients that is associated with in-hospital mortality. We planned to determine the relationship between NLR and outcomes in major trauma patients. The aim was to observe the discriminative ability of initial NLR as a predictor of mortality at hospital discharge and ICU admission following major trauma.

Method

This is a retrospective cohort study involving all major trauma patients meeting criteria for inclusion into the Alfred Health Trauma Registry (AHTR) and were admitted directly to the Alfred hospital over a 24-month period (January 2018 to December 2019). The initial NLR was calculated for each patient and was compared against the shock index (SI), lactate and revised trauma score (RTS). Outcomes observed were mortality at hospital discharge and ICU admission. We assessed the predictive capacity of each test using the receiver operating characteristic (ROC) curve and performed area under the curve analysis to compare their performance. Additionally, NLR was dichotomised with a cutoff of 10 and plotted on a Kaplan Meier curve to discriminate time to death.

Results

Data was collected for 1,687 major trauma patients that were included in that 24-month period. Of these patients, in-hospital mortality occurred in 165 (9.77%) patients and 725 (42.92%) patients required ICU admission. The median NLR was 6.84 (IQR 3.89-11.52) with the majority of NLR values falling between the range of 0-10. Initial NLR was the worst performing test of the four scoring systems, with RTS performing best overall in our study. NLR had an AUROC of 0.46 (95% CI: 0.40-0.52) for prediction or mortality and AUROC of 0.53 (95% CI: 0.50-0.56) for prediction of ICU admission. The AUROCs of initial NLR for both mortality at hospital discharge and ICU admission was significantly lower than SI, lactate and RTS. When NLR was dichotomised with a cutoff of 10, a high NLR did not predict increased mortality or time to death.

Conclusions

Initial NLR is not predictive of outcomes in major trauma. It demonstrates poor discriminative ability to predict mortality at hospital discharge and ICU admission. The inflammatory response as measured by neutrophil and lymphocyte counts are highly variable during the initial phase following injury and does not correlate with outcomes. These findings suggest that further research should investigate other uses for NLR, such as NLR ≥48 hours or monitoring NLR as a trend over time to predict outcomes.
ABSTRACT

Background
Advance care planning is a process which allows individuals to outline preferences for future medical care, in the event that they lose the ability to make treatment decisions themselves. Uptake of advance care planning in Australia is reportedly low, and there are concerns regarding advance care planning document quality. The current literature reports barriers to the uptake of advance care planning. However, little is known in the Australian setting about barriers to advance care planning across culturally and linguistically diverse communities.

Aim
The study aimed to determine the uptake and quality of advance care planning at a large public health service in Melbourne, Australia. The study also aimed to explore health professional insights on the barriers to and enablers of advance care planning across culturally and linguistically diverse communities.

Methods
The study adopts a mixed-methods design, and was conducted in three parts:
- Part 1: retrospective audit of advance care planning documentation prevalence
- Part 2: retrospective audit of advance care planning documentation quality
- Part 3: semi-structured interviews with health professionals on advance care planning barriers and enablers across culturally and linguistically diverse communities

Results
The study identified a low prevalence of advance care planning completed by the person (36.0%). Uptake of advance care planning completed by the person was lower across culturally and linguistically diverse communities, with lower prevalence for those born outside Australia (30.0%) compared to those born in Australia (40.7%). Diverse cultural and moral views influence if and how an individual chooses to engage with advance care planning. Document quality was variable, which creates challenges for decision-making with advance care planning documents.

Conclusion
This study is one of the few Australian studies to explore health professional views on the barriers to advance care planning across culturally and linguistically diverse communities. The barriers include ambiguity in processes, difficulties of communication in advance care planning discussions, and the challenges of understanding diverse cultural views which inform how an individual chooses to engage with advance care planning. Future policy should endeavour to improve uptake and quality of advance care planning by demonstrating respect for the diverse cultural and moral views that inform if, and how an individual chooses to engage with advance care planning.
ABSTRACT

Background
Benign oesophagogastric conditions commonly require complex surgical procedures. These procedures include anti-reflux surgery, the rates of which have increased significantly in recent years, and simultaneously, so too have the rates of postoperative complications. Recurrent hiatus hernia, and reflux and obstructive symptoms, are the most common postoperative complications, occurring in up to 40% of cases, and significantly impact patients’ quality of life. Currently, patient selection for further management is difficult, as there are no objective diagnostic algorithms to assess postoperative symptoms and guide further management. This poses a major diagnostic challenge for clinicians. Our central aim for this project was to evaluate whether, in distinct circumstances, diagnostic algorithms could be crafted to deliver clinically significant value.

Method
The project goal was to determine whether diagnostic algorithms for symptomatic patients post-oesophagogastric surgery can be developed, and to perform a discovery analysis to establish whether they can be applied following different oesophagogastric surgical procedures. We conducted four distinct studies to test our central hypothesis and endeavour to fulfill our project goal. Studies were interlinked, as they were evaluating the performance of similar investigational modalities but each under different circumstances. For each study, patient data was retrieved from a database and patients were included in the study according to the inclusion and exclusion criteria. Then patients were split into their relevant cohorts and compared based on different variables. The data was analysed and interpreted, and diagnostic thresholds were generated for significant variables.

Study one: oesophageal acid exposure and pressure dynamics within the oesophagus were assessed on pH monitoring and oesophageal manometry, respectively.

Study two: nuclear scintigraphy was used to analyse differences in oesophageal and gastric transit.

Study three: oesophageal manometry was used to analyse differences in pressure dynamics within the oesophagus.

Study four: significant findings from the previous studies were collated and a proposed diagnostic algorithm for symptomatic patients post-oesophagogastric surgery was developed.

Results
Study one: symptomatic patients compared to asymptomatic patients post-hiatus hernia repair and fundoplication had significantly higher oesophageal acid exposure in all pH variables and more severe impairment in oesophageal peristalsis. Symptomatic patients compared to asymptomatic patients post-fundoplication had significantly higher total acid exposure.

Study two: symptomatic patients had significantly higher proportion of counts retained within the intrathoracic herniated stomach.

Study three: symptomatic patients had significantly higher LOS relaxation and integrated relaxation pressure than asymptomatic patients.

Study four: a diagnostic algorithm for symptomatic patients post-hiatus hernia repair and fundoplication was developed.

Conclusions
This project strongly supports the proposition that developing diagnostic algorithms that are specific to new postoperative anatomy is not only feasible, but also likely to be clinically valuable. Multiple novel variables were significantly associated with reflux and/or obstructive symptoms in postoperative patients. These results culminated in the development of a proposed diagnostic algorithm for patients post-hiatus hernia repair and fundoplication, fulfilling and surpassing the goal of our project. Ultimately, we demonstrated the feasibility of developing specific diagnostic algorithms for surgical conditions, utilizing novel variables from existing and validated investigations. .
My name is Rana Sawires and I’ve finished my fourth year of medicine. I chose this project because I’m interested in paediatrics and wanted to gain some experience in research so I could see its real-life clinical implications. I’ve learned so many countless skills this year, including data management and collection, statistical analysis, as well as how to use new programs for the project. I’ve learned how to think critically about data, and not to take things at face value as well as how to see where the limitations are in a given study design and how we can account for or justify them. Above all, I’ve learned a lot about taking ownership of a research project, being ready to make mistakes and learn from them, and to constantly strive for better. This year has been so amazing and I can only thank my wonderful supervisors, Jim and Michael for being such wonderful mentors and supports throughout it. I hope that I will be able to take the skills I’ve learned this year and apply them to future research and in my clinical practice. For anyone doing a BMedSc(Hons), don’t be afraid to make mistakes, don’t be afraid to ask for help, but mostly, don’t be afraid to make the project your own and shape it! Feel free to reach out to me if you have any questions!

ABSTRACT

Background

Febrile seizures are the commonest type of seizure in occurring in the first few years of life, mostly affecting children aged six months to five years old. While largely benign, the incidence of each febrile seizure increases the risk of recurrence, afebrile seizures and epilepsy. Viruses are the most frequent cause of febrile illnesses in which a febrile seizure occurs. Febrile seizure incidence also appears to follow a seasonal trend.

Aims

To identify patterns of febrile seizure incidence across different seasons and locations with specific viral activity, and to establish a framework for analysing virus circulation data with common illnesses within a shared region and population.

Method

Our study was an ecological study of Victorian presentations of febrile seizures and respiratory virus detection. We obtained independent datasets of emergency department febrile seizure presentations at Monash Health and all respiratory multiplex PCR tests performed at Monash Health from January 2010- December 2019 in order to observe common trends in virus circulation and febrile seizure incidence. Trends were studied temporally through mixed effects Poisson regression analysis of the monthly incidence of febrile seizures and positive PCR tests. Peak viral seasons were defined as monthly virus detection in the 3rd quartile of our distribution and were used to calculate peak season risk ratios. Trends were additionally studied geo-temporally using hotspot analysis by applying Getis-Ord Gi* statistics, and cluster and outlier analysis using Anselin Local Moran’s I statistics.

Results

We found a 1.75-2.06 annual RR of febrile seizure incidence in June-September. Temporal analysis of our data showed this peak in febrile seizures was attributable to circulating viruses in this season, and virus modelling showed correlation with adenovirus (1.14 peak season RR), influenza A (1.05 peak season RR), influenza B (1.03 peak season RR), human metapneumovirus (1.21 peak season RR), picornavirus (1.16 peak season RR) and RSV (1.18 peak season RR). Adenovirus was more common in younger children and in those presenting with mild febrile seizures, while influenza B was associated with febrile seizures in the extremes of our age groups and with more severe febrile seizures. Geo-temporal analysis confirmed hotspots of febrile seizures, influenza A, adenovirus and HMPV in metropolitan Melbourne, but further research will determine the relationship between the febrile seizure and viral findings.

Conclusion

Our ecological study statistically demonstrates the recognised winter peak in febrile seizure incidence and ascribes the seasonal relationship to several viral infections which affect the community. We have also identified clusters of febrile seizures and positively detected viruses in metropolitan Melbourne. Further geo-temporal directions for this study include comparing groups of the data through time to establish the significance of correlations between viral and febrile seizure clusters. We have successfully created a framework for temporal analysis of viral incidence datasets with common illnesses of interest and have forged a new path in adding a geo-temporal component to such a framework. This lays the groundwork for future analysis of common illnesses of interests with large viral circulation datasets to inform health practitioners and public health policy alike.
ABSTRACT

Background

Children with Down syndrome (DS) are highly vulnerable to having sleep disordered breathing (SDB) due to their unique craniofacial characteristics and reduced muscle tone which predispose to airway obstruction. SDB is associated with intermittent hypoxia and sleep disruption and can result in daytime deficits. Assessing the detail of sleep quality in children with DS is needed to understand how SDB affects this group of children particularly, and this may provide a better insight into optimising daytime function in children with DS. To date, there are limited studies that have analysed sleep quality in children with DS, and none have used electroencephalogram (EEG) spectral analysis. This study aimed to determine whether SDB exerts a different effect on sleep in children with DS compared to typically developing (TD) children.

Methods

Children with DS and SDB (n=44) were matched for age and gender with the TD children without SDB (n=44, TD-), and additionally matched for SDB severity with TD children with SDB (n=44, TD+). All groups underwent overnight polysomnography to have their sleep characteristics and respiratory measures examined. Sleep quality was determined using several measures: sleep macro-architecture (time spent in various sleep states), sleep micro-architecture using EEG spectral analysis (quantification of EEG activity in various sleep states), and slow wave activity (an indicator of sleep drive). Sleep micro-architecture analysis included determining spectral power in main EEG frequencies: delta (0.5–3.9 Hz), theta (4 – 7.9 Hz), alpha (8 – 11.9 Hz), sigma (12 – 13.9 Hz), beta (14 – 30 Hz) and total power (0.5 – 30 Hz) in each sleep stage (N1, N2, N3, and REM).

Results

Demographic characteristics were similar between groups. Key differences in respiratory measures identified that children with DS had greater hypoxic exposure than TD+ children with matched severity of SDB, and more respiratory events during REM sleep. Sleep macro-architecture assessment in children with DS demonstrated more wakefulness during the night and increased time spent in N2 sleep. In terms of sleep micro-architecture, the DS group had higher EEG total (p<0.01), delta (p<0.001), theta (p<0.05), sigma (p<0.001), and beta power (p<0.001) in REM sleep. Children with DS had reduced slow wave activity across the night compared to the TD+ group (p<0.05). In contrast, there were no differences in sleep macro or micro-architecture between TD+ and TD-.  

Conclusions

This study identified that in contrast to TD children, children with DS had more disrupted sleep, reflecting a greater effect of SDB in children with DS. Sleep macro and micro-architecture collectively suggest more frequent awakeness and poorly consolidated REM sleep in children with DS. This difference may be related to greater hypoxia in children with DS or be a feature of the DS condition itself. Future research is needed to explore the potential contribution of DS to the changes in sleep macro and micro-architecture. Our findings of altered sleep architecture in children with DS and SDB support the implementation of SDB screening for early detection and treatment to optimise sleep quality and therefore daytime functioning and quality of life.
Mr Pravik Solanki

Models of care for the trans, gender diverse and non-binary community in Victoria: a quantitative comparison

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ABSTRACT

Background

Victoria’s current healthcare system has uncoordinated pathways, rising referrals to services, and persistently long wait lists for trans, gender diverse and non-binary adults seeking Hormone Therapy (HT) and other gender-affirming treatments. HT can be approved in the World Professional Association for Trans Health (WPATH) model offered by mental health clinicians, or Informed Consent (IC) models increasingly offered by general practitioners. However, no study worldwide has empirically compared clients and their assessments in these two models, and few have focused on the health needs of non-binary people. Moreover, clients with ‘complex health needs’ remain poorly characterised, despite the consensus that they would benefit from comprehensive WPATH assessments.

Aims

The three aims of this study were to characterise and compare WPATH and IC model clients, to characterise and compare transgender and non-binary clients, and to characterise complex health needs by identifying characteristics associated with psychiatric diagnoses and longer assessments for HT.

Method

We conducted a cross-sectional audit of clients approved for gender-affirming treatment at Monash Health Gender Clinic (WPATH model) and Equinox (IC model). Clients with a first appointment between March 2017 – March 2019 with a completed assessment by June 2020 were included. Data collection was from scanned medical records (Monash Health Gender Clinic) or an existing dataset (Equinox). Data analysis was conducted on R, involving Benjamini-Hochberg post-hoc adjustments to limit the false discovery rate, and a backwards stepwise approach to include only relevant predictors in regression models.

Results

WPATH model clients had a significantly greater number of psychiatric diagnoses than IC model clients (mean 1.4 vs 1.1 diagnoses, p<0.001), being significantly more likely to have a diagnosis of an anxiety disorder (47% vs 36%, χ²(1)=5.1, p=0.024), borderline personality disorder (12% vs 5%, χ²(1)=8.3, p=0.004), or autism spectrum disorder (12% vs 5%, χ²(1)=6.5, p=0.011). Additionally, WPATH assessments for HT were significantly longer than IC assessments (mean 5.9 vs 2.6 sessions, p<0.001). Non-binary clients had a significantly greater number of psychiatric diagnoses than transgender clients (mean 1.7 vs 1.1 diagnoses, p<0.001), being significantly more likely to have a diagnosis of borderline personality disorder (16% vs 6%, χ²(1)=10.5, p=0.001). Additionally, non-binary people comprised a significantly greater proportion of clients approved for HT in an IC model than the WPATH model (27% vs 15%, χ²(1)=5.6, p=0.018), with IC assessments taking a significantly greater number of sessions for non-binary clients than transgender clients (mean 3.2 vs 2.4 sessions, p<0.001). Independent associations were found between the number of psychiatric diagnoses and non-binary identity (β=0.686, p=0.001) or healthcare card ownership (β=0.427, p=0.017), between depression diagnoses and regional/remote residence (aOR 2.229, p=0.011), and between anxiety disorder diagnoses and non-binary identity (aOR 2.833, p=0.012) or employment (aOR 0.463, p=0.016). No characteristics independently influencing the length of WPATH assessments for HT were identified.

Conclusion

This is the first study worldwide to compare WPATH and IC model clients and their assessments, providing insights to guide the development of health services in Victoria. Further studies adopting prospective and/or mixed-methods approaches would add to this evolving field, for which there is growing need.
Mr Abhishekh Srinivas

Anatomical feasibility of endovascular intervention for Type-A aortic dissections

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3 Department of Cardiothoracic Surgery, Monash Health

ABSTRACT

Background
Type-A aortic dissections (ADs) represent a significant life-threatening abnormality of the aorta, possessing a mortality rate of between one to two percent per hour initially, with less than 20% of patients surviving within the first fortnight of onset. As such, with few exceptions, the management of Type-A ADs is heralded as a surgical emergency, with the current gold-standard of treatment being open surgical repair (OSR). However, up to 20% of all patients remain unsuitable for major OSR, due to reasons of concurrent comorbidities, age or simply patient frailty. Additionally, mortality of these operations remains unacceptably high, with figures in the range of 25%. Consequently, there is a strong interest in minimally invasive endovascular surgery of the ascending aorta and determining the characteristics of Type-A AD patients who would be suited for this.

Method
We conducted a retrospective cohort study of all Type-A AD patients who presented to Monash Health between January 2002 and November 2019. High-quality CT-angiograms were obtained and analysed using multiplanar reconstruction to determine quantitative and qualitative variables pertaining to anatomy of the dissected aorta, including dissection entry tear location, aortic length and width, and supra-aortic vessel characteristics. Data obtained from imaging analysis was then compared to known instructions for use (IFU) for five endovascular devices- Zenith A-branch, Zenith Ascend, Tag Thoracic Branch Endoprosthesis (TBE), Valiant Navion and a valve-carrying conduit proposed by Rylski et al. to determine patient suitability for endovascular intervention.

Results
102 patients were included in our analysis. In analysing anatomy of the dissected aorta, we documented marked variance in site of entry tear when compared to previous feasibility studies in the literature, and this variance does not appear to be significantly affected by age, ethnicity or gender across our analysed patients. 54% of all patients had a tear within the aortic root, making it the most common dissection entry tear location in our study. Arch-vessel involvement in the dissection was not as commonly seen within our study, with only 24% of all cases’ dissection extending into the brachiocephalic trunk, compared to previous studies in the literature documenting figures of up to 45%. Utilising data from angiography scans, a cumulative total of 39% of all patients were suited for endovascular intervention. This is in sharp contrast to previous feasibility study results of up to 70% of all cases being suited for endovascularly treating Type-A ADs. Of our five analysed devices, the Tag TBE is best suited to our patient population, providing a minimally invasive therapeutic option for 34% of all cases.

Conclusions
Endovascular treatment of acute Type-A AD is desirable, particularly when considering the pre-operative and post-operative benefits, as well as the broadened scope of patients to which this therapeutic intervention can be extended to. However, our study has shown that it still remains far from being the standard treatment. Dissection of the supra-aortic branch vessels, location of the entry tear and a large aortic diameter at the level of the proximal and distal LZs were the most common factors to preclude the usage of endovascular intervention for treating Type-A ADs in most patients, and particular attention must be given to these characteristics when constructing and developing next-generation stent grafts.
ABSTRACT

Background

The only thrombolytic drug treatment for Acute Ischaemic Stroke is recombinant tissue-type plasminogen activator (tPA). tPA activates plasminogen into its active form plasmin which cleaves the fibrin surrounding the blood clot. However, recanalisation only occurs in <30% of AIS patients that receive tPA. Furthermore, 6% of recanalised patients are still at risk of symptomatic intracerebral haemorrhage (sICH). Moreover, ~40% of AIS patients that received tPA and failed to recanalise are at risk of functional deterioration. Plasmin once formed is inhibited by-anti-plasmin forming plasmin anti-plasmin complexes (PAPs). PAP formation indirectly reflects the amount of plasmin. Though plasmin has a vital role in the plasminogen activating system, no study has assessed whether the plasmin generating capacity in plasma could be a predictor to AIS patient’s clinical outcome. We determined whether PAP complex generation formed ex vivo in plasma treated with tPA reflects actual in vivo generated PAP complex levels post tPA-thrombolysis and also whether the degree of PAP formation correlates with the clinical outcome after tPA treatment.

Methods

We obtained plasma from 84 AIS patients from a stroke biobank in Hungary. Plasma samples were obtained from AIS patients immediately before thrombolysis, 1 hr post-thrombolysis, and 24 hr post-thrombolysis. Plasma samples from 38 non-AIS patient plasma were used as controls. Control and pre thrombolysed AIS patient plasma samples were treated with tPA with and without the presence of fibrin cofactor. Ex vivo generated PAP and levels of in vivo generated PAP complex after tPA-thrombolysis were measured with PAP ELISA kit. Fibrin zymography and western blotting was performed to evaluate changes in tPA activity and levels of plasminogen & anti-plasmin before and after in vivo tPA-thrombolysis. A regression analysis was conducted to assess any correlation between changes in fibrinolytic markers and the clinical parameters.

Results

We found large variability in the fold change of ex vivo generated PAP complex in AIS patients (~146) and control (~36.97) after treatment with tPA indicating that there is a marked difference in individuals to respond to tPA treatment ex vivo. Plasma from pre-thrombolysed AIS patients contained significantly higher PAP levels that control plasma indicative of increased fibrinolytic activity in AIS patients. Of interest, a significant correlation was seen between ex vivo tPA-induced PAP complex generation with actual in vivo generated PAP complex 1 hour after tPA administration (Pearson; r=0.9406, p<0.0001). Though there were no significant correlation found between the degree of PAP formation with clinical outcome, there was a trend that for each fold-increase in ex vivo PAP complex there was a 2.2% increase neurological improvement (p=0.054).

Conclusions

There is a large variability in the capacity of plasma to respond to tPA treatment ex vivo. This is also reflected the degree of in vivo tPA-induced PAP complexed formed ex vivo predicts the actual in vivo generated PAP complex levels formed 1 hour after tPA administration. Further research is needed using a larger plasma sample biobank in order to determine whether the degree of tPA-induced PAP formation formed ex vivo predicts patient outcome a larger data set.
Ms Elizabeth Suo
Heart transplant – what is the cost of delayed referral?

Supervisor Names and Institute Affiliations:
A/Prof Ingrid Hopper (School of Public Health and Preventative Medicine)
Professor David Kaye (Alfred Health)

ABSTRACT

Background
Heart failure (HF) is a complex disease syndrome with an increasing incidence globally. It is recognised that a proportion of patients with HF are referred late to specialist centres for evaluation of advanced HF therapies. Late referrals put patients at higher risk of complications which may compromise eligibility for cardiac transplant and incur greater healthcare costs. There is a paucity in the medical literature worldwide in regards to referral patterns, due to the lack of a clear definition of late referral. In contrast, other medical specialties outline clear definitions of late referral, associated complications and impacts on healthcare systems. This thesis aims to define and explore the impacts of late referrals, compare characteristics and resource usage timely and late referrals, in an Australian context.

Aims
1. To create a definition for late referral to a specialist heart failure centre.
2. Identify differences in patient characteristics in those referred in a timely manner and those referred late.
3. Quantify the in-hospital resource usage associated with late referral to the Australian healthcare system.

Methods
A retrospective observational study was conducted at the Alfred Hospital of patients who received a cardiac transplant between 2016 and 2019. Data were sourced from individual electronic medical records which included (1) demographic and clinical status at the time of referral; (2) Late referral criteria; (3) Date of referral, listing and transplant surgery; (4) In-hospital resource usage at the time of transplant surgery. The late referral criteria were derived from a previous Australian paper which outlined markers of advanced heart failure that should prompt referral to advanced HF services. Primary outcome measures included length of stay and costs of transplant admission. For statistical analysis, Mann-Whitney U tests and Chi-square tests were used to identify significant differences between timely and late referral groups.

Results
A total of 80 patients were included in the study. The median age was 52 years at the time of referral with a male predominance (78%) in the cohort. A late referral definition was developed based on the distribution of the number of criteria patients fulfilled, which was the “presence of four or more components for more than six months”. Those referred late had higher rates of HF symptoms, comorbidities and hospitalisations at the time of referral. They had a longer duration of time between first diagnosis and date of referral. Patients referred late incurred greater costs at the time of the transplant admission, costing 28% more than those referred in a timely manner.

Conclusion
This is the first study to develop a definition for what constitutes a late referral to a specialist HF centre. Application of this definition identified a cohort of patients as likely late referrals who were significantly different to those referred in a timely manner in terms of clinical status, duration to referral and costs. These findings have laid the groundwork for further cardiology referral research in Australia, and will ultimately lead to improved access to cardiac transplant for patients with advanced HF.
Mr Antony Takla  
Terminal Anaesthesia: The Ethics of Sedation to Unconsciousness in End of Life Care

Supervisor Names and Institute Affiliations:  
Professor Julian Savulescu (Uehiro Centre for Practical Ethics, Oxford University)  
Professor Dominic Wilkinson (Uehiro Centre for Practical Ethics, Oxford University)  
A/ Professor Giuliana Fuscaldo (Monash University)

I did my BMedSci(Hons) in 2020 after completing year 4C in 2019. The reason why I decided to do a BMedSci(Hons) was to gain more experience in research and all the associated skills that come along with that (drafting manuscripts, delivering concise presentations and preparing conference posters). I particularly enjoyed the ethics program that is run in conjunction with the Uehiro Centre for Practical ethics because it was very different from anything I had done before and it really opened my eyes and challenged me in new ways. I really enjoyed reading different arguments from various ethicists on contentious issues in medicine and learning how to formulate and present my own arguments. Getting to visit Oxford, though short-lived due to the pandemic, was also quite a unique and memorable experience. I truly hope by the time students are reading this, international travel is back on the table and students can enjoy the full experience abroad. I highly recommend this program, and I am happy to be contacted about my prospective students in the future at: atak43@student.monash.edu

ABSTRACT

Background

End of life care (EOLC) refers to palliative care for patients who are imminently dying. Management includes holistic care and symptom management. While there have been considerable advances in EOLC, a quarter to a third of all terminally ill patients experience refractory symptoms that require sedation. Terminal sedation (TS) refers to the practice of administering sedatives to help manage refractory symptoms in dying patients. Professional guidelines indicate that sedatives should be carefully titrated, aiming to provide the lowest dose of sedation to achieve comfort; it is thought that aiming directly at unconsciousness would be both unnecessary and unethical. In this thesis, I explore some problems with this line of argument and propose a version of TS that I label “Terminal Anaesthesia” (TA) for some dying patients. TA is the administration of an anaesthetic agent (such as propofol) to a dying patient with the clear aim of bringing about immediate unconsciousness (based on a competent patient request). I outline the ethical case for TA as a way of respecting patients’ wishes and of ensuring true patient comfort in their last few hours or days of life. I respond to some potential objections, especially around the moral equivalence of TA and euthanasia. I reject the claim that one ought to never aim directly at reducing consciousness in palliative care, contending that this can be morally good or at least morally neutral in some circumstances. In addition, I set out to investigate the attitudes of the general public in the UK towards various forms of sedation in EOLC. This was done to build on my ethical analysis through a process of reflective equilibrium.I performed an anonymous online survey including two separate samples of the UK public (total n=509). Seventy-two percent of participants indicated that it would like to have the option of TA available in their EOLC, however, 64% indicated they would likely use it. More than two-thirds of participants disagreed with a statement that doctors should never be allowed to make a dying patient completely unconscious. More than 50% of participants believed that TA and euthanasia were not equivalent, however, a third believed they were. Responses to questions of providing artificial nutrition and hydration to a patient receiving TS were divided. No statistically significant differences were found between the two surveys in relation to key questions regarding the use of TS or TA in EOLC. Ultimately, I argue that there is a strong ethical case in favour of TA and my survey suggests that there would be overwhelming support for this EOLC option from the UK general public. Reluctance from physicians and policymakers to provide deliberate sedation to unconsciousness at the end of life should be reconsidered. Policies ought to better reflect public preferences (underpinned by sound moral arguments) about the full range of options that should be available to dying patients receiving EOLC.
Ms Katrina Yiying Tan

The Melanoma SPOT: Study of Pathways Of Treatment

Supervisor Names and Institute Affiliations:
Associate Professor Victoria Mar1,2
Dr Yan Pan1
1 Victorian Melanoma Service, Alfred Hospital
2 School of Public Health and Preventive Medicine, Monash University

ABSTRACT

Background

Missed opportunities for the diagnosis of melanoma, as well as in follow-up care, carry grave consequences to long-term prognosis, particularly for rural Australians who already face significant barriers to healthcare. To date, an assessment of pathways to diagnosis and follow-up of melanoma with direct comparison between rural and metropolitan patients has not been performed. We aimed to describe the clinical pathways to melanoma diagnosis and of follow-up for rural and metropolitan patients, highlighting gaps in care and areas in need of future investigation.

Methods

Two retrospective questionnaires were conducted. 123 consecutive patients who presented to the Victorian Melanoma Service (VMS) between February and August 2020 completed the survey regarding pathways to diagnosis. 90 patients who had been seen at the VMS between October 2018 and June 2019 completed the survey inquiring about follow-up care received in their first-year post-melanoma. Types of doctors seen, frequencies, outcomes, delay times and barriers including COVID were recorded and assessed.

Results

Pathways to melanoma diagnosis did not differ between rural and metropolitan patients. The most common pathway for all patients was GP α biopsy, representing 33.33% of experiences. There was a non-significant trend for rural patients to be more reassured that their lesion was benign (OR, 1.44; 95% CI, 0.44-4.37) though they were still as likely as metropolitan patients to have diagnostic biopsy within one-month of initial consult (OR, 1.13; 95% CI, 0.24-4.44, p=0.85). Rural patients faced significantly greater difficulty accessing health services (p<0.01), however, pathways to melanoma diagnosis were not associated with thickness of tumour at diagnosis in this cohort.

Although rural patients appeared to be more active in follow-up, provision of care did not differ between rural or metropolitan patients. Dermatologists were the most common doctor seen for follow-up of both metropolitan and rural patients (64% metropolitan; 46% rural), skin GPs were a close second for rural patients (31% rural; 15% metropolitan). Frequency of follow-up was more associated with the thickness of patients’ original tumours and did not differ according to rurality. Rural patients were more likely to report feeling ‘very confident’ in conducting self-skin examinations (p<0.05).

COVID and its lockdowns led to delayed diagnostic biopsies (2.5%), impacted 7% of overall pathways, and affected 25% of follow-up pathways, 87% of which were delays in skin checks by at least one month.

Conclusion

Our descriptive analysis clearly demonstrates the variance and complexity of melanoma diagnostic pathways, and it highlights the potential for greater SSE performance in both pathways to diagnosis and pathways of follow-up care. We were able to shed light on the rather ambiguous experiences faced by rural patients, particularly the role of barriers to health services. Pathways to diagnosis for rural patients were unable to explain why rural patients tend to develop thicker tumours compared to metropolitan patients. The finding that barriers exist at all, requires further investigations as to alternative modes for the delivery of care. We captured some unintended consequences of COVID, the true impact of which will be more obvious in the months to come.

Undertaking a BMedSc(Hons) year was one of the best decisions I’ve made while studying medicine. It was a great way to introduce some new challenges and learn different skills, especially after finishing the notorious 4th year of medicine. I went into the year with little knowledge about how research is actually conducted but I came out knowing, and having personally experienced, how to recruit patients, how to analyse data and how to write up a mini-thesis; invaluable skills that I know will help me in years to come. I was lucky to have undertaken this research year with my supervisors A/Prof Victoria Mar and Dr Yan Pan, both of whom gave me incredible feedback, provided unyielding support and solidified my hopes of pursuing further research in dermatology. Any student hoping to broaden their knowledge in their field of desire and hoping to gain research skills to serve them beyond their undergraduate degree, should definitely consider a BMedSc(Hons) year.
Miss Dhiya Surya Tarina

Topical Wound Healing Formulations in the Treatment of Chronic Wounds Associated with Diabetic Complications

Supervisor Names and Institute Affiliations:
Dr. Tom Karagiannis from the Department of Diabetes Central Clinical School Monash University.

ABSTRACT

Background

Chronic wounds arising from diabetic complications commonly found in elderly adults are characterized by the inability to progress into normal wound healing due to the underlying metabolic conditions that result in wound aggravation. Treatment over the years commonly use topical cream-based ointments to provide a proper environment that retained moisture for cell proliferation to occur. This study investigated the efficacy of four topical medications towards wound healing. Dimethicone and sorbitol are a silicone-based topical moisturizer and a sugar-based topical ointment respectively that provides a moisturizing effect towards the stratum corneum. Petrolatum is an occlusive topical ointment that retains moisture. The efficacy of a petrolatum derivative enhanced with antioxidants (AEP) was also investigated to account the possibility of removing reactive oxygen species to improve wound healing, which has been known to contribute to the chronicity of these wounds.

Method

A splinted excisional wound model was applied to three mice strains; a wild type healthy control strain (C57BL/6 J), non-diabetic phenotype healthy strain (db/h) and type 2 diabetic strain (db/db) strain. These mice consisted of five groups (n=6) with one group left untreated and the four remaining groups different topical treatments on one excisional wound with the other wound left untreated. Daily wound monitoring was conducted along with wound changes and digital photographs done twice a week then once a week after fourteen days. C7BL6/J and db/h were culled on day 21 while the db/db strain was culled on day 56 with emergency culls conducted ad libitum. Tissues of the healed wound was embedded in paraffin wax, then cut and stained with Haematoxylin & Eosin (H&E), Masson’s trichrome (MT), and Picrosirius red (PSR) stains to assess inflammation and collagen deposition respectively. Wound closure along with type I and type III collagen were analyzed using Fiji Is Just Image-J software program. Results were statistically analyzed with two way ANOVA (analysis of variance) using GraphPad PRISM.

Results

Re-epithelialization rate increased the most with petrolatum, followed by sorbitol, AEP, then dimethicone showing the slowest rate. Scarring improved mostly with AEP and dimethicone. Hair growth was shown more in mice treated with petrolatum and dimethicone. H&E stains show improvement in inflammation from all treatment except for sorbitol. Treatment groups assessed through MT and PSR and does not show increase in collagen deposition compared to the untreated group. None of the data show any statistical significance (p>0.05).

Conclusions

Chronic diabetic wounds requires treatment that implements all the treatments that show improvement in different aspects of wound healing. Petrolatum and sorbitol improve re-epithelialization while AEP and dimethicone improve scarring. Inflammation was also improved through these treatments but collagen deposition did not increase which may be interpreted as a the wound already showing proper scarring in the later stages of wound healing. Future studies should investigate how further healing can be achieved when combined with stem cell therapies to target wound closure on a molecular level.
Ms Emma Grace Thompson

Societal Consensus on Germline Gene Editing Unpacked

Supervisor Names and Institute Affiliations:
Dr Katrien Devolder (Uehiro Centre for Practical Ethics, University of Oxford)
Dr César Palacios-González (Uehiro Centre for Practical Ethics, University of Oxford)
Professor Catherine Mills (Monash Bioethics Centre, Monash University)

ABSTRACT

Background
Germline gene editing is a rapidly evolving biotechnology with potentially high stakes. In order to decide if and how it should be used in humans, a framework is needed to ensure ethically justified and democratically legitimate regulatory decisions. Since the International Summit on Human Gene Editing in 2015, the term “broad societal consensus” has become synonymous with the germline gene editing debate. However, the literature fails to adequately explain what this concept means and why it might be valued when it comes to determining the future of germline gene editing.

Aim
This thesis unpacks the meaning of and justification for “broad societal consensus” as a precondition to the clinical application of germline gene editing in humans.

Methodology and Findings
The thesis is grounded in the scientific, clinical and regulatory landscape of germline gene editing to provide context for further discussion. The complexity of the ethical arguments in the germline gene editing debate is introduced and reasonable disagreement is shown on the appropriateness of its use in humans. This includes an exploration of the arguments for and against germline gene editing in relation to principles such as beneficence, identity, enhancement, non-maleficence, social justice, human rights and dignity. Finally, answers are provided for how we might develop an ethically justified policy to regulate germline gene editing in the setting of diverse moral, religious and sociocultural views.

Conclusion
I defend the notion of societal consensus proposed by Baylis, but I advance the theory into a more meaningful and workable framework.
Ms Lauren Siaomei Tong

The utility of ultrasound scan for the diagnostic evaluation of acute appendicitis in children

Supervisor Names and Institute Affiliations:
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Department of Paediatric Surgery, Monash Childrens Hospital
Department of Paediatrics, School of Clinical Sciences at Monash Health, Monash University

ABSTRACT

Background

Acute appendicitis is the most common surgical emergency in children. It is classified into simple (non-perforated) and complex (perforated) disease which have differing management. Clinical diagnosis and classification of paediatric appendicitis can be challenging, with atypical presentations and limited communication skills, so abdominal ultrasound scan (USS) is commonly performed. Its accuracy and utility is multifactorial and incompletely explored in Australian literature. Sonographic features particularly may have value in diagnosing and differentiating simple and complex appendicitis. We aimed to determine USS’ accuracy, and identify sonographic features to detect and differentiate acute appendicitis in children.

Method

Single-centre retrospective cohort study at a tertiary hospital over 29 months (1st January 2017- 31st May 2019). We included all USS of children with suspected appendicitis, and compared these with operative outcome: No appendicectomy (NoA), Negative appendicectomy (NegA), Simple appendicitis (SA) and Complex appendicitis (CA). NegA was defined histologically, SA and CA on intraoperative findings. We excluded children with previous appendicectomy or a pre-existing condition causing abdominal pain. Diagnostic accuracy was reported as overall accuracy, sensitivity, specificity, predictivity and likelihood ratios. Receiver operating characteristic (ROC) curve and multiple logistic regression analysis predicted utility of specific sonographic features for diagnosis and differentiation of appendicitis, extracted from a standard sonographer’s proforma.

Results

A total of 934 USS were analysed, with median age 10.7 (1.2-18.4) years and 46.3% male. Prevalence of appendicitis was 36% (n=339), of which 12% (n=113) had CA. More than half (52%) of appendicectomy patients had a pre-operative USS, of which 52% were diagnostic. Overall accuracy for appendicitis was 89.4% with sensitivity 85% [95% CI: 80-88], specificity 92% [95% CI: 90-94], PPV 86% [95% CI: 82-89] and NPV 91% [95% CI: 89-93]. Sonographic features suggesting appendicitis included presence of an appendicolith (p=0.003), hyperaemia (p=0.001), non-compressibility (p=0.029), absent luminal gas (p=0.004) and diameter above 7mm (AUC 0.92, [95% CI: 0.90-0.94]); with secondary features including focal pain (p<0.001) and peri-appendiceal echogenic fat (p<0.001). USS signs suggestive of CA were the absence of a blind ending (p<0.001), appendicolith (p=0.003), diameter above 10.1mm (AUC 0.63, [95% CI: 0.57-0.69]), no focal pain (p=0.040) and the presence of peri-appendiceal fluid (p=0.004).

Conclusions

USS has good accuracy despite frequent non-diagnostic scans, and may be helpful to diagnose appendicitis in clinically ambiguous paediatric presentations. Presence of specific sonographic features can aid diagnosis and differentiation of the disease. This maximises USS’ utility to improve clinical decision-making and counselling, and optimises appropriate care for children.

I chose to undertake an honours year as it provides more time to explore the research world, learn new skills, and pursue extracurricular activities. With a keen interest in paediatrics, I initially chose a prospective clinical study with the Department of Paediatric Surgery at Monash Children’s Hospital. Although the pandemic sent us home after six months of set up, I’m grateful for the opportunity to complete this retrospective project, and learn about a new topic! I’d like to thank my inspirational supervisors who we are privileged to work with, as well as passionate alumni, committees, friends and family who have supported us throughout this evolving year.

My advice to prospective students would be to choose a project you’re interested in, submit ethics applications in the previous year (if you need to recruit your own patients), and keep up your commitments outside med! Dedicating a year for research may seem daunting, but now is a great time to learn the ropes and build a strong foundation of skills for the future.

Feel free to contact me at:
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Ms Madeleine Chuen Ying Tse

Intercoastal catheter drainage treatment failure in adult thoracic trauma and its associated factors.

Supervisor Names and Institute Affiliations:
Professor Mark Fitzgerald – Director of Trauma Services, Alfred Health; Director, National Trauma Research Institute; Department of Surgery, Central Clinical School, Monash University
Professor Biswadev Mitra – Director of Emergency Medicine Research, Alfred Health; Head of Clinical Research, National Trauma Research Institute, Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University

ABSTRACT

Background

Intercoastal catheter (ICC) insertion is a common and essential procedure during treatment of thoracic trauma. The subsequent management is poorly understood, and complication rates vary greatly. Incorrect timing of removal may lead to recurrent pneumothorax, retained haemothorax and infection, which require invasive reintervention. This project aimed to determine the circumstances associated with ICC removal failure and develop a checklist to reduce complication rates.

Method

Failure was defined as any patient who requires invasive reintervention after their ICC is removed for the initial traumatic indication, or suffers any clinically significant adverse effect that can be attributed to ICC removal.

1. Systematic review – Six databases were searched for experimental and observational studies published from 1990 to April 2020 that describe ICC removal in adult trauma patients and the number that failed. The proportion of failure was pooled using a random-effects model and qualitative synthesis was conducted for associated variables.

2. Survey of expert opinion – Clinicians from Victoria’s two adult major trauma services were surveyed anonymously on the criteria they consider essential for ICC removal. Their specialty and years of experience were also obtained.

3. Retrospective cohort study – Trauma patients ≥16 years who underwent ICC insertion and removal between 2018-2019 were extracted from the Alfred Health Trauma Registry. ICC removal failure and the types of reintervention were reported as proportions. Variables relating to demographics, injury and interventions were compared using univariable and multivariable logistic regression.

4. Development of an ICC removal checklist – ICC-specific variables were collected for the first 100 patients from the cohort study and analysed using multivariable logistic regression.

Results

Meta-analysis of 17 studies involving 3785 ICC removals revealed a failure rate of 7% (95% CI 5-9%), although the included studies demonstrated significant heterogeneity (p<0.001). The retrospective cohort study of 357 ICC removals among 457 patients treated at the Alfred Hospital had a 7.6% failure rate, with almost 90% of those patients requiring an additional ICC.

The following risk factors for ICC removal failure were identified:

a) high chest Abbreviated Injury Scale
b) thin chest wall
c) ICCs inserted by non-surgery trained operators
d) requirement for mechanical ventilation, and
e) haemopneumothorax.

The following protective factors were identified:

a) trial of clamping
b) drainage volume threshold of <150-200ml/day
c) use of continuous suction, and
d) weaning with water-seal.

The survey revealed significant variability in clinical practice among expert clinicians. Five factors were chosen by >50% of respondents:

i) oxygen saturation >90% on room air
ii) no requirement for suction
iii) no air leak for ≥24hours
iv) pleural drainage volume threshold
v) no residual pneumothorax on chest X-ray.

Univariable analyses determined that the optimal volume cut-off was <200ml/day and drainage duration was ≥3 days. These six factors were combined to create an ICC removal checklist and resulted in an area under receiver-operator characteristic curve of 0.81 (95% CI 0.67-0.95), which has excellent discriminative ability for ICC removal failure.

Conclusions

Failure of ICC removal was common and there was a paucity of evidence on the factors associated with failure and limited guidelines to direct clinical practice. An ICC removal checklist has been developed which warrants prospective validation in order to facilitate standardisation of practice that will help future research in identifying variables that will reduce ICC drainage treatment failure in adult thoracic trauma.
Background
Infants born preterm often suffer respiratory distress and require ventilatory support. Whilst efforts are made to use non-invasive forms of ventilation wherever possible, many infants will still require intubation and invasive ventilation. Prolonged intubation is associated with an increased risk of bronchopulmonary dysplasia, and therefore clinicians will attempt extubation as early as possible. However, this increases the risk of reintubation. There have been various attempts made to predict which infants will be extubated successfully without the need for reintubation using clinical parameters. However, the performance of these predictive methods is suboptimal. Analysis of events that co-occur – i.e. co-occurrence - has shown success in the development of predictive algorithms in adult and paediatric intensive care settings, but this form of analysis is novel in the neonatal intensive care unit.

Aims
To investigate demographic factors and co-occurring events which may be predictive for reintubation in very low birth weight neonates.

Method
Demographic features and clinical events were collected from electronic health records of very low birth weight infants at a tertiary NICU in Sweden from 2017-2020. Three groups of infants were compared: never intubated infants, infants extubated successfully on first attempt and infants who required reintubation. Demographic variables were compared between groups using one-way ANOVA. Python coding language was used to write code to identify events that co-occurred in these groups of infants and to calculate scores relating to the probability of events co-occurring. Co-occurrences of all types of events and events related to intubation, extubation and reintubation were compared between the three infant groups using principles of Bayesian probability.

Results
Sixty-two infants were included: 37 never intubated infants, 13 successfully extubated infants and 12 reintubated infants. Infants who required reintubation were of lower gestational age and birth weight compared to successfully extubated infants. Other demographic features such as APGAR scores and length of stay only differed between never intubated infants and infants who required intubation, regardless of the outcome of extubation. Co-occurrence analysis was unable to demonstrate clinical events predictive for intubation, extubation or reintubation. Contradictory and counterintuitive results indicated flaws in our methodology.

Conclusions
Birth weight and gestation at birth were the only factors predictive for reintubation in this study. The methodology we used for co-occurrence analysis was not predictive for intubation, extubation or reintubation. In light of my findings, this method will require modification and re-evaluation in the NICU setting for prediction of successful extubation in the future.
Effect of umbilical cord blood cell therapy on grey matter vascular injury in the growth-restricted fetal brain

ABSTRACT

Background

Fetal growth restriction (FGR) is a pregnancy-related condition where the fetus does not reach its biological growth potential and is associated with significant morbidity and mortality. At present, there are no established therapies available for treatment of neuropathologies related to FGR. Umbilical cord blood (UCB) contains a rich mixture of stem and progenitor cells with neurotrophic, angiogenic and immunomodulatory properties and has been suggested as a potential treatment. We examined the neuropathological and neurovascular changes in highly vulnerable grey matter regions of the brain in FGR, including the hippocampus, cortex, basal ganglia and thalamus, in an ovine model of growth restriction. We also studied the potential of UCB therapy to promote vascular remodelling and tissue repair.

Method

Surgery was performed in twin-bearing pregnant ewes at 105 days’ gestation to induce FGR in one fetus. UCB therapy was administered at 125 days’ gestation. Post-mortem was performed at 135 days’ gestation and brain tissue collected. Histological and immunohistochemistry staining were used to investigate neuronal cell count and morphology (H&E), blood vessel number and morphology (laminin), cellular apoptosis (caspase-3), microglia number and morphology (Ki67) and cellular proliferation (Ki67).

Results

Twenty-one fetuses were included in 4 groups: control (n = 6), FGR (n =5), control + UCB (n=5) and FGR + UCB (n= 5). The FGR lambs were growth restricted compared with the control lambs (3.03 ± 0.29 kg vs 4.66 ± 0.14 kg; p = 0.002). There was no significant variation in neuronal number or morphology, blood vessel number and morphology, cellular apoptosis, microglial number and morphology or cellular proliferation between the FGR and control cohort. UCB therapy increased blood vessel number and decreased average vessel size and % area stained with laminin across multiple grey matter brain regions. UCB therapy also reduced activated microglia in the thalamus and ventral CA1.

Conclusions

The lack of difference in neuropathology between FGR and control cohorts in the examined brain regions may indicate that the grey matter is less vulnerable to injury. UCB therapy promoted vascular remodelling and reduced microglial activation across multiple brain regions. The vascular remodelling process may be part of an angiogenic response.
Background
Inflammatory bowel disease (IBD) is a chronic gastro-intestinal disease that carries a significant global health burden. IBD aetiology has been linked with the microbiota and the immune response. The current study aims to characterise the immune phenotype in macrophages driven by two candidate bacteria, isolates 66 and 152, that have been derived from inflammatory and non-inflammatory mucosal tissue, respectively, from paediatric IBD patients.

Method
Confirmation of identification of bacterial isolates 66 and 152 was achieved via 16S rRNA gene sequencing. Growth curves of the bacterial isolates 66 and 152 were performed under anaerobic conditions over 30 hours. For stimulation experiments, bacterial isolates were cultured, harvested after 24-hours and heat-killed. THP-1 monocytes were differentiated into macrophages using a formyl ester (PMA). Heat-killed isolates and inflammatory controls, lipopolysaccharide (LPS) and Enteropathogenic E. coli (EPEC), at various concentrations were used to stimulate THP-1 macrophages for 2 or 4 hours. Cell cytotoxicity was determined via LDH release assay. Cytokine gene expression was determined via RNA extraction and subsequent qPCR analysis of converted cDNA.

Results
Isolate 66 grew at a faster rate during the exponential phase compared to isolate 152, but both isolates reached stationary-phase after 24 hours. There was variability in THP-1 cytotoxicity when incubated with both isolates as well as with the inflammatory controls (LPS and EPEC). However, there was no significant difference in THP-1 cytotoxicity between any of the groups including the non-stimulated control. With respect to gene expression, there was marked induction of IL-6 and TNF expression and a smaller increase in IL-10 expression following stimulation with LPS or EPEC for either 2 or 4 hours. The higher concentration of both bacterial isolates 66 and 152 (10µg/mL) induced approximately a 10-fold increase in IL-6 and IL-10 expression compared with the non-stimulated control. However, in the current study there was no difference between the ability of the two isolates 66 and 152 to induce cytokine gene expression in the THP-1 macrophages.

Conclusions
These preliminary data suggest that THP-1 macrophages are a suitable model for characterisation of bacterial influence on immune cells. While both novel isolates increased expression in both inflammatory and anti-inflammatory cytokines IL-6 and IL-10 respectively, there appears to be no difference between the isolates driving immune responses in THP-1 macrophages, despite them being associated with different IBD tissue phenotypes in situ. This research will pave the way for further functional characterisation studies using bacteria derived from IBD microbiomes.
ABSTRACT

Background
Injury causes a significant morbidity and years lived with disability. Pain and post-traumatic stress disorder (PTSD) are two common and prominent disabling conditions post-injury that currently receive low levels of treatment. A stepped-collaborative care intervention is known to provide better post-traumatic care and help prevent the burden of injury. Previous studies have evaluated the feasibility of an early-stepped collaborative care intervention in reducing pain and PTSD in trauma survivors and showed that it is readily implemented in North American healthcare settings.

Objectives
The aim of this study was to examine the feasibility of implementing a stepped-collaborative care intervention to reduce the severity of pain and PTSD symptoms in trauma survivors in Victoria.

Method
This study recruited adult major trauma patients admitted to The Alfred hospital living in Victoria. People were excluded if they had prior or acquired cognitive impairment, were injured through self-harm and during psychosis, if they have a history of violence. Participants were eligible if they met risk criteria for developing persistent pain or PTSD. Participants were randomized into stepped-collaborative care intervention or enhanced usual care group. Data were collected from electronic medical records and in study interviews, with data collectors blinded to group allocation. Measures of pain, PTSD, depression, anxiety and substance use and satisfaction with treatment were included in study interviews at baseline and one month.

Results
Of all the trauma admissions screened between October 2019 and April 2020, 62 participants were eligible and approached. Forty eight people declined to the study predominantly because they did not have any concerns, or they could not be contacted within 28 days of injury. Out of 34 truly eligible participants who were at risk and had concerns about pain or mental health, 17 participants consented to participate (50%). At one month follow up, intervention participants had lower mean mental health symptoms score; (Cohen’s effect size; PTSD d = 2.26, depression d = 2.16 and anxiety = 2.19). There were no differences between groups on satisfaction with treatment or willingness of treatment at baseline or one-month.

Discussion
The current study found that reaching the targeted population is feasible in a Victorian major trauma services, as we could recruit 50% of eligible cases who expressed concerns with their mental health or pain after their injury. The preliminary study analyses showed some treatment benefits by one month post-enrolment in the study. Future analysis of the whole study cohort of 60 patients up to 6-months post-injury may reveal stronger treatment effects.

Conclusions
The current study provides preliminary support for the acceptability and effectiveness of an early stepped collaborative care intervention in Victoria, Australia.
Ms Pramasari Rajanna Edie Wijaya

Female Genital Cosmetic Surgery: Perspectives of Health Workers and Other Professionals Who Work With Women’s Bodies

Supervisor Names and Institute Affiliations:
Dr Maggie Kirkman and Professor Jane Fisher

ABSTRACT

Background

Although there is an increasing demand for FGCS, there are still limited published data on the benefits, risks, and clinical indications of FGCS. This lack of scientific basis of the procedure has led to strong criticism from several professional organizations. Despite the criticisms, websites advertising FGCS still depict the procedure as a simple, safe procedure with minimal risks. Without a significant number of studies, it will be difficult to establish how FGCS is viewed by professionals who deal with women’s bodies.

Method

21 health and non-health professionals were recruited for individual semi-structured interviews. The data was managed in NVivo 12 and analysed using thematic analysis method, coding it to themes.

Results

Health professionals’ indication for FGCS were similar to non-health professionals’ justification for non-surgical genital modifications: A complex mix of functional, cosmetic and psychological concerns. Participants have shown an acknowledgement of genital diversity, yet still valuing a certain range of aesthetic standard.

Conclusions

These findings showed that health professionals and other professionals who deal with women’s bodies perpetuate the rigid aesthetic standard of genital appearance that governs the policing of women’s bodies. A comprehensive education on the importance of valuing genital diversity needs to be incorporated in the education of future medical professionals in order to be able to challenge these aesthetic standards.
Mr Alan Linkow Xue

Using PSMA PET Scans to Predict Histologic Outcomes at Biopsy and Surgery

Supervisor Names and Institute Affiliations:
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ABSTRACT

Background
To prevent the overtreatment of indolent PCa, risk stratification is used to treat lower-risk PCa with conservative treatment. However, literature shows that under current risk stratification categories, many intermediate risk cancers that are believed to be suitable for conservative surveillance treatment actually harbor more aggressive, undetected disease. This is shown by a higher grade cancer present at surgery than biopsy, a process known as pathologic upgrading.

PSMA PET scans are a novel PET scan that are specific for the PSMA protein, found overexpressed on PCa cells. They have been shown to outperform conventional imaging in detecting PCa metastases and post-treatment recurrence. Emerging data show PSMA PET scans image the primary tumour with remarkable accuracy, and the SUVmax, a measure of maximum signal intensity, correlates to tumour grade. We investigated whether PSMA PET scan is predictive of final tumour grade and pathologic upgrading.

Methods
We reviewed a prospectively maintained database of men who had received multiparametric MRI (mpMRI), 68-Ga PSMA PET/CT, and undergone transperineal template biopsy from November 2015 to September 2020. Men were excluded if they had received treatment prior or if scans were not performed in a 6-month period. Variables collected included SUVmax, as well as standard clinical variables, including age, PI-RADS score, PSA density, and Gleason Grade.

The primary outcome was the percentage of Gleason score pattern 4 disease (%GS4) in the index tumour on biopsy specimen and on radical pathology (RP) specimen. These were dichotomized as above or below 3 thresholds: 10%, 20%, and 50%. The secondary outcome was the presence of pathological upgrading, defined as having Gleason Grade Group (GG) 1 or 2 disease on biopsy and Gleason GG 3 or higher on RP specimen.

Logistic regression analysis was performed using the SUVmax as a single variable, and with clinical variables for adjustment. ROC curve analysis was performed and cutoffs maximizing sensitivity and specificity were obtained.

Results
284 patients received biopsy, 139 patients went on to receive surgery, 84 patients were included in the upgrading analysis. SUVmax was found to predict percentage pattern 4 disease on biopsy at 10%, 20%, and 50%. (p<0.0001 in all 3 models) SUVmax was found to predict percentage pattern 4 disease at RP at 20% (p<0.0001) and 50% (p<0.0001), however was not an independent predictor in the 10% model (p=0.079). SUVmax was a nonsignificant predictor of pathologic upgrading (p=0.053). On ROC curve analysis, a SUVmax cutoff value of 5.39 predicted upgrading with a sensitivity and specificity of 50% and 81% respectively. A cutoff value of 5.41 predicted +/- 50% GS4 disease with a sensitivity and specificity of 72% and 77% on biopsy and 70% and 75% on surgery respectively.

Conclusions
Our study validates the predictive power of the SUVmax measurement on PSMA PET to predict histological outcomes. Our results also strongly suggest the SUVmax correlates at lower percentages of pattern 4 disease. However, a more robust population is required to conclusively assert the added value of PSMA PET in a primary risk stratification setting.

What a year 2020 has been! After abandoning a project at King’s College London in March, (apparently there was some kind of pandemic going around) starting a new project was no easy task. However, my supervisors helped me find a new, COVID-safe project that still gave me a rewarding BMedSc(Hons) year. The Honours year has been a great year to think about future career directions, spend time on pursuits outside of medicine, and to challenge myself. It’s a very different type of learning than what we’ve done previously, but has taught me so much about what good research looks like. I’d encourage prospective BMedSc(Hons) students to take on a project with more responsibility (for example, performing the statistical analysis), as it’ll prepare you well for future years as a doctor, when you’re expected to do research with far less support. When choosing supervisors/projects, I’d encourage students to look for supportive supervisors with interesting research questions, rather than trying to find the exact topic you’re interested in. Overall, it’s been a rewarding, albeit challenging year.

Happy to speak to students about organising a project overseas, surgical research, or general life advice (warning: not too good at that last part):

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Mr Daniel Ning-Yuan Yan

Is there a Difference in the Health-Related Quality of Life of People Living with HIV compared to People Living without HIV in Australia?

Supervisor Names and Institute Affiliations:
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Central Clinical School – Department of Infectious Diseases

ABSTRACT

Background
HIV remains a significant global health problem. Effective and accessible antiretroviral therapy (ART) has led to a decrease in mortality of people living with HIV (PLWH), and therefore an increase in life-expectancy and number of PLWH. Promoting an individual’s quality of life (QoL) is a key treatment priority in chronic care. Investigation into factors that affect QoL in PLWH has been challenging, as relationships between HIV in Australia and socioeconomic, psychological and lifestyle factors are complex.

Aims
To identify and assess the reported health-related quality of life (HRQoL) in PLWH, assess differences in HRQoL between HIV positive individuals and a similar HIV negative population, and to identify factors associated with HRQoL.

Method
Data for this project was obtained from the Melbourne HIV Cohort Study, a prospective cohort study conducted from 2011 with five-year follow-up data available. HIV positive and negative participants were recruited from six study sites in metropolitan Melbourne. The aims of the Melbourne HIV Cohort Study were to investigate how health in PLWH changes over time compared to a similar HIV negative population of men who have sex with men (MSM). Adults over the age of 18 with no previous antiretroviral exposure were enrolled into two groups, HIV positive cases or HIV negative controls. Controls had to identify as MSM. Clinical history and investigations, and a patient filled lifestyle questionnaire at was collected at baseline and annual visits for up to five years. Outcomes of HRQoL were measured using the Assessing Quality of Life-6D (AQoL-6D) scale. Additional mental health assessments were made utilised the Depression, Anxiety, Stress Scale 21 (DASS-21). Statistical analysis of baseline and three-year follow-up questionnaire results conducted in Stata (version 15.1) involved Mann-Whitney U and Fisher’s exact tests for comparison between groups, linear regression for HRQoL predictors, and Wilcoxon signed-rank tests for differences over time in HRQoL.

Results
Sixty-two HIV positive cases, 48 HIV negative controls were recruited. Thirty-three participants were lost to follow-up (LTFU) at three years; 27 cases, six controls. Overall AQoL-6D scores were significantly lower amongst cases compared to controls at baseline (83.5 (IQR 77.2-88.6) vs 87.3 (IQR 82.1-91.8), p=0.022). This was also observed in mental health and coping subdomains (mental health: 68.8 (IQR 56.3-79.7) vs 78.1 (IQR 68.8-81.3), p=0.0385; coping: 75.0 (IQR 66.7-75.0) vs 79.2 (IQR 75.9-91.7), p=0.0022). No significant differences in AQoL-6D scores between cases and controls remained at follow-up, except in coping (75.0 (IQR 66.7-83.3) vs 75.0 (IQR 75.0-91.7), p=0.0354). A significant improvement over time was identified amongst cases in the mental health subdomain (75.0 (IQR 56.3-81.3) to 81.3 (IQR 62.5-91.3), p=0.0428). Increased depression and anxiety were associated with poorer HRQoL in baseline multivariate analysis. No predictors of HRQoL over time were identified due to limited statistical power.

Conclusions
Our results highlight HRQoL was significantly lower in PLWH and influenced by poorer mental health at time of diagnosis and treatment initiation but improved significantly at three-year follow-up. This demonstrates the importance of addressing mental health as part of routine care, particularly at diagnosis and/or treatment commencement.
Ms Sze Wing Serine Yau

The Effect of Maternal Social Determinants of Health on Neonatal Outcomes

Supervisor Names and Institute Affiliations:
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Dr Mary-Ann Davey – Department of Obstetrics and Gynaecology, Monash University

ABSTRACT

Background

Health outcomes of neonates can be influenced by the social factors of their mothers. The existing literature examining the association between maternal social determinants of health and adverse neonatal outcomes is diverse and heterogenous in that they use different definitions for the social factors and have been performed in populations with different characteristics. However, there has been limited literature examining the association in the Victorian population.

Methods

We conducted a population-based retrospective cohort study using routinely collected data extracted from the Victorian Perinatal Data Collection (VPDC). The study population consisted of all singleton livebirths in Victoria, Australia from 1 January 2014 to 31 December 2018. We aimed to investigate the association between maternal social determinants of health and adverse neonatal outcomes in the Victorian population. The social determinants we analysed were socioeconomic status (SES) represented by the Index of Relative Socio-economic Disadvantage (IRSD) quintiles, maternal residence, maternal region of birth and maternal Indigenous status. The outcomes we examined were neonatal death, NICU/SCN admission (adjusted odds ratio (OR) 1.24, 95% confidence interval (CI) 1.20–1.29), transfer to tertiary centre, preterm birth (adjusted OR 1.22, 95% CI 1.16–1.28), SGA, low Apgar score, RDS and birth asphyxia. Rural maternal residence showed increased risk of NICU/SCN admission (adjusted OR 1.15, 95% CI 1.12–1.18), transfer to tertiary centre, preterm birth (adjusted OR 1.16, 95% CI 1.12–1.21) and RDS. Amongst the maternal regions of birth, infants of Southern and Central Asia-born mothers were found to be consistently at increased odds of a number of adverse neonatal outcomes including neonatal death, NICU/SCN admission (adjusted OR 1.16, 95% CI 1.13–1.20), preterm birth (adjusted OR 1.06 95% CI 1.01–1.12), SGA and LBW. Infants born to Indigenous mothers had greater odds of NICU/SCN admission (adjusted OR 1.28, 95% CI 1.19–1.38), transfer to tertiary centre, preterm birth (adjusted OR 1.38, 95% CI 1.24–1.54), SGA and LBW compared to infants born to non-Indigenous mothers.

Conclusions

We identified that the maternal social determinants of health had varying effects on neonatal health outcomes in Victoria using a population-based database. Discrepancies between neonatal health outcomes continue to exist based on social inequality. The results of our study may be used to guide clinical practice in ways that can help improve the health of neonates born in Victoria.
ABSTRACT

Background

There have been ongoing international efforts in the last few decades to identify individuals at high risk of developing psychosis similar to preventive efforts in other diseases like diabetes and heart disease. These individuals are known as “psychosis risk” or “ultra-highrisk” patients. This research has been motivated by the significant morbidity, mortality and societal burden associated with psychotic disorders. Researchers hope that by identifying and engaging these patients before they develop psychosis, they can positively alter the trajectory of their natural history while these individuals are in adolescence and early adulthood. Fruitful clinical outcomes include not only a delay or prevention in psychosis onset, but also the amelioration of existing clinical distress in these patients who often suffer from other non-psychotic comorbidities like anxiety, depression, and substance use disorders.

However, the field of psychosis risk research has faced numerous challenges to its validity as a viable diagnosis. Current methods to identify “high-risk” psychosis patients have a low positive predictive value, meaning that many patients who are labelled as ultra-high risk do not develop psychosis. Moreover, this “transition rate” has declined in recent years, with recent meta-analyses suggesting a three-year psychosis risk of 26-36%. There has also been a dearth of high-quality evidence supporting interventions for psychosis risk patients. Consequently, some commentators have questioned the ethical justification behind disclosing a psychosis risk diagnosis, arguing that the harms of disclosure may outweigh the benefits. Such harms are especially pertinent in psychosis risk because of concerns like stigma and discrimination in a young clinical population. Emerging research has also hypothesised that disclosure may accelerate the onset of psychosis by linking the stress caused from a diagnosis to our general understanding that psychosocial stress contributes to the aetiology of psychotic disorders.

Despite ongoing discussion in the bioethical literature, these concerns over the morality of disclosure in psychosis risk patients are not directly addressed in psychosis risk clinical guidelines. Additionally, only one paper by Mittal and colleagues at the time of writing has outlined a normative disclosure strategy for psychosis risk patients.

In light of these concerns, this thesis examines the ethical justification of disclosure to psychosis risk patients. I first primarily identify and discuss the ethical principles at stake in disclosure before then drawing key lessons from ethical dilemmas in the disclosure of other diseases. Then, explore the normative weight of each ethical principle when applied to psychosis risk disclosure. I next critique Mittal et al.’s three-model disclosure strategy to highlight its shortcomings as a coherent method of disclosure before then defending my own presumptive, defeasible framework for psychosis risk disclosure. In doing so, I have also created a clinically actionable, principle-based framework grounded on my extensive ethical analysis of disclosure in psychosis risk patients.
Ms Beverley Zhong

The Origins of Inflammation in Heart Failure with a Preserved Ejection Fraction

Supervisor Names and Institute Affiliations:
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ABSTRACT

Background
The pathophysiology of heart failure with a preserved ejection fraction (HFpEF) is not entirely understood. Recently, there have been considerations towards a theoretical framework where conditions such as obesity and diabetes mellitus cause a state of systemic inflammation, leading to endothelial dysfunction and thus heart failure (HF). Endothelial dysfunction causes monocytes and macrophages to produce inflammation and fibrotic markers, such as transforming growth factor-beta (TGF-ß) and matrix metallopeptidase (MMP), which lead to increased collagen deposition in the interstitial space and degradation of the extracellular matrix (ECM). HFpEF patients are commonly female, older and obese. Obesity is known to cause fatty liver disease, and there is limited research on the relationship between the liver and heart. Here, I investigate the relationship between the liver and heart, with a primary focus on inflammation through cell cultures, mice and human serum studies.

Method
Co-cultures utilised human cardiac fibroblast cells (HCF) and HepG2 cells. A $^3$H-proline incorporation assay was performed on co-cultured cells to determine collagen levels with the addition of lipopolysaccharides and HepG2 cells to HCF cells. HepG2 condition media was also used in a separate study to confirm a direct relationship. Secondly, mice mRNA gene expression was performed to observe fibrotic and inflammatory markers in the high-fat diet and normal chow diet mice. Lastly, human serum assays were analysed to compare inflammatory markers in HFpEF and healthy control patients. We also compared inflammation levels between arterial and hepatic blood samples.

Results
We found that hepG2 cells cause an increase in collagen levels in HCF cells, and HepG2 condition media supported these results. We observed elevated expression of some fibrotic and inflammatory markers in high-fat diet mice compared to normal chow diet mice. Lastly, some inflammatory markers were significantly higher in the HFpEF group compared to the healthy control group.

Conclusions
We discovered that there is a relationship between the liver and the heart, where the former seems to compound the effects of inflammation. In particular, we were able to support the theoretical framework of obesity causing systemic inflammation, possibly leading to the structural changes observed in the heart in HFpEF. This finding indicates the possibility of inflammatory markers as treatment targets for the management of HFpEF, an area in which there is currently no treatments.
Mr Jonathan Gerard Zhou

Comparison of frequent attenders to the emergency department between an Australian and a Canadian academic tertiary hospital

Supervisor Names and Institute Affiliations:

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Department of Epidemiology and Preventive Medicine
Monash University School of Public Health and Preventive Medicine

Dr Ivy Cheng
Sunnybrook Health Sciences Centre, Toronto, ON, Canada

ABSTRACT

Background
Frequent attenders to the ED constitute a small percentage of the total ED population but account for a substantial proportion of visits. They are a vulnerable population in society with multiple complex needs and produce significant costs to healthcare systems. Research is needed to guide the creation of interventions to improve the quality of care of this population and reduce costs. To be effective, interventions should be highly tailored to the characteristics of frequent attenders.

We aimed to determine the characteristics and resource consumption of frequent attenders at an Australian hospital (The Alfred) and a Canadian hospital (Sunnybrook Health Sciences Centre).

Methods
We conducted a descriptive, retrospective and observational study using clinical and administrative data from The Alfred and Sunnybrook. Data from January 1, 2018 to December 31, 2019 were used to define patients as nonfrequent attenders (less than four visits in 12 months) and frequent attenders (four or more visits in 12 months). Secondary analyses involved highly frequent attenders (18 or more visits in 12 months) and analysis of frequent attenders by age groups. We used multivariate logistic regression to determine risk factors for frequent attendance at The Alfred and Sunnybrook.

Results
At The Alfred, frequent attenders accounted for 5.8% of the total ED population in 2019 but represented 22.4% of the total visits. At Sunnybrook, frequent attenders made up 4.9% of the total ED population but were responsible for 17.5% of the total visits. Being aged 65 years and older was a significant predictor of frequent attendance at The Alfred (adjusted OR=2.64) and Sunnybrook (adjusted OR=2.58). At both hospitals, more frequent attenders aged 18-24 years were female, while more were male in the 65 years and older age group.

Compared to nonfrequent.attender visits, a greater proportion of frequent attendant visits at The Alfred and Sunnybrook were triaged at high acuity and resulted in inpatient admission. Visiting during the night shift was a significant predictor of frequent attendance at Sunnybrook (adjusted OR=1.19) but not at The Alfred.

At both hospitals, frequent attenders aged 18-24 years and 25-44 years had substantial rates of mental and behavioural disorders. Multiple drug use and alcohol use were common among these age groups. Frequent attenders aged 65 years and older had higher rates of physical diseases, including chronic diseases such as chronic obstructive pulmonary disease and heart failure. A greater number of physical diseases were predictors of frequent attendance at Sunnybrook than at The Alfred.

Conclusion
This study described the characteristics of frequent attenders at The Alfred and Sunnybrook. Important differences were observed both within and between these populations. Future interventions designed to reduce frequent ED visits at The Alfred and Sunnybrook should be tailored to the relevant needs of frequent attenders. Their high resource consumption highlights their economic burden and the need for intervention.
Emma Thompson – High Street in Oxford

This is the main street in the centre of Oxford, lined by historic cafes, retail shops and many of Oxford University’s colleges. As students researching with the Uehiro Centre for Practical Ethics at Oxford University, we rode our bikes up and down this street many times each day before returning to Australia at the start of the COVID-19 pandemic.