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# MRSS ANNUAL BMEDSC (HONS) YEARBOOK 2021





## **FRONT COVER**

### **Carine Wessels – The beginning of a lifelong journey**

Watercolour painting of a day 5 embryo, representing the honours year as the beginning of a career-long journey in research.

## **INSIDE FRONT COVER**

### **Keeth Mayakaduwege – Fetal Ultrasound**

This image is a fetal ultrasound taken in a mother's second trimester. Currently, 2 million babies worldwide are stillborn every year and as a result millions of families suffer through this tragedy. However, many late pregnancy stillbirths are preventable with improved antenatal care. In our project, we sought to evaluate an Australian bundle of care that aims to reduce late gestational stillbirths. The patient consented to the use of this image.

# 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 after two incredibly challenging years. You should all feel extremely 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 hope that it has challenged you and given you an appreciation of: how new knowledge is created, how research can be translated into 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 how our bodies function in health and disease and how we should best treat and manage diseases! We also hope that you will have much more confidence in your ability to read and critically evaluate new research findings and 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 everyone else who has devoted their time to help you learn during the year. A particular thanks to all of the 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. The Course would not be possible without them. Thank you also to the MRSS committee, particularly your BMedSc(Hons) Student Representative Rhea Singh. Rhea did an excellent job at passing on your questions and comments and providing feedback on the program, helping to improve your own experience as well as that of future cohorts. I would also like to thank Rhea for helping to organise the BMedSc(Hons) conference and People's Choice assessment teams! I am sure that everyone agrees that the conference 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.

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

## Message from MRSS

Congratulations everyone on completing the BMedSc(Hons) course for 2021!!! Despite all the challenges and surprises that have occurred throughout the year, we have all achieved so much and made it through to the other end. If I think back to the beginning of the year, many of us were thrown into the deep end, having very little experience in research and not knowing what the year ahead entailed. Fast forward to the BMedSc(Hons) Conference, and it was amazing to see the breadth and depth of research that our cohort has conducted and all the hard work and new skills that we have learnt. It was incredible to see how our research can make meaningful contributions to medical research – contributions that I am sure we will continue to make throughout our careers. By finishing a year full of hurdles, we have demonstrated that we have the ability to adapt, learn, work hard, and thrive in unfamiliar and difficult environments. I think we should all be proud of everything that we have achieved throughout the year. With new skills, more knowledge, and greater confidence in research, I am certain that this is only the beginning of many of our research careers. It has been a privilege serving as your student representative and thank you for giving me this opportunity. I look forward to graduating and working alongside you all in the near future! On behalf of the cohort, I would also like to extend my gratitude to all those who made the year possible. In particular, thank you to A/Prof Megan Wallace, Jessica Lai, heads of schools, the Course Management Committee, and all the supervisors for their generous support, guidance, and encouragement.

**Rhea Singh, BMedSc(Hons) student representative  
Medical Research Student Society (MRSS)**

# Esha Abraham

## Positivity and Risk Factors for *Trichomonas Vaginalis* Among Women Attending a Sexual Health Clinic in Melbourne, 2006-2019

Supervisor Names and Institute Affiliations:

A/Professor Eric Chow<sup>1,2,3</sup>, Dr Tiffany Phillips<sup>1,2</sup>, Professor Christopher Fairley<sup>1,2</sup>

1. Melbourne Sexual Health Centre, Alfred Health, Melbourne, Victoria, Australia
2. Central Clinical School, Monash University, Melbourne, Victoria, Australia
3. Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Victoria, Australia



I was fortunate enough to be able to complete my BMedSc(Hons) at the Melbourne Sexual Health Centre this year. I decided to do an honours year because I wanted a break from clinical medicine and to develop my research skills. I selected this project as it allowed me to delve deeper into women's health from a different perspective. Eric, Kit, and Tiffany were amazing supervisors, and I am so grateful for all the support and guidance I've received this year. This year has improved my critical thinking and communication skills and has been a deeply enriching experience.

Feel free to contact me at:  
eabr0001@student.monash.edu

### ABSTRACT

#### Background

There is limited data on epidemiological trends of *Trichomonas vaginalis* (TV) in Victoria as it is not a notifiable disease. This study aimed to examine the positivity of TV in women at the Melbourne Sexual Health Centre (MSHC) over the last 14 years and identify associated factors.

#### Method

All women aged  $\geq 16$  years who presented to MSHC between 2006 and 2019 were included. The diagnostic method was changed from culture to nucleic acid amplification test (NAAT) in August 2018. The positivity of TV each year was calculated, and temporal trends were examined using the chi-squared trend test. A generalised estimating equations multivariable logistic regression was performed to examine factors associated with TV positivity.

#### Results

Between 2006 and 2019, 69,739 women were tested for TV, and 294 tested positive (0.42%, 95% CI 0.37-0.47). TV positivity increased significantly from 0.27% (95% CI 0.15-0.45) in 2006 to 1.57% (95% CI 1.17-2.06) in 2019 ( $p_{\text{trend}} < 0.001$ ). The positivity by culture (0.34%, 95% CI 0.30-0.39) was significantly lower than the positivity by NAAT (1.68%, 95% CI 1.32-2.11) ( $p < 0.001$ ). Multivariable analysis adjusted for the year; diagnostic method; age; concurrent chlamydia, gonorrhoea, and syphilis; injecting drug use in the last year; sex worker status; Indigenous status; condom use in the last year; time in Australia; and previous STI diagnosis.

The positivity of TV increased significantly by 21% each year (aOR 1.21; 95% CI 1.12-1.31). TV positivity was significantly associated with age  $\geq 35$  years (aOR 3.47; 95% CI 2.26-5.35); injecting drug use (aOR 6.99; 95% CI 4.11-11.87);

concurrent chlamydia (aOR 1.77; 95% CI 1.05-2.99); and concurrent syphilis (aOR 21.55; 95% CI 6.96-66.78).

#### Conclusion

The positivity of TV is rising among women attending a sexual health clinic in Melbourne. Associated factors include age  $\geq 35$  years; injecting drug use in the last 12 months; concurrent chlamydia; and concurrent syphilis.



# Irvan Muhammad Alfian

## An Analysis of Fluidigm Biomark™ Array Data for Placental Inflammasomes in Human Idiopathic Fetal Growth Restriction Affected Pregnancies

Supervisors: Dr Padma Murthi and Prof Chrishan Samuel

Department of Pharmacology, Monash Biomedicine Discovery Institute, Monash University



Hi, I am Irvan, a medical student from Universitas Indonesia. I had the opportunity to complete my Honours year at Monash University from 2020 to 2021. Unfortunately, travel restrictions to Australia due to the COVID-19 pandemic were in place throughout the entire year, therefore, my Honours project had to be done remotely. My thesis was focused on human placentas and pregnancy complications, which were topics that I was familiar with. Overall, the experience of working under the guidance of both of my supervisors was invaluable to me. I gained more knowledge about how to write a scientific research paper from the past year alone. Even though the pandemic made it much more challenging and limited the project in terms of access and communication, in the end, I am grateful and proud to have finished it with satisfying results. Lastly, a personal note from me to future students: it would be helpful if you choose a topic that you are interested in and make sure that you put your heart into it. Build a great relationship with your supervisors as they are your everything during Honours year. Feel free to contact me if you are looking for further insights.

### ABSTRACT

#### Introduction

Fetal growth restriction (FGR) is one of the major pregnancy complications resulting in maternal and perinatal mortality. It is commonly associated with placental insufficiency and exacerbated by placental inflammation. The novel inflammatory pathways governed by the multimeric inflammasomes in the pathogenesis of FGR are largely unknown.

#### Aims

The first aim was to analyse placental gene expression profiles for components of the inflammasome pathway and further quantification of mRNA of candidate inflammasomes was analysed using Real-Time PCR. The second aim was to correlate the inflammasomes gene expression profiles with maternal age, gestational age (pre-term vs term differences), fetal birth weight, placental weight, and birth weight to placental weight ratio.

#### Methods

Gene expression using the cycle threshold (CT) values were analysed by  $2^{-\Delta\Delta CT}$  methodology for the inflammasomes including 7 danger-associated molecular patterns (DAMPs) genes (NLRP3, NLRC5, CASP1, CASP3, CASP8, NOD2, and NFκB1), 3 pathogen-associated molecular patterns (PAMPs) genes (TLR2, TLR5, TLR6), 4 cytokines (IFNγ, IL-1β, IL-6, and IL-10), and 2 housekeeping genes (18S rRNA and GAPDH), which were measured using the Fluidigm Biomark™ Array in third-trimester placental tissues with gestational age ranging from 27-40/41 weeks from FGR pregnancies (n=25) and gestation-matched uncomplicated control pregnancies (n=25). Further quantification relative to 18S rRNA was performed for the 7 DAMPs genes and 4 cytokines that were independently validated using Real-Time PCR. Statistical significances and gene expression correlations were performed in FGR and gestation-matched

control pregnancies using GraphPad Prism V8.0.

#### Results

From the Fluidigm Biomark™ Array, gene expression of all genes tested were present in both FGR and control placentae. From the independent validation data, mRNA expression for NLRP3, NLRC5, CASP1, CASP3, CASP8, NOD2, NFκB1, IFNγ, IL-1β, and IL-6 showed a significant increase in FGR compared with control pregnancies (n=25/group, p<0.001, Mann-Whitney U test). However, a significant decrease in the mRNA expression of the anti-inflammatory cytokine, IL-10 was found in FGR compared with control pregnancies (p<0.001, Mann-Whitney U test). Spearman's correlation test in control pregnancies demonstrated a significant correlation between CASP1 and gestational age (r=0.662, p<0.001), birth weight (r=0.668, p<0.001), and placental weight (r=0.692, p<0.001), NOD2 and placental weight (r=0.456, p=0.022), and NLRP3 and birth weight to placental weight ratio (r=0.448, p=0.025). However, in FGR, a significant correlation was observed between CASP3 and gestational age (r=0.579, p=0.003), birth weight (r=0.651, p<0.001), and placental weight (r=0.657, p<0.001) and NLRP3 and gestational age (r=0.558, p=0.004). NLRP3, CASP1, and CASP3 mRNA expression was significantly increased in term control and term FGR compared with pre-term control and pre-term FGR, respectively (p<0.001, Mann-Whitney U test).

#### Conclusion

These results show that the placental gene expression for the components of the inflammasome pathway is differentially expressed in FGR compared with control pregnancies. Further protein expression analyses and functional studies of these genes are warranted to provide the molecular mechanisms of inflammasomes and cytokines in the aetiology of FGR.

# Asare Amofo

## Incidence, Risk Factors and Prediction of Stillbirths in Victoria

Supervisor Names and Institute Affiliations:

Dr Daniel Lorber Rolnik, Professor Euan Wallace

School of Clinical Sciences, Safer Care Victoria, Monash Health



Hi! My Name is Asare Amofo and I undertook my BMedSc(Hons) year at the School of Clinical Sciences after my fourth year of medical school. I chose to do an honours year to gain some broader experience in research and selected an O&G based project after my exposure to women's health during my clinical rotations. During this year I've learnt a lot of new skills such as how to write up a literature review and how to perform statistical analysis on large datasets. I feel that I have a much better grasp on research skills which should be useful in my future career. I was also lucky enough to have a supervisor that guided and supported me throughout the whole year, which made my project run smoothly.

Overall, I enjoyed my honours year a lot and would highly recommend an honours year to anyone who is thinking about doing one, even if you are sitting on the fence about it.

If you have any questions email me at [aamo0001@student.monash.edu](mailto:aamo0001@student.monash.edu).

## ABSTRACT

### Background

New preventative measures and standards of care have led to a decrease in the rates of stillbirth globally over the past 20 years. However, maternal characteristics and the profile of risk factors for stillbirth have also been changing, with increasing rates of obesity, decreasing rates of smoking and new subgroups at higher risk being identified (e.g., South Asian women). There is a need for an updated study on how these risk factors have changed over the past 20 years and how strongly they contribute to stillbirths in Australia.

Developing a robust stillbirth predictive model remains a challenge, with poor accuracy, lack of validation and many models using the same developmental approach. Hence there is a need to investigate how alternative statistical approaches perform in estimating stillbirth risk.

### Aim

Our first aim was to identify trends and risk factors and the changing strength of association between risk factors and stillbirths at Monash Health over last two decades. We also aimed to develop, internally validate, and compare predictive models for stillbirth using different statistical approaches (logistic regression and competing risks regression).

### Method

We performed two studies in this project; a retrospective cohort study analysis of Monash Health data analysing risk factors and trends over 20 years and a prognostic study using 5 years of state-wide data to develop and compare predictive models. For both studies analysis excluded terminations of pregnancy, multiple pregnancies, and gestation less than 24 weeks. We reported rates of occurrence of risk factors and the odds ratio and 95% confidence intervals for each time 5-year time period (2000-2004, 2005-2009, 2010-

2014 and 2015-2019). Scatter plots of individual birthweights against gestational and 10th, 50th and 90th centile charts were produced. For our prognostic study we compared two predictive models developed using logistic regression and competing risks regression. These models were developed using predictors available in early pregnancy and performance was assessed by comparing the area under the receiver operating characteristic (AUROC) and sensitivities at a 5% and 10% false positive rate.

### Results

In our risk factor and trends over time analysis we identified body mass index, advanced maternal age, parous status, region of birth, pre-existing hypertension, birthweight less than the 10th percentile, pre-eclampsia, antiphospholipid syndrome and smoking as risk factors for stillbirth in the study cohort. Rates of stillbirth in the study cohort decreased from 6.6 stillbirths per 1000 livebirths to 4.9 stillbirths per 1000 livebirths. Decreasing rates of maternal smoking, pre-eclampsia, and neonates with a birthweight less than the 10th percentile were reported and increases in the median BMI, rates of congenital abnormalities and mean maternal age were reported. The AUROC for the logistic regression model was 0.603 and 0.607 for the competing risk model showing comparable performance.

### Conclusion

There has been a shift in the distribution of stillbirth causes with lower rates of fetal growth restriction and pre-eclampsia being attributable to stillbirths and increasing rates of congenital abnormalities which likely reflect improvements in screening. Use of maternal characteristics in logistic regression and competing risks models provide significant early stillbirth prediction and perform similarly however accuracy remains poor.



# Anisija Gillian

## The impact of maternal age on the risk of Caesarean section

Supervisor Names and Institute Affiliations: Professor Ben W. Mol<sup>1,2</sup> and Dr Daniel L. Rolnik<sup>1,2</sup>

<sup>1</sup>Monash University, Melbourne, Australia

<sup>2</sup>Department of Obstetrics & Gynaecology, Monash Health, Melbourne, Australia



I completed a BMedSc(Hons) after my fourth year of medicine. I initially wasn't planning on doing a BMedSc(Hons) in 2021 but when I decided to look into some of the available projects I was fascinated by all the opportunities and realised how exciting it would be to spend a year involved in research. I decided to do a project in O&G which is the area of medicine I'm currently most interested in pursuing. I had no experience with research before this year, which was scary at first however I learnt a lot very quickly. This year was definitely a significant learning curve for me and involved a lot of self-directed work, which was both challenging and liberating. I am so grateful for all the knowledge and skills I have gained this year, which I believe will be incredibly useful in my future career and I would recommend a BMedSc(Hons) to anyone looking to widen their skillset and try something different. It has also been amazing to have the opportunity to work with and learn from my supervisors Professor Ben Mol and Dr Daniel Rolnik, who taught me so much this year.

I am happy to answer any questions, feel free to contact me at [anisijag@gmail.com](mailto:anisijag@gmail.com)

## ABSTRACT

### Background

Caesarean section (CS) rates have increased over recent decades in Australia, while simultaneously, the mean maternal age of pregnant women is also rising. These trends are important because the increased risk of CS with advanced maternal age (AMA) is well-established in existing literature. Non-progressive labour and suspected fetal distress are the two most common indications for an emergency CS that involve different disease processes and may therefore be impacted differently by maternal age. Despite this, very few studies have explored the impact of maternal age on the specific indication for CS, which is what our study aimed to assess.

### Method

We conducted a retrospective cohort study including nulliparous women who attempted vaginal birth with liveborn singletons at Monash Health from 2000 to 2020. We completed a subgroup analysis including only low-risk women to explore the association between age and the indication for CS without the influences of maternal comorbidities and complications. We calculated the frequency of various labour outcomes, including unassisted vaginal birth, CS for fetal distress, and CS for non-progressive labour by maternal age category and calculated odds ratios with 95% confidence intervals. We conducted multinomial logistic regression to investigate a possible linear association between age and the odds of CS, before creating restricted cubic spline curves to investigate a possible non-linear association. Subsequently, we recreated these spline curves stratifying participants by birth weight category to assess the influence of birth weight on this continuous association between maternal age and indication for CS. Finally, we created Kaplan-Meier and cumulative incidence curves to analyse the duration of labour

until birth for different birth modes by maternal age category.

### Results

Nulliparous women aged  $\geq 40$  years were 2.71 times as likely to require a CS for fetal distress compared to the reference group of women aged 20 to 24 years (95%CI 2.23 to 3.29). Furthermore, women aged  $\geq 40$  years were at a 2.80 times greater odds of CS for non-progressive labour (95%CI 2.36 to 3.33). In the low-risk subgroup, the odds of CS for fetal distress increased by 2.81 times in the  $\geq 40$ -year-old age group (95%CI 1.23 to 6.41) and the odds of CS for non-progressive labour increased by 3.43 times (95%CI 1.81 to 6.50). There was a non-linear association between continuous maternal age and the odds of CS for fetal distress and CS for non-progressive labour, where the odds of CS for both indications increase progressively with advancing age. Birth weight had a significant impact on the risk of CS for non-progressive labour only. Furthermore, the duration of labour to vaginal birth was greatest in older women, however, the time to CS was shorter with AMA.

### Conclusion

AMA had a significant impact on increasing the risk of CS for both fetal distress and non-progressive labour. This association remained significant in the subgroup of low-risk women, ultimately suggesting that the impact of maternal age on CS risk is independent of the impact of pregnancy complications and comorbidities regardless of the indication.

# Ahmad Basalamah

## Impact of the COVID-19 Pandemic on Monash University Nursing and Allied Health Student Placements and Course Completions in 2020

Supervisor Names and Institute Affiliations:

Dr Eleanor Mitchell and Dr Keith Sutton

Monash Rural Health



I'm a student from University of Indonesia and I was born in 1999. During my Honours year, I was unable to go to Australia due to the pandemic and until now, I haven't got the opportunity to visit Monash University nor meet my supervisors in person. I immediately got interested in my project ever since I saw the title and plus, Eleanor and Keith, my supervisors are both very lovely people. I learned a lot from my Honours year and of course, my Honours year has been one of the greatest opportunities and achievement I had in my life.

### ABSTRACT

#### Background

In early 2020, COVID-19 caused a pandemic resulting in lockdowns all around the world. The State of Victoria, Australia experienced 2 lockdowns in 2020 that resulted in changes to tertiary education delivery. Clinical placements are critical to meet graduate registration requirements for most health professional qualifying vocational degrees. Interruptions to clinical placements have the potential to delay student course completion, which could affect the availability of the health workforce. This study sought to identify the impact of COVID-19 on the number of Monash University, nursing and allied health student clinical placements, and understand the ways in which COVID-19 affected health student placements.

#### Methods

Data collected for the Nursing and Allied Health Graduate Outcomes Tracking study was used for this study. The number and characteristics of student placements undertaken during 2020 were compared to those completed in the previous two years (2018 and 2019). Data were analysed with Chi-squared and Poisson regression analysis.

#### Results

The results obtained showed the number of placements for occupational therapy were unaffected ( $p>0.05$ ) and physiotherapy were less affected ( $p<0.001$ ) than nursing and midwifery ( $p<0.001$ ) and paramedicine ( $p<0.001$ ). These latter two courses showed a significant decrease in the number of placements, to almost 50% of the previous years. Similarly, placements in occupational therapy ( $p>0.05$ ) and physiotherapy were of a similar length ( $p>0.05$ ), while nursing and midwifery ( $p<0.001$ ) and paramedicine ( $p<0.001$ ) had shorter placement hours compared

to the previous two years. Most of the courses showed their first-year students had decreased numbers of placements ( $p<0.001$ ), except for Occupational Therapy ( $p>0.05$ ). The mid- and final-year students were less affected or unaffected, as their numbers remain mostly similar, except for final-year Physiotherapy students, who had no placements. Placements in all location classifications declined in 2020, although not disproportionately. Some agency types declined in number and proportion during 2020, such as NGOs and School-based placements, whereas Community Centres were unaffected.

#### Conclusion

In conclusion, the COVID-19 pandemic decreased the number of clinical placements and changed some of their characteristics. The effect of COVID-19 restrictions also varied upon different health professional courses as Paramedicine and Nursing and Midwifery were more affected in all aspects compared to Occupational Therapy and Physiotherapy. This research highlights the impact of COVID-19 restrictions on health professional students. Contrary to Government recommendations, COVID-19 affected the placements for final year students, hence the impact on the junior health workforce may be quite significant and warrants further investigation.



# Viecky Mirsa Putri Betavani

## The effect of treatment of sleep disordered breathing on sleep quality in children with Down syndrome

Supervisor Names and Institute Affiliations:

1. Professor Rosemary S.C. Horne

2. Dr Lisa M. Walter

Department of Paediatrics, Monash University

The Ritchie Centre, Hudson Institute of Medical Research



Hi there! I am Viecky and a fourth-year medical student from Universitas Indonesia. I had the pleasure of undertaking my Honours year in department of paediatrics with Professor Rosemary Horne and Dr Lisa Walter. My research project that I took has led me to expand my knowledge and gain a lot of perspectives in children especially children with Down syndrome. As I studied them, I became more aware of their health and how it could affect their well-being and I would like to help them to improve their quality of life in the future. I also learned how to design research and was able to improve my writing skills. One thing that I can say to the future students is to get out of your comfort zone and grab the chance to take on the Honours year. I can say that taking an Honours year has been the best decision I have ever made and also a life-changing experience. I got to learn new things in the research field and greatly enjoyed working with clinicians and researchers who are experts in their field with diverse backgrounds and perspectives.

I am more than happy to be contacted about anything via  
vput0005@student.monash.edu

### ABSTRACT

#### Background

In children, sleep is at a lifetime maximum and is important for growth and development. However, sleep disordered breathing (SDB) which forms a spectrum from primary snoring (PS) to obstructive sleep apnoea (OSA) can cause sleep disruption. OSA affects 1%-6% of typically developing (TD) children and impacts on their daytime functioning. OSA is much more common in children with Down syndrome (DS) and affects up to 90% of children due to their unique craniofacial characteristics, reduced muscle tone, and obesity. Treatment of SDB in TD children has been found to be effective in improving SDB severity, but studies in children with DS remain limited. The current study aimed to assess changes in SDB severity and conventionally scored sleep macro-architecture. Sleep micro-architecture was assessed using spectral analysis which is a more sensitive measurement of sleep disruption in children with DS following treatment. We hypothesised that treatment of SDB would reduce SDB severity and improve sleep quality in children with DS.

#### Method

Children with DS ( $n=24$ ) completed a follow up polysomnographic (PSG) study within 2 years of their baseline study. We investigated outcomes in two groups of children with DS, children who were treated ( $n=9$ ) following their baseline study and children who had no treatment ( $n=15$ ). Sleep quality was determined by sleep macro-architecture (time spent in different sleep states), sleep micro-architecture using EEG spectral analysis, and slow wave analysis (indicates sleep drive). SDB severity was measured using the obstructive apnoea hypopnea index (OAHI). We compared changes in SDB severity and sleep quality between children at baseline and follow up in both groups. SDB severity, sleep macro-architecture and sleep micro-architecture data between baseline and follow up for

both groups were compared using the Wilcoxon signed rank test and Mann-Whitney U tests were used to compare data between treated and untreated groups at baseline and follow up.

#### Results

The treated group at baseline had more severe OSA compared to the untreated group. OSA was significantly improved in children who were treated at follow up. There were no significant differences in sleep macro-architecture parameters from baseline to follow up in either the treated or untreated group. Children at follow up who had treatment had decreased SDB severity indicated by decreased OAHI. From sleep micro-architecture, differences were mostly found during NREM sleep compared to REM sleep. Children at baseline who were treated had lower theta, alpha, sigma, and beta power compared to the untreated group. However, the children who were treated had increased sigma power at follow up that indicates sleep improvement.

#### Conclusion

Treatment of SDB was found to be effective in reducing OSA severity in DS children with SDB. SDB treatment did not improve sleep macro-architecture. Increased sigma power during NREM sleep at follow up in children who received treatment suggests an increase of sleep spindles known to maintain sleep, which indicates improvement in sleep quality. The improvement of both sleep quality and SDB severity in children with DS following treatment will likely improve their quality of life.

# Yasmine Syifa Nabila Budi

## Interventions for Parents of Children with Autism Spectrum Disorder (ASD): An Umbrella Review

Supervisor Names and Institute Affiliations:

Professor Katrina William

Dr Georgina Cox

School of Clinical Sciences, Departments of Pediatrics and Education Research, Monash University



I had a very good time working with Professor Katrina Williams and Dr Georgina Cox, they were very helpful and accomodating despite the time difference and the fact that I couldn't be on site during the course of the research year. I also felt very lucky to be able to do this project under my supervisors' guidance because they gave me new knowledge regarding qualitative research that is still very lacking and quite rare to find in Indonesia. Being able to do a new way of analysing and looking through my data is a very valuable experience for me and I am forever thankful for this experience provided by Monash. In short, the experience that I had during this year was so valuable and I believe will be very helpful for my future both as a clinician and also a researcher. Good luck for the next batch and I hope you have the same experience as I did.

### ABSTRACT

#### Introduction

Parents of children with ASD are prone to various mental health conditions such as, depression, anxiety disorder, high stress levels, and lower level of well-being or quality of life. These difficulties can arise for many reasons and at different times during their child's life. The stress could come from the act of caregiving, isolation from peers, inability to communicate needs with clinicians and their support system, or inability to use healthy coping mechanisms. Parent intervention is needed to prevent and manage mental health problems so parents and their family can thrive.

#### Objective

This umbrella systematic review evaluated and synthesised published systematic reviews or meta-analyses reporting interventions for parents of children with ASD. This study is presented with two aims. The first to assess the effectiveness of parent interventions and the second to assess the quality of each included review.

#### Methods

This research uses established methods for umbrella systematic reviews and a qualitative approach for data synthesis and analysis.

#### Result

We include 9 Systematic Reviews and Meta-Analyses, there are 6 Parent interventions with 6 different outcomes, the methods of intervention are conventional psychological therapies, such as Mindfulness (N=1467), Acceptance and Commitment Therapy (ACT) (N=168), Cognitive Behavioral Therapy (CBT) (N=309), Parent education (N=975), Parent Support Groups (N=124) and Psychointervention (N=909), were reported to have favorable outcomes. The quality of the reviews varied, with 4 reviews with high risk of bias, 4 reviews with a low risk of bias, this happens due to the heterogeneity and low data presented in each review. For mindfulness, for example, parental stress,

depression and anxiety levels of parents were reduced. Reviews included interventions from high income countries such as the USA, Australia and the UK. Parent interventions were delivered under clinician supervision as hospital-based, home-delivered and online, for example with online forums.

#### Conclusion

Parents of children with ASD are likely to benefit from psychological interventions and support, with evidence emerging of reduced mental health problems and increased well being and overall quality of life. However, because there is very little data presented right now, there is not enough evidence that is available to aid services development. These findings would be very beneficial in terms of finding the best setting and implementation of the intervention for parents of children with ASD.



# Ashleigh Carolan

## A combination therapeutic approach to Granulosa Cell Tumours

Supervisor Names and Institute Affiliations:

Dr Simon Chu and Professor Peter Fuller (Hudson Institute of Medical Research)



I completed my BMedSc(Hons) after my fourth year of medicine. Following a stressful year of studying, I felt it would be a welcome break to try something new (with no exams!). I decided to take on a lab-based project for a few reasons; firstly, I liked the idea of having a hands-on project where I could learn new practical skills. Secondly, due to COVID restrictions, I wanted a project where I could go into an office/lab each day and have face-to-face interactions with colleagues. I know many students with clinical projects had to work from home, which can be very isolating. During the year, I met lots of great people from all backgrounds, not just clinical. My advice to future students would be to choose a supervisor that is the right fit for you and make sure you are both on the same page about your goals for the year. I was lucky that my supervisor was available almost every day for help and encouraged me to take every opportunity that the honours year presents.

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### ABSTRACT

Granulosa cell tumours (GCT) are uncommon ovarian cancers characterised by an indolent clinical course and significant late recurrence rates. Furthermore, these tumours are unique from other ovarian cancers, with a majority secreting estrogen and inhibin. Aside from invasive surgery, there are limited therapeutic options. Chemotherapy is not effective and associated with severe adverse effects, highlighting the need for targeted therapies in GCT.

Our laboratory has previously shown that targeting X-linked Inhibitor of Apoptosis Protein (XIAP) using small molecule inhibitors known Smac-mimetics, is a compelling combination therapeutic strategy in GCT. XIAP inhibition sensitises cancer cells to anti-cancer therapies through regulating key pro-survival pathways, namely NFκB.

We hypothesised that XIAP inhibition using Smac-mimetics combined with established drugs targeting additional pathogenic pathways would provide a novel therapeutic strategy for GCT. To determine the most effective combination agents, we performed a high-throughput drug screen (HTS) using both an FDA-approved and an anti-cancer compound library (1μM each compound) +/- a Smac-mimetic called Compound A (500nM). We used two cell lines, KGN (GCT-derived) and hGrC1 (transformed normal granulosa cells). Cell viability was determined using a fluorescence assay (alamarBlue) following 72 hours of treatment. For further investigation, we selected YM155 (survivin inhibitor) and Panobinostat (HDAC inhibitor). Using cell proliferation and viability assays, we demonstrated that YM155 is highly effective as a single agent at 50nM. Additionally, 100nM Panobinostat acted synergistically with 500nM Compound A. The use of both agents led to an increase in apoptosis at these same concentrations, as demonstrated by increased caspase

3/7 activity. We validated these results by assessing apoptosis using flow cytometry with Annexin V dye. A mechanistic profile for the compounds was determined using real-time PCR and luciferase reporter assays. Panobinostat demonstrated an increase in NFκB activity, which decreased when combined with Compound A. This finding was accompanied by an increase in TNFα expression, suggesting that there is activation of the extrinsic pathway of apoptosis. The addition of Compound A to Panobinostat, appears to inhibit NFκB, which enhances the activity of apoptosis. 25nM YM155 showed a slight decrease in survivin and XIAP expression after 24 hours of treatment, however the results were not significant, and experiments should be repeated at a higher dose. These results represent two different promising therapeutic strategies for GCT, leading to potential clinical translation.

# Adya Choudhary

## Using Cervical Length for the Prediction of Preterm Birth

Supervisor Names and Institute Affiliations:

Dr Rui Wang, Professor Ben Mol, Dr Kirsten Palmer, A/Professor Harry Georgiou. Department of Obstetrics and Gynaecology, School of Clinical Sciences, Monash University.



Medical research has always intrigued me, so to gain some first-hand insight as to how it all occurs, I undertook a BMedSc(Hons) year after completing fourth year in 2020. O&G was a speciality that stood out to me during placement, and I felt a BMedSc(Hons) project would help further this interest. This year has been extremely educational, rewarding, and valuable, and through the guidance of my incredible supervisors I have felt supported every step of the way. I have gained key skills relating to data analysis and scientific writing and have become familiar with the research process – all of which will aid me in the future.

This experience has confirmed that research is something I would like to pursue more of in the future, and the knowledge and confidence I've gained will equip me to do so. I would definitely recommend a BMedSc(Hons) to anyone interested in undertaking medical research in a safe and comfortable environment.

Feel free to contact me at:  
acho0010@student.monash.edu

## ABSTRACT

### Background

Preterm Birth is an increasing global health issue associated with complications. Cervical length has been identified as a promising prognostic tool for preterm birth. However, existing studies on this topic usually consider such a prognostic factor question as a question on diagnostic accuracy, dichotomise cervical, and ignore time as part of the outcome, resulting in inconsistent evidence and limiting their implication. In addition, there is limited evidence on the variation in the prognostic capacity in different populations (nulliparous vs multiparous women), and with multiple cervical length measurements on preterm birth.

### Aims

The aims were to evaluate 1) the predictive capacity of mid-trimester cervical length for preterm birth in asymptomatic, singleton pregnancies, considering preterm birth as both time-to-event and binary outcomes; 2) whether the predictive capacity varies in nulliparous and multiparous women; and 3) the predictive capacity of a change in cervical length.

### Method

This was a secondary analysis of the PPeTaL study, which was a prospective cohort study conducted between 2017 – 2020. In this thesis, asymptomatic, singleton pregnancies with at least one cervical length measurement between 16 – 24 weeks (prognostic factor of interest) were included. The outcomes assessed were preterm birth, extreme preterm birth (birth < 34 weeks), and spontaneous preterm birth. The PROGRESS framework was followed. Cox regression and Logistic regression were performed, adjusting for important confounding factors, to assess the prognostic capacity of cervical length (Aim 1). An interaction between cervical length and parity was added to the logistic regression to assess variation in the

prognostic capacity of cervical length in nulliparous and multiparous women on preterm birth (Aim 2). An additional logistic regression was performed to evaluate the prognostic value of a change in cervical length on preterm birth (Aim 3).

### Results

We identified 367 asymptomatic, singleton women with at-least one cervical ultrasound measurement between 16-24 weeks. In this cohort, 138 (37.6%) were nulliparous. There were 91 (24.8%) preterm births, 35 (9.5%) extreme preterm births and 68 (18.5%) spontaneous preterm births. Women with a longer cervix were associated with a decreased hazard of preterm birth (adjusted hazard ratio[aHR] 0.63, 95% confidence interval [CI] 0.49 – 0.80), extreme preterm birth (aHR 0.49 95% CI 0.36 – 0.68), and spontaneous preterm birth (aHR 0.57, 95% CI 0.43 – 0.77). Logistic regression showed similar findings. No significant interaction between the predictive capacity of cervical length and parity was found for preterm birth (p value 0.141) and extreme preterm birth (p value 0.149). There is insufficient evidence that change in cervical length was associated with preterm birth (adjusted odds ratio[aOR] 1.55, 95% CI 0.36 – 6.35) or extreme preterm birth (aOR 2.04, 95%CI 0.28 – 14.86).

### Conclusion

Women with a shorter mid-trimester cervical length are more likely to have preterm birth and extreme preterm birth and such an association is present in all cervical lengths. No significant difference on the prognostic capacity of cervical length between nulliparous and multiparous women was found. We also did not find a change in cervical length to be a predictor for preterm birth, however our study was underpowered for our last 2 aims.

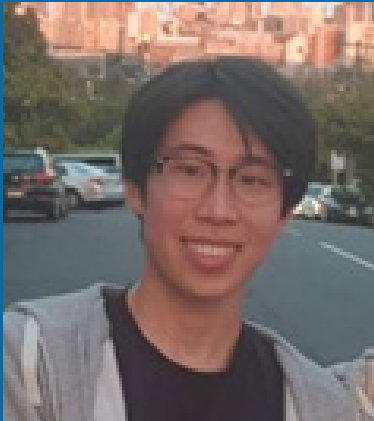


# Gumin Chung

## Can eye movements predict speed perception?

Supervisor Names and Institute Affiliations:

Dr Nicholas Price, Biomedicine Discovery Institute



I chose this project because the work sounded interesting.

## ABSTRACT

### Background

Smooth pursuit, the visual tracking of a moving stimulus, is a voluntary eye movement critical for hunting, survival, and every-day functioning. Dysfunction is associated with psychiatric conditions known for visual symptoms, such as schizophrenia (hallucinations) and autism (atypical facial recognition). Pursuit is driven by motion signals on the retina. However, the eye movements generate additional motion on the retina, and are compensated for by an efferent motor signal, making pursuit a “closed loop feedback system”. Similarly, an efferent copy of eye motion is used in the sensory realms of the brain to contextualise object motion derived from retinal slip speed. The extent to which eye motion affects perceptual sensitivity to speed changes during smooth pursuit is unknown. Here we show that speed perception relies solely on retinal image slip speed, with no association with eye speed.

### Method

We measured eye speeds of four subjects during the visual tracking of a moving stimulus with a random 100ms period of increased speed, and asked them to press a button when they detected the speed increment.

### Results

We found that there was no difference in eye speeds between trials in which the perceptual report of speed modulation was a true hit, false hit, or a miss, even when stimulus speeds differed greatly.

### Conclusions

We expect our findings to provide a basis for further investigation into the role of retinal slip speed and associated brain areas in speed perception. Eventually, this may shed light into the pathophysiology of visual dysfunction in schizophrenia and autism.

# Jack Davidson

## Oxygen delivery to preterm infants – are oxygen saturation targets achieved in practice?

Supervisor Names and Institute Affiliations:

A/Professor Kenneth Tan (Monash Newborn, Department of Paediatrics, Monash Children's Hospital)

Dr Risha Bhatia (Monash Newborn, Department of Paediatrics, Monash Children's Hospital)



Hi, my name is Jack and I completed my honours degree at Monash Newborn at the Monash Children's Hospital. My study was a quality assurance project where we looked at the oxygen saturations of infants born <28 weeks' gestation and whether or not these are being kept within the target levels of 91-95%. I chose to do my project with Monash Newborn because I'm really interested in paediatrics and I had great supervisors to support me. I learned lots about how to effectively search the literature and identify gaps in the literature, as well as what is required to conduct my own project. I was also given lots of opportunities to keep up my clinical experience in the NICU which was a great balance to my year! In 2022 I will be completing my 5th and final year of medicine. Feel free to message me on Facebook or by email if you have any questions about research in general or what it was like doing research at Monash Newborn.

### ABSTRACT

#### Background

Retinopathy of prematurity (ROP) is a major cause of visual impairment in extremely preterm infants (EPIs). A key risk factor for ROP is high neonatal oxygen saturations (SpO<sub>2</sub>). An increase in the incidence of ROP over the past decade can be partly attributed to a shift towards higher SpO<sub>2</sub> targets in order to reduce infant mortality. SpO<sub>2</sub> targeting is managed by nursing adjustment of the fraction of inspired oxygen (FiO<sub>2</sub>). Studies show that infants only spend 40-60% of the time within the target range. Increasing compliance with these targets may reduce ROP rates. Potential means for improving this compliance include staff education, visual reminders of SpO<sub>2</sub> targets and FiO<sub>2</sub> titration guidelines.

#### Aims

The primary aim was to determine the proportion of time that EPIs spent within the Monash Newborn SpO<sub>2</sub> targets of 91-95%. I then wanted to assess for potential barriers that nurses face when targeting an SpO<sub>2</sub> range.

#### Methods

This was a prospective observational cohort study that formed the first phase of a quality improvement (QI) initiative aiming to reduce ROP rates at Monash Newborn. All infants born <28 weeks' gestational age (GA) and admitted to Monash Newborn over a six-month period were included in the study. SpO<sub>2</sub> data were recorded minutely for the first 14 days of life for each infant. Frequency distributions were used to report the time spent below, within and above the target range for all SpO<sub>2</sub> values and then exclusively when the FiO<sub>2</sub> >0.21. I then surveyed nurses at Monash Newborn, aiming to address the following three areas: 1) awareness of SpO<sub>2</sub> target compliance rates at Monash Newborn, 2) nurses' opinions on potential barriers to target compliance and 3) nurses' current SpO<sub>2</sub> targeting practices.

#### Results

Thirty-four infants <28 weeks' gestation were admitted to Monash Newborn during the six months between 08/03/2021 – 27/08/2021 and their SpO<sub>2</sub> analysed. For all FiO<sub>2</sub> values, infants spent 48.04% of the time within, 40.77% above and 11.20% below the target ranges of 91-95%. After excluding periods where the FiO<sub>2</sub> was 0.21, infants spent 58.30% of time within the target range, 26.02% above and 15.68% below. There were 91 completed responses to the nursing survey, with 52.75% having at least 5 years' experience working in a neonatal setting. Three-quarters (75.82%) of respondents believed that infants spent at least 70% of the time within the target range, whilst only 2 believed that infants spent <50% of the time within the target range. The majority (94.44%) believed they would benefit from further neonatal oxygen targeting education. Nurse-to-infant ratios, being overworked, and general infant instability were not seen by the nurses as significant barriers to SpO<sub>2</sub> targeting.

#### Conclusion

Compliance with SpO<sub>2</sub> targets at Monash Newborn is poor and infants spend a large amount of time in hyperoxia (>95%). It appears there may be a lack of awareness with regards to target compliance amongst nurses. There is, therefore, a need to implement interventions such as staff education to improve compliance with SpO<sub>2</sub> targets with the aim of reducing ROP rates at Monash Newborn.

# Georgia Dawson

## Contemporary Trends in Perinatal Outcomes Following Instrumental Vaginal Births. The Victorian Context

### Supervisor Names and Institute Affiliations:

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4. Safer Care Victoria, Melbourne Victoria, Australia

5. Department of Obstetrics and Gynaecology, Monash Health, Clayton Victoria, Australia

6. Department of Health, Victorian State Government, Victoria, Australia



I completed the BMedSc(Hons) year in my penultimate year (2021), before commencing final year of the Bachelor of Medical Science and Doctor of Medicine in 2022. I chose my research project within the obstetric speciality as I enjoy both the surgical and medical aspects of this field. I also believed my project was a relevant and concerning aspect of current care, of which I could provide applicable research.

During my project, I learnt research is a challenging yet worthwhile practice. I would definitely recommend this year to all upcoming students, and my advice would primarily be to plan ahead. Throughout the year, many people experience setbacks or are awaiting approval/patients/access to data. If you plan ahead, these setbacks can be anticipated, and alternate arrangements planned. Secondly, talk to other students about your projects. The year researching from home/within your laboratory/or office can be isolating, however if you maintain a support system of other BMedSc(Hons) students, you can encourage and help one another.

For future students, I am always happy to be contacted and offer assistance so please do not hesitate to reach out.

## ABSTRACT

### Background

Approximately 15% of all births in Victoria are completed by Instrumental Vaginal Births (IVB), and this rate appears to be rising. Recent fatalities associated with IVB have questioned whether the rates IVB morbidities are increasing and going unrecognised within practice. These factors have highlighted the importance of understanding fetal harms associated with IVB, an area currently lacking significant literature.

### Aims

To ascertain the current risk of individual instruments in causing fetal morbidity and mortality. Further, to assess temporal trends in outcomes overtime and what risk factors increase adverse fetal outcomes, including location of birth and maternal demographics.

### Methods

A retrospective study from 2010-2019, using Victorian population data from the Victorian Perinatal Data Collection (VPCD). The study cohort included babies of  $\geq 28$  weeks' gestation, free of congenital anomalies, singleton and twin births, and excluded terminations of pregnancy. Demographic characteristics for mother and baby were appraised over the study period. Exposure variables included year, location and method of birth, as well as indication for IVB, and maternal parity, age, and country of birth. Outcome variables analysed were all potential fetal morbidities following IVB, including mortality. Statistical analysis was performed to calculate relative risks, rates of morbidities by exposure variables, and significant trend changes overtime.

### Results

Our cohort included 484,496 total vaginal births from 481,826 women. Of these, twenty-three percent ( $n=110,874$ ) were IVB. Rates of IVB increased from 20.7% to 25.4% ( $p<0.01$ ) over the study period,

driven by an increase in forceps births from 7.5% to 12.2% ( $p<0.01$ ). Forceps were associated with a significant increased risk of endotracheal intubation, facial nerve damage, scalp bruising, feeding problems, other birth injuries, and NICU admissions. Vacuum births were statistically associated with intracranial and extracranial haemorrhages, skull fractures, and asphyxia. Overtime, rates of some vacuum associated morbidities decreased (skull fractures 3.1 to 0.7 per 1000 vacuum assisted births;  $p=0.03$ ) where others increased (subgaleal haemorrhage 0.4 to 2.8 per 1000 vacuum assisted births;  $p=0.03$ ). Rates of forceps associated morbidities increased (including facial nerve trauma 1.1 to 3.6 per 1000 forceps assisted births;  $p=0.02$ , and NICU admission 10.1 to 19.2 per 1000 forceps assisted births;  $p=0.01$ ). Additionally, rates of morbidity were more likely in rural and regional compared to metropolitan centres ( $p<0.01$ ) and were greatest among nulliparous ( $p<0.01$ ), younger mothers ( $p<0.01$ ), and those born in Australia ( $p<0.01$ ).

### Conclusion

The benefits and maternal harms following IVB are well studied, however fetal harms are less conclusive. Our study showed statistically significant risks between instruments, and fetal harms may be increasing, particularly among forceps and those performed in regional and rural centres. These results support ongoing analysis of adverse outcomes following IVB to inform best practice, shared decision making, and training recommendations. We also suggest further analysis into the long-term complications following IVB.



# Mihika de Bruyne

## Factors influencing willingness to pay to avoid postoperative nausea and vomiting

Supervisor Names and Institute Affiliations:

Associate Professor Jai Darvall and Professor Kate Leslie AO FAHMS

The Royal Melbourne Hospital Department of Anaesthesia and Pain Management

School of Public Health and Preventive Medicine, Monash University



I did my BMedSc(Hons) this year after finishing 4C in 2020. I had the pleasure of completing my honours year in the anaesthetics department of The Royal Melbourne Hospital where I was involved in recruitment for a large clinical trial investigating the use of chewing gum to treat postoperative nausea and vomiting. My project was a substudy using data collected as part of this trial regarding willingness to pay to avoid postoperative nausea and vomiting. My supervisors and the anaesthetic research team were amazing and provided many opportunities to learn more about anaesthetic research as well as working on clinical skills. I had a great experience exploring the world of clinical research and the year has provided me with many new skills and some much-needed perspective as I embark on my final year of medical school. I would highly recommend a BMedSc(Hons) to anyone looking to expand their horizons beyond just clinical medicine and I am happy to be contacted by any future students.

## ABSTRACT

### Background

Nausea and vomiting are common postoperative side effects of anaesthesia, which are distressing to patients and contribute to greater healthcare costs. To properly understand the impact of postoperative nausea and vomiting (PONV) we need to establish the value that patients place on preventing suffering associated with PONV. This can be assessed via willingness to pay (WTP), in which patients are asked directly how much money they would hypothetically pay to avoid an outcome. There are currently no Australian or New Zealand data on WTP to avoid PONV and research into factors influencing WTP to avoid PONV are lacking. We aimed to analyse the effects of age, ethnicity, income, past history of PONV or motion sickness, current preoperative nausea and experience of PONV in the post anaesthesia care unit (PACU) on WTP to avoid PONV in an Australian and New Zealand population.

### Method

Data from the ongoing CHEWY (Chewing gum to treat postoperative nausea and Emesis in Women) clinical trial were used in this analysis. Demographic factors including age, ethnicity and income were recorded in a preoperative survey along with past history of PONV or motion sickness and current preoperative nausea. All participants were asked for their WTP preoperatively, and those who experienced PONV in the PACU were asked again about WTP at 24 hours postoperatively. Statistical analysis involved linear regressions for the influence of demographic factors, past history of PONV and current preoperative nausea on WTP, and a Wilcoxon signed-rank test to analyse change in WTP following experience of PONV in the PACU.

### Results

A total of 642 patients were included, of whom 430 provided preoperative WTP

and 108 provided both preoperative and postoperative WTP. The median WTP was \$50 both preoperatively and postoperatively, with interquartile ranges \$20 - \$100 and \$15 - \$100 respectively. There was a statistically significant association between increasing income bracket and increasing WTP to prevent PONV ( $p < 0.001$ ). Experience of PONV was significantly associated with an increase in individual WTP ( $p < 0.001$ ). There were no statistically significant associations between age, ethnicity, past history of PONV/motion sickness or current preoperative nausea with WTP to avoid PONV.

### Conclusion

To our knowledge this is the first study to analyse WTP to avoid PONV in an Australian population. We found that income and experience of PONV in the PACU significantly increased WTP while age, ethnicity, past history of PONV or motion sickness and current preoperative nausea did not significantly influence WTP. These findings will be used for cost-benefit analysis in the CHEWY trial to provide evidence for the use of chewing gum as a low-cost drug-free alternative to ondansetron. More broadly, our findings contribute novel Australian data to the existing knowledge regarding WTP to avoid PONV. Future research into the impact of current preoperative nausea and ethnicity is warranted.

# Raysha Farah

## Assessing Glymphatic Clearance in a Preclinical Model of Amyotrophic Lateral Sclerosis

Supervisor Names and Institute Affiliations:

A/Professor David Wright, Department of Neuroscience, Monash Central Clinical School

Dr Akram Zamani, Department of Neuroscience, Monash Central Clinical School



Early in medical school at Universitas Indonesia, I became increasingly intrigued with performing research translatable to the clinic as it's a great mix between patient interaction and scientific research. My journey towards being a 'physician-scientist' developed during every summer off my medical school, where I would spend months in a lab. I would love a degree that proves my researching skills. The BMedSc(Hons) from Monash University is a perfect match for me to develop my skills in research.

My research focuses on the diagnosis of amyotrophic lateral sclerosis (ALS). My lab utilises dynamic contrast-enhanced MRI and MATLAB to analyse physiological changes in the brain's glymphatic system, potentially becoming biomarkers for ALS diagnosis. One of the highlights of this program is working with cutting-edge technology with my supervisors while diagnosing complex diseases such as ALS. I also had the opportunity to co-author a journal that hopefully would be translatable to the clinic. The rigorous research methodologies used have shaped me into a better researcher and makes me increasingly committed that research will be part of my career as a doctor. I highly recommend this program to anyone, especially medical students who want to become a researcher in the future.

### ABSTRACT

#### Background

Neurodegenerative diseases are chronic and inexorable conditions characterised by the presence of insoluble aggregates of abnormally ubiquitinated and phosphorylated proteins. Transactive response DNA-binding protein 43 (TDP-43) is one such protein implicated in the neurodegenerative process and is a hallmark characteristic of amyotrophic lateral sclerosis (ALS). Following the discovery of the glymphatic system as a pathway to clear solutes and deliver metabolites, it has been suggested to contribute to both the initiation and progression of neurodegenerative diseases such as Alzheimer's Disease (AD) with multiple lines of evidence suggesting possible impairment of the glymphatic system in ALS.

#### Method

This project assesses the function of the glymphatic system using an adult transgenic mouse model of ALS with overexpression of cytoplasmic human TDP-43 (hTDP-43 $\Delta$ NLS) that is suppressible by doxycycline (Dox). To evaluate for overall health and symptoms, mice were weighed and assessed for their sensorimotor coordination, balance, and stamina using the accelerating rotarod test at one-week post-Dox for the female cohort and one and three weeks post-Dox feeding for the male cohort. In-vivo DCE-MRI was performed using 9.4T/20 MRI with T1-w acquired utilizing the 3D FLASH sequence in the TDP-43 transgenic and littermate controls three weeks and one week after cessation of Dox feed corresponding to symptomatic and asymptomatic stages of the disease. The normalised signal increase over baseline was calculated at each time point using MATLAB to evaluate glymphatic clearance. TDP-43 immunohistological staining was performed on frozen sections to confirm TDP-43 pathology.

#### Results

At three weeks post-Dox (symptomatic time point), DCE-MRI analysis showed reduced glymphatic clearance throughout the whole brain, limbic system, pons, and spinal cord of TDP-43 mice accompanied with body weight loss. At one week post-Dox (asymptomatic time point), DCE-MRI analysis also showed reduced glymphatic clearance in the whole brain, limbic system, pons, and spinal cord of TDP-43 mice accompanied with increased expression of TDP-43.

#### Conclusion

These results highlight the potential of the glymphatic system involvement in disease pathology and as an important therapeutic target and potential biomarker of ALS susceptibility, severity, and prognosis. This study suggests that the glymphatic system is impaired at the symptomatic time point at the whole-brain level, limbic system, pons, and spinal cord. The finding that impaired glymphatic clearance is found in the limbic system may indicate the possibility of developing cognitive and metabolic changes, symptoms typically found in ALS. Importantly, pons and spinal cord impaired glymphatic clearance may indicate the possibility of developing motor impairments in later stages of ALS due to impaired glymphatic clearance that might promote the pathological TDP-43 spread along the corticospinal tract that possibly results in muscle paralysis. While the relationship between glymphatic clearance and disease progression remains to be elucidated, these results demonstrate that alterations in the glymphatic system occur early in the course of ALS, and worsen as the disease progresses and therefore could represent a therapeutic target in the treatment of ALS.

# Rebecca Farquharson

## Time between the onset of symptoms and healthcare seeking among men and women attending the Melbourne Sexual Health Centre

### Supervisor Names and Institute Affiliations:

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<sup>2</sup>Melbourne Sexual Health Centre, Alfred Health, Melbourne, Victoria, Australia

<sup>3</sup>Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne,

Melbourne, Victoria, Australia

The Ritchie Centre, Department of Obstetrics and Gynaecology, Monash University  
Safer Care Victoria, Department of Health and Human Services



Hi! My name is Rebecca, and I had the pleasure of completing my BMedSc(Hons) year at the Melbourne Sexual Health Centre (MSHC) in Carlton. I have developed an interest in public health throughout the medical degree, and was drawn to the intersection of public health and sexual health in my project. I was also keen to try something outside of clinical medicine.

I have learnt so much this year – about research, time management, organisation and asking for help. I am very grateful for the opportunity honours has given me to develop my written and oral communication skills, and to experience what it is like to work in a research office.

MSHC is an extremely friendly and welcoming environment, and I feel incredibly lucky to have undertaken my research here. I would highly recommend MSHC to any students with an interest in sexual health or epidemiology, and am happy to be contacted by anyone interested in pursuing research at MSHC.

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## ABSTRACT

### Background

Rates of bacterial sexually transmitted infections (STIs) are rising in Australia. A key factor affecting the transmission and thus rates of STIs is the duration of infectiousness. Early healthcare seeking following symptom onset can reduce the duration of infectiousness. However, the factors influencing time to healthcare seeking among patients with STI-associated symptoms remain unclear.

### Aims

We aimed to examine time to healthcare seeking following the onset of STI-associated symptoms by risk group and by STI diagnosis, and to identify explanatory factors associated with delayed healthcare seeking among patients attending a sexual health clinic in Melbourne.

### Methods

This study was a retrospective analysis of symptomatic consultations at the Melbourne Sexual Health Centre (MSHC) between 10 August 2017 and 31 December 2020. We assessed differences in reported time to healthcare seeking by risk group and by diagnosis. Multivariable logistic regression was performed to explore factors associated with delayed healthcare seeking, which was defined as a symptom duration of greater than seven days prior to clinic attendance.

### Results

The final sample included 7,032 patients: 1,844 men who have sex with men (MSM), 2,777 men who have sex with women only (MSW) and 2,411 women. Time to healthcare seeking was significantly shorter in MSM than MSW among those with non-gonococcal urethritis, genital warts and anal warts (all  $p < 0.001$ ). Time to healthcare seeking was significantly shorter in patients with gonococcal urethritis than patients with non-gonococcal urethritis ( $p < 0.001$ ), in

patients with candidiasis than patients with bacterial vaginosis ( $p < 0.001$ ), and in patients with genital herpes than patients with primary syphilis ( $p < 0.001$ ). Delayed healthcare seeking was common, seen among 34.5% of MSM, 52.5% of MSW, and 45.9% of women. Men who delayed healthcare seeking were less likely to be MSM (adjusted odds ratio (aOR) 0.75; 95% confidence interval (CI) 0.68 – 0.81) or taking HIV pre-exposure prophylaxis (PrEP) (aOR 0.64; 95% CI 0.57 – 0.73). Conversely, men who delayed healthcare seeking were more likely to report no recent sexual partners (aOR 1.75; 95% CI 1.42 – 2.16), report a previous STI (aOR 1.16; 95% CI 1.04 – 1.28), have fewer male partners (ptrend=0.001), have fewer female partners (ptrend=0.009), or reside a further distance from the clinic (ptrend<0.001). Women who delayed healthcare seeking were more likely to report no recent vaginal or anal sex (aOR 1.54; 95% CI 1.19 – 1.99), have fewer male partners (ptrend=0.001), or reside a further distance from the clinic (ptrend=0.049).

### Conclusion

Time to healthcare seeking varied by risk group and by diagnosis at MSHC, and delayed healthcare seeking was common. Men with STI risk factors, including MSM, men taking PrEP, and men with a higher number of sexual partners, were less likely to delay healthcare seeking. Promotion of early healthcare seeking among lower-risk groups, including MSW, in addition to currently targeted higher-risk groups, may assist in reducing STI-associated morbidity. Men and women who resided a further distance from MSHC were more likely to delay healthcare seeking. This suggests that access to healthcare is a barrier towards early healthcare seeking that must be addressed.



# Isabel Foo

## Attentional biases across the menstrual cycle and in premenstrual mood disorders

Supervisor Names and Institute Affiliations:

A/Professor Caroline Gurvich, Dr Elizabeth Thomas, Dr Eveline Mu

Monash Alfred Psychiatry research centre (MAPrc)/Central clinical school (CCS)



I completed my BMedSc(Hons) year at the Monash Alfred Psychiatry research centre (MAPrc) after Year 4C. As someone who did not have any previous research experience, I thought doing an honours year would be a great opportunity to see what being a researcher is like and to develop some research skills. My project was part of a larger observational trial and I was involved in recruitment, data collection and analysis. This was a great experience and I also enjoyed interacting with participants and maintaining some clinical skills. Despite the inevitable challenges that were encountered throughout the year, I was well supported at MAPrc being surrounded by an amazing group honours students from different courses, as well as having the guidance of three incredible supervisors (who I would highly recommend if you are interested in women's mental health!). Overall, this year has not only given me an opportunity to explore the world of clinical research in a supportive environment but has also allowed me to develop my critical thinking, communication, and organisational skills. I would highly recommend giving it a go even if you are a little nervous about it (like I was).

Happy to be contacted at  
ifoo1@student.monash.edu!

## ABSTRACT

### Background

Premenstrual mood disorders are characterised by the experience of psychological and physical symptoms which are severe enough to impact daily function. These symptoms occur during the second half of the menstrual cycle known as the luteal phase. A negative attentional bias (increased allocation of attention towards negative stimuli) has been observed in other mood disorders such as depression and anxiety. It has been suggested that this bias may play a role in maintaining and facilitating these altered mood states. In the context of the menstrual cycle and premenstrual mood disorders, it is of interest as to whether a negative attentional bias is present during the luteal phase and whether there is a correlation between the increase in symptom severity in this phase and a bias towards negative stimuli. The emotional antisaccade task enables measurement of emotional attentional biases and has not yet been employed in relation to the menstrual cycle and premenstrual mood symptoms.

### Aims

1. To explore whether there is a greater attentional bias towards negative stimuli (i.e. increased antisaccade latency/error rate to negative compared with positive stimuli) in the luteal compared with the follicular phase.
2. To explore whether there is a correlation between the change in attentional bias to negative stimuli (i.e. change in antisaccade latency/error rate to negative stimuli) and the change in severity of depressive and anxiety symptoms between follicular and luteal phase.

### Method

Fifteen women were tracked for two menstrual cycles where the severity of premenstrual symptoms was recorded with the Daily Record of Severity of Problems (DRSP). Participants also completed

saccadic eye tracking assessments once in their follicular and once in their luteal phase. Latency and error rates from the antisaccade task were used as measures of attentional biases. Repeat measure ANOVAs with phase (follicular vs luteal) and stimuli (positive vs negative) as within subject factors were conducted to compare latencies and error rates between phases. Correlations were conducted to compare symptom change measured by the DRSP with changes in latency and error rates between phases.

### Results

There were no significant differences in latencies or error rates to negative compared with positive stimuli in the luteal phase. There was also no significant increase in latencies or error rates to negative stimuli in the luteal, compared with the follicular phase. Despite the lack of statistical significance, the overall pattern of findings suggested longer latencies and higher error rates towards negative stimuli during the luteal phase. Positive correlations and trends were found between premenstrual symptoms and latencies and error rates to negative stimuli.

### Conclusion

No significant negative attentional bias was observed in the luteal phase. However, the overall pattern of our results suggest that premenstrual mood symptoms may be associated with an increased negative attentional bias in the luteal phase. These findings add to a growing body of literature suggesting a relationship between negative attentional biases and premenstrual mood disorders. Further research is required to fully explore these relationships, which may lead to improved understanding and management of premenstrual mood disorders in future.

# Isobel Galloway

## Outcomes and Withholding or Withdrawal of Life Sustaining Treatment in Extremely Preterm Infants

Supervisor Names and Institute Affiliations:

Associate Professor Kenneth Tan

Monash Children's Hospital, Monash Newborn, Melbourne, Australia

Associate Professor Charles Christoph Roehr

National Perinatal Epidemiology Unit - Clinical Trials Unit, Nuffield Department of Population Health Medical Sciences Division, University of Oxford



After a massive year 4C in the middle of a pandemic, I was very excited to pivot my energy in a different direction. I had originally planned a project based at John Radcliffe Hospital in Oxford; however I was still unable to travel in 2021. Eventually, we came to a modified project at Monash Newborn which combined my interests in paediatrics, acute care and obstetrics in a niche of Neonatology that has not been studied in great detail. I loved the opportunity to explore research, something I strive to do throughout my career. My supervisors were fantastic in providing the necessary insight and advice I needed to conduct my project. The Department of Paediatrics is also an amazing place to do a BMedSc(Hons).

For anyone considering doing a BMedSc(Hons), my advice would be to just do it! I thoroughly enjoyed using my brain in a more analytical way compared to cramming it with medical knowledge! Additionally, you learn so many valuable skills about research and develop an academic independence and confidence. Doing a year of research is also very inspiring when you see all the interesting things you could investigate.

I'm very happy for anyone to contact me about anything BMedSc(Hons) related at [igal0001@student.monash.edu](mailto:igal0001@student.monash.edu) or [isobeljsgalloway@gmail.com](mailto:isobeljsgalloway@gmail.com)

### ABSTRACT

#### Background

Outcomes in extremely preterm (EPT) infants vary substantially both between and within countries. The literature suggests variation may be because of differences in population demographics, intensity and uptake of evidence-based practices and the attitudes towards managing periviable infants. There is also significant variation in end-of-life practices however, less is known about how this might affect outcomes. Our study investigated this knowledge gap to understand the implications withholding and withdrawal of life sustaining treatment (WWLST) might have on outcomes of EPT infants.

#### Aims

Our study assessed outcomes in a 6-year (2015 to 2020) EPT cohort admitted to Monash Children's Hospital (MCH). The primary aim was to identify the factors which predicted mortality and in-hospital morbidity and create multivariate models to aid in prognostication. The secondary aim was to investigate the WWLST practices and their effect on mortality.

#### Methods

This single-unit retrospective cohort study looked at infants <27 weeks admitted to the Monash Children's Hospital (MCH) neonatal intensive care unit (NICU) without severe congenital anomalies. Data collected included maternal and infant demographics, antenatal and birth history, respiratory practices and outcomes, in-hospital morbidities, death and WWLST factors. Existing data collected for submission to the Australian and New Zealand Neonatal Network (ANZNN) were used. Missing data were collected using electronic medical records (EMR). Finally, a high-risk subgroup of infants who died or had a severe morbidity was identified and data on WWLST practices and outcomes were collected. Summary statistics and unadjusted odds ratios for

the composite outcome mortality and in-hospital morbidities and each separately were calculated. Multivariate models were created to identify predictors of these outcomes. Survival analysis was also performed.

#### Results

Our cohort of 278 infants had low mortality (15%) but high in-hospital morbidity (85%) rates. Eighty-eight percent of infants either died or had an in-hospital morbidity. Our models performed well in classification testing and predictive factors were as expected. Two-thirds of infants that died did so in the first 13 days and risk factors were most influential in this period. In 53.7% of infants, at least one discussion about WWLST occurred. WWLST preceded death in 83% of our infants. The main reason for WWLST practices was to prevent expected poor long-term outcomes, indicating an emphasis on quality of life. After at least one WWLST discussion, 77.3% of infants had WWLST. Infants about whom WWLST discussions occurred were 95.1 times more likely to die than those that about whom these discussions did not occur. Most of those infants who did not undergo WWLST after a WWLST discussion survived (7 out of 10). This indicates the major role WWLST has in EPT mortality and raises ethical and clinical practice questions which should be an area of further research.

#### Conclusion

While predictors of outcomes in our cohort were expected, we discovered that WWLST practices have significant implications on the mortality of EPT infants at the MCH NICU. Future research should focus on comparing these practices and outcomes with other NICUs to determine their contribution to variable outcomes in EPT infants.

# Laura Gilbertson

## The ethics of expanded terminal sedation in end of life care

Supervisor Names and Institute Affiliations:

Professor Justin Oakley (Monash University); Professor Dominic Wilkinson (University of Oxford); Dr Benjamin Davies (University of Oxford)



Overall, I really enjoyed my Honours year! I wanted to try something different after finishing fourth year last year. I think Honours is a great way to take a year off from medicine whilst still having a productive and fun year. I chose my topic because I am interested in geriatric medicine and end of life care. I have always enjoyed studying ethics and decided that whatever work I do in the future bioethics will be relevant. I did find it tough meeting with my supervisors on Zoom and working from home, but my supervisors were incredibly supportive of me and were amazing at providing feedback. Ultimately, I think that an Honours year is a great opportunity to test out medical research within a supported environment. My advice would be to pursue a project that you are interested in and not stress too much about how it relates to your future career.

### ABSTRACT

#### Background

Despite significant advancements in palliative care, some patients still suffer greatly at the end of life. There are a range of treatment options available to alleviate suffering in dying patients, some of which elicit significant moral controversy. Terminal sedation [TS] refers to the use of sedatives in dying patients until the point of death. The capacity for sedatives to relieve suffering must be weighed against two key risks: unconsciousness until the point of death and the potential for hastening of death.

The following limits are commonly applied to TS: (1) symptoms should be refractory (all other treatment has failed), (2) sedatives should be administered proportionally to symptoms, and (3) the patient should be imminently dying. Expanded terminal sedation [ETS] describes the use of sedation at the end of life which extends beyond one or more of these limits. That is, symptoms are not refractory, and/or sedatives are administered rapidly (i.e. not proportionally), and/or death is not imminent.

#### Body

This thesis investigates the moral permissibility of expanded terminal sedation. I first review the moral reasoning behind each of the individual limits applied to TS. I find that the arguments for the limits do not clearly outweigh the arguments against. At least in some circumstances, the practice of ETS is morally permissible. The literature is yet to explore exactly what these circumstances look like.

Using theoretical argumentation, I describe some of the circumstances in which ETS is morally permissible. I contextually limit the discussion to Victoria, Australia; a jurisdiction where assisted dying is legal. I argue that patients have a right to access means of suffering relief at the end of life, including ETS. In circumstances where sedation is clinically appropriate to relieve

suffering, it should be made available to the patient, even if the patient does not meet the traditional criteria for TS.

I argue that ETS is morally permissible in the following end of life scenarios in Victoria: (1) cases of non-refractory suffering where earlier treatment options (e.g. opioids) are likely to fail, (2) the use of rapid sedation where gradual sedation is likely to be ineffective or where unconsciousness is a clinically desirable outcome, (3) the patient has less than six months to live and meets all other criteria for assisted dying in Victoria, and (4) the patient has less than six months to live, is suffering intolerably, lacks decision-making capacity, and sedation is considered to be in their best interests (based on their known values and clinical expertise).

#### Conclusion

This thesis explores the expansion of TS in the context of current assisted dying laws in Victoria, Australia. Whilst remaining two distinct practices, there is scope for some degree of convergence between the criteria for assisted dying and the criteria for ETS. Dying patients who are ineligible for TS (or even assisted dying) should not be left to endure their suffering. ETS provides one means to bridge this gap.



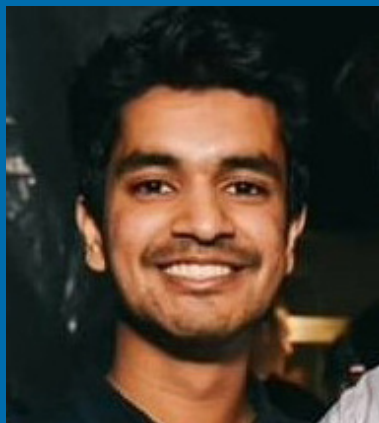
## Breast Arterial Calcification: A Novel Marker for Cardiovascular Disease in Women

Supervisor Names and Institute Affiliations:

Supervisors: A/Professor Nitesh Nerlekar, Dr Adam Brown

Monash Heart, Monash Health

Monash University, Melbourne



I undertook my BMedSc(Hons) at Monash Heart after completing fourth year medicine. Having developed a keen interest in cardiology in 3rd year, I thought a BMedSc(Hons) would provide me with an excellent opportunity to further my understanding of the field while developing research skills. I was fortunate enough to get the opportunity to work on a wonderful project looking at a better way to identify cardiovascular risk in women using mammograms. The project allowed me to get involved in several aspects of research from obtaining ethics approval to writing up manuscripts; invaluable skills which I will no doubt use in the future. Despite not being able to conduct our originally planned prospective cohort study due to the COVID-19 pandemic, I was thankfully supported by my supervisor who conceived alternate studies I could conduct as part of my Honours year. I had a thoroughly enjoyable year and look forward to pursuing a career as an academic-clinician. I would definitely recommend doing a BMedSc(Hons) for anyone interested in getting involved in research.

If you have any questions about my project or the BMedSc(Hons) experience, please feel free to email me at [vgoe0001@student.monash.edu](mailto:vgoe0001@student.monash.edu).

## ABSTRACT

### Background

Breast arterial calcification (BAC) assessed on screening mammography has been reported as a surrogate marker for cardiovascular disease (CVD) in women. Current risk markers underestimate risk in women, thus, BAC presents an exciting opportunity in cardiology.

Despite significant interest in BAC, there exists several evidence gaps. These include, poor understanding of BAC prevalence, its determinants and the mechanism by which it associates with atherosclerosis. Atherosclerosis and BAC have been associated with inflammation; therefore, an inflammatory link remains possible. Additionally, the value of BAC, beyond CVD risk factors, in predicting incident CVD has not been well investigated.

### Objectives

1. Evaluate the contemporary literature reporting BAC
2. Investigate inflammation as a mechanism linking BAC with CVD, using epicardial adipose tissue (EAT) and peri-coronary adipose tissue (PCAT) as surrogate inflammatory biomarkers
3. Investigate association of BAC with incident CVD and determine its value for CVD risk stratification

### Methods

We conducted three studies to address our objectives.

1. A systematic-review and meta-analysis including all research articles reporting BAC. Results of studies were combined to generate pooled results and determine the associations of BAC with CVD.
2. A cross-sectional study of women who previously underwent digital mammography and coronary computed tomography angiography (CCTA) at Monash Health. Mammograms were reviewed for BAC. Coronary artery disease (CAD) was defined as the presence of any coronary atheroma on CCTA. EAT and PCAT were evaluated using validated semi-automated software.
3. A retrospective cohort study of women who underwent digital mammography and

invasive coronary angiography (ICA) at any future timepoint. Mammograms were reviewed for BAC. ICA reports were reviewed with obstructive CAD defined as luminal stenosis  $\geq 50\%$  within a coronary vessel.

### Results

1. There were 77 studies (104,710 patients) included. Pooled BAC prevalence was 22% (95%CI:19-25%) with cumulatively increasing prevalence annually. Significant BAC predictors were age, hypertension, diabetes, hypercholesterolemia ( $p < 0.01$ ). BAC was associated with CAD (OR 2.65, 95%CI:2.17-3.23,  $p < 0.01$ ) and non-coronary vascular disease (ES 0.80, 95%CI:0.51-1.09,  $p < 0.01$ ). BAC associated with incident cardiovascular events (HR 1.61, 95%CI:1.11-2.32,  $p = 0.001$ ).

2. BAC was present in 37 (24%) patients. BAC-positive patients were older with greater hypertension and dyslipidemia ( $p < 0.01$ ). EAT volume was significantly higher in BAC-positive individuals ( $110.2 \pm 40\text{mL}$  vs  $94.4 \pm 41\text{mL}$ ,  $p = 0.02$ ), however, this difference was not significant after adjusting for confounders ( $p = 0.26$ ). There were no differences in either EAT density nor PCAT attenuation based on BAC ( $p > 0.05$ ). Both BAC and EAT volume were independently associated with CAD and CVD risk ( $p < 0.05$ ).

3. BAC was prevalent in 13 (29%) patients with a median follow-up time of 480 days (IQR 210-1161). BAC was an independent predictor of incident CAD (adjusted RR 3.12, 95%CI:1.67-5.81,  $p < 0.001$ ). ROC analysis demonstrated that BAC provides incremental value beyond cardiac risk factors when used for CAD risk prediction ( $p = 0.03$ ).

### Conclusion

Our results demonstrate that BAC is an increasingly prevalent marker, sharing significant associations with CVD. BAC appears to provide incremental value beyond CVD risk factors when incorporated with CVD risk algorithms. Mechanistic understanding of this association is poorly explained using dynamic inflammatory surrogates, and instead, BAC may be a representation of a lifetime exposure to CVD risk factors.

# Madeline Laidley Green

## Feasibility of Right Brachiocephalic Vein Access for the Resuscitation of Shocked Adult Trauma Patients

### 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

Doctor Simon Hendel – Head of Trauma Anaesthesia, Alfred Health; Lecturer, Department of Anaesthesiology and Perioperative Medicine, Central Clinical School, Monash University; Clinical Research Fellow, National Trauma Research Institute



I completed my BMedSc(Hons) between 4D and 5C at the National Trauma Research Institute (NTRI). I'm interested in critical care and saw this year as an opportunity to gain exposure in this area while I began to explore the world of research. I developed my project in conjunction with Professor Fitzgerald at the NTRI to create a research year that allowed me to gain research skills and simultaneously be involved in the clinical environment. I believe that this allowed me to see how research integrates with and influences clinical practice.

I am so grateful for the guidance of my supervisors, who helped me navigate planning and completing my research projects. I've learnt an enormous amount about research and developed my critical thinking skills which will benefit my clinical practice in the future. I feel much better placed to get involved in future research projects.

This year has (somewhat unexpectedly) ignited a passion for research that I hope to carry into my medical career. I highly recommend the year for anyone who is interested in integrating research with clinical practice in the future!

Happy to be asked any questions:  
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## ABSTRACT

### Background

Severe blood loss (haemorrhagic shock) is the most common cause of preventable death after injury. Management includes haemorrhage control and replacing the lost circulating blood volume, which requires venous access. Obtaining intravenous access in trauma patients is challenging due to circulatory collapse in shock. This thesis explores a novel solution to obtaining venous access in trauma resuscitation - the right brachiocephalic vein (RBCV).

### Aims

This thesis aimed to investigate the feasibility of accessing the RBCV in shocked adult trauma patients.

This was done by:

- Investigating RBCV characteristics in major trauma patients
- Proposing a visualisation and access technique based upon biometrics
- Assessing the collapse of the RBCV in shocked trauma subjects

### Methods and Results

#### RBCV Characteristics in Major Trauma Patients

Methods: A retrospective review of 46 major trauma patients was conducted. Computerized Tomography (CT) scans of 25 shocked and 21 non-shocked adult trauma patients (on arrival to ED) were analysed to investigate if the RBCV collapses in shock. The diameter of the RBCV, right internal jugular vein (RIJV) and inferior vena cava (IVC) were measured.

Results: The RBCV was found to have a larger diameter than the RIJV and IVC in both shocked and non-shocked subjects. Whilst a statistically significant difference in RBCV diameter between shocked and non-shocked subjects was found ( $p < 0.05$ ), this difference was not large enough to be clinically significant. No statistically significant difference was found for the RIJV and IVC. Further study is required as subjects may not have been shocked at time of CT scan.

### Development of Visualisation and Access Method

Methods: Biometrics were analysed from CT scans of trauma patients to propose a landmark-based technique for ultrasound visualisation and venous access of the RBCV with the head in the neutral position (as required for trauma resuscitation).

Results: The supraclavicular fossa adjacent to the lateral border of the attachment of the clavicular head of the right sternocleidomastoid muscle (RSCM) was selected as the surface landmark for ultrasound probe placement and needle skin puncture. The left anterior superior iliac spine (LASIS) was selected as the directional landmark for probe angulation and needle advancement.

The proposed landmark-based technique was trialled on two cadavers by five Trauma Consultants, who all had successful attempts at gaining access.

### Assessing the RBCV in Shock

Methods: A prospective cohort study was designed to assess for potential collapse of the RBCV in shocked adult trauma patients during trauma resuscitation. Ultrasonography was used to visualise the RBCV and measure the diameter of the vein pre and post resuscitation.

Results: Due to COVID-19 restrictions, two of the planned 20 subjects have been recruited. Preliminary findings suggest that the RBCV does not collapse in severely shocked trauma patients. The proposed landmark-based technique allowed successful ultrasonographic visualisation of the RBCV in 60 seconds.

### Conclusion

Venous access using the RBCV is likely to be feasible, however further research is required. This new method of venous access may enhance resuscitation of haemorrhagic shock and lead to improved outcomes after injury.

# Ahinsa Gunatilaka

## The protective effect of maternal immunisation on preterm birth and stillbirth: does timing or number of vaccines given together matter?

Supervisor Names and Institute Affiliations:

Professor Michelle Giles – Department of Obstetrics and Gynaecology, Monash Health

Dr Daniel Rolnik – Department of Obstetrics and Gynaecology, Monash Health



I completed the BMedSc(Hons) in 2021 after completing my fourth year of Medicine as I wanted to learn more about medical research in a more formal and structured way, and it seemed like a good option after the challenging year that 2020 presented. The Honours year had its own set of challenges, in particular adjusting to a more self-directed style of learning than I was used to. Overall, I came to enjoy the flexibility that the year provided, and it was very satisfying to see all the work come together by the end. Throughout this process I was able to develop and refine my critical thinking and academic writing skills, which will be useful for understanding and contributing to the literature during my future career in Medicine. I would be happy to be contacted by any future BMedSc(Hons) students thinking of undertaking a project in Obstetrics & Gynaecology.

### ABSTRACT

#### Background

Preterm birth (PTB) and stillbirth are responsible for a large proportion of neonatal and early childhood morbidity and mortality, worldwide. Rates of both outcomes are higher in Australian Indigenous populations, and globally, most cases occur in low-middle income settings. In Australia, pertussis and influenza vaccines are recommended in pregnancy for their disease-specific benefits. Some studies have suggested possible associations with reductions in PTB and stillbirth, although the evidence is conflicting.

#### Aims

This study had three aims: i) to determine whether maternal vaccination in this study population showed a protective effect against preterm birth and stillbirth, ii) to determine whether any association with reduced rates of adverse outcomes remained when timing of vaccination was accounted for, and iii) to explore any difference in magnitude of protection when multiple vaccines were given simultaneously, compared to when one or no vaccines were given.

#### Methods

This was a retrospective data linkage study using data from Monash Health, Victoria from 2017-2020. Pregnancy, vaccine exposure, and birth information was retrieved from the Birthing Outcome System (BOS) for all deliveries in this period, and specific dates of vaccination were obtained from the Immunisation Program System (ImPS). These datasets were merged, and the study population included 7,292 women with known dates of vaccination, and 2,178 unvaccinated women. Unadjusted incidence rates were calculated for vaccinated and unvaccinated groups per 1,000 person-weeks. To account for timing of vaccination, immortal time and survivorship bias, Cox proportional hazards models were used to determine unadjusted and adjusted

hazard ratios, analysing vaccines as time-dependent exposures. To calculate rates of outcomes when multiple vaccines were given, Poisson regression models were used, which also account for the time-dependent nature of vaccination.

#### Results

The unadjusted incidence rate of PTB <37 weeks amongst vaccinated women was lower than that of unvaccinated women (7.2 vs. 12.8 per 1,000 person-weeks,  $p < 0.001$ ). For stillbirth, the incidence rate was lower in the vaccinated group compared to the unvaccinated group (0.2 vs. 1.9 per 1,000 person-weeks,  $p < 0.001$ ). Cox proportional hazards models showed an adjusted hazard ratio of 0.76 (95%CI 0.61,0.92;  $p < 0.004$ ) for PTB in the pertussis vaccine group. There was no significant difference in stillbirth in the pertussis vaccine group (aHR 0.54; 95%CI 0.22,1.32;  $p < 0.18$ ). The influenza vaccine group showed non-significant adjusted hazard ratios for both outcomes. Poisson regression demonstrated that for PTB and stillbirth, incidence rates of giving both vaccines together were lower than those of giving no vaccine or influenza vaccine only, but similar to the rates if only pertussis vaccine was given.

#### Conclusion

Few studies have adequately accounted for timing of vaccination, or combined influenza and pertussis vaccines. This study demonstrates a protective association of influenza and pertussis vaccines against PTB and stillbirth in this study population, but shows that when adjusted for timing of vaccination, the protective effect is reduced. For both outcomes, giving both vaccines had a similar effect to giving pertussis vaccine only. These findings, and findings of subsequent larger-scale studies, may have implications for maternal vaccine recommendations to reduce rates of PTB and stillbirth.



# Uni Liuxin Han

## Understanding the Growth and Development of Children Born in the COVID-19 Pandemic

Supervisor Names and Institute Affiliations:

A/Professor Rachel Hill<sup>1</sup>

Professor Suresh Sundram<sup>1,2</sup>

1.Department of Psychiatry, School of Clinical Sciences, Monash University

2.Monash Medical Centre, Monash Health, Melbourne, Australia



Hello! My name is Uni and I undertook my Honours year with the Department of Psychiatry at the School of Clinical Sciences. Honours was a fantastic opportunity as a student to delve into the crazy and fascinating world of research, and to gain a host of invaluable skills. As the background for my project sprung from the intersection of behavioural neuroscience and molecular psychiatry, I found I was able to read very broadly about the various ongoing lines of inquiry that aim to unravel the mysteries of the mind, and the complexities underlying the pathogenesis of mental illness. It was also very rewarding to have the challenge of working with big data using bioinformatic platforms and tools.

One of the highlights of Honours is the people you get to meet along the way - I was extremely fortunate to be welcomed into an amazing laboratory group and I am incredibly grateful for the support from my supervisors, and all the postdoctorates and fellow students!

If anyone reading this is interested in undertaking an Honours project in psychiatry, you are very welcome to contact me at uni.h@protonmail.com with any questions.

## ABSTRACT

### Background

The COVID-19 pandemic has created an unprecedented set of global health challenges. Given the novelty of the SARS-CoV-2 virus, the short, medium, and long-term risks of SARS-CoV-2 infection are poorly understood. Historically, it has been well documented that maternal infection during pregnancy, even in the absence of vertical transmission, is linked to increased risk of neurodevelopmental disorders in offspring. Moreover, this association has been studied in animal models, which have shown that maternal infection and subsequent immune activation results in reproducible behavioural deficits, as well as neurochemical, neuroanatomic and neurophysiologic abnormalities. Taking this together, there is a pressing need to monitor and characterise the developmental trajectories of children whose mothers were exposed to SARS-CoV-2 during the COVID-19 pandemic. Ongoing lines of neuroscientific inquiry support further investigation of the molecular and biological mechanisms underlying how risk is conferred in utero to offspring.

### Aims

1. To assess and characterise the short-term impact of maternal exposure to SARS-CoV-2 during pregnancy on the neurodevelopment of offspring
2. Investigate potential underlying biological mechanisms by which infection with SARS-CoV-2 may disrupt neurodevelopment

### Method

This matched prospective cohort study enrolled 9 mother-infant dyads (n=4 COVID-exposed women and infants and n=5 unexposed women and infants). Infant anthropometry was collected at 3 months and retrospectively from birth records. Early neurodevelopmental outcomes were measured using the Hammersmith Infant Neurological Exam, Vineland-3 and

Sensory Profile-2. We collected buccal swab specimens from SARS-CoV-2 exposed and control infants, and after extraction and bisulphite conversion of DNA, compared the methylation profiles of exposed and control infants using the Infinium MethylationEPIC microarray.

### Results

We found that there were no statistically significant associations between SARS-CoV-2 exposed infants (n=4) and matched controls (n=5) in terms of early growth and neurodevelopmental outcomes at 3 months. There were significant differences in the methylome of SARS-CoV-2 exposed infants compared to the control cohort. We found one differentially methylated position (cg06758191), located in the gene body of AFAP1 that was hypomethylated in the SARS-CoV-2 exposed cohort that was significant after multiple correction ( $p < 0.00083$ ). We also identified two differentially methylated regions that were significant after multiple correction; a hypomethylated intergenic region located in chromosome 6p proximal to the genes ZP57 and HLA-F ( $p < 0.004$ ), and a hypomethylated region in the promoter and body of the gene GAREM2 ( $p < 0.036$ ). Gene ontology enrichment analysis revealed differential methylation in genes corresponding to pathways relevant to neurodevelopment and synaptic signalling.

### Conclusion

While significantly limited by our small sample size, we found that the early growth and neurodevelopmental outcomes in our SARS-CoV-2 exposed cohort have been largely favourable. At this timepoint, we are unable to draw conclusions about whether the methylomic changes we identified do confer increased neurodevelopmental risk. However, our results support that MIA may significantly alter the foetal methylome, which may in turn exert long-lasting effects on gene expression and phenotype.

# Jessica Hinh

## Management Practices for Pneumonia in Low- and Middle-Income Countries: An Audit of Médecins Sans Frontières Practices in 9 Countries

Supervisor Names and Institute Affiliations:

Geoff Chan –

- School of Public Health and Preventative Sciences, Monash University
- Burnet Institute, Melbourne

Dr Philipp du Cros –

- Burnet Institute, Melbourne
- Médecins Sans Frontières-Operational Centre Amsterdam



I knew pretty early on during med school that I wanted to do a BMedSc(Hons) between fourth and final year to try something a little bit different and to learn some research skills. I had also developed a keen interest in global health, and wanted to further explore this through research.

I had the great privilege of delving into research and global health under the supervision of Geoff and Phil at the Burnet Institute. I undertook a mixed-methods study which gave me invaluable experience in the analytical processes of both qualitative and quantitative research. The Burnet also fostered a wonderful student culture that thoroughly enhanced my experience, which included a mentoring program, casual job opportunities, and a student conference

It should be acknowledged that completing this year was undoubtedly tough. Be prepared for periods of stress (especially the month before your thesis is due!), late nights, and lots of coffee. However, the invaluable skills, experiences, and support gained have made it all worth it!

For anyone considering doing a BMedSc(Hons) in a similar area, please feel free to contact me:  
jhin0001@student.monash.edu

## ABSTRACT

### Background

Pneumonia remains one of the leading causes of death worldwide and its disease burden disproportionately impacts those in low- and middle-income countries (LMICs). Therefore, much effort is still required to drastically reduce rates of morbidity and mortality from pneumonia. Although many initiatives, strategies, and guidelines have been circulated on how to address this issue, the slow decline in progress highlights the 'know-do' gap between evidence-based recommendations and the practices occurring in resource-limited settings. We aimed to describe pneumonia practices - the use of guidelines, diagnosis and management, referrals, and oxygen therapy – as well as challenges and barriers faced by healthcare workers (HCWs) within Médecins Sans Frontières (MSF) projects.

### Method

We conducted a multi-country mixed-methods study amongst MSF HCWs using structured surveys and semi-structured interviews. The study was conducted between June and August 2021 in 9 countries where MSF projects were offering routine pneumonia care. Quantitative data was descriptively analysed for frequency and proportion using R, while qualitative data was thematically analysed. Data from the quantitative and qualitative components of the study were collected and analysed separately, but interpreted together.

### Results

32 HCWs participated in the survey, and 10 HCWs were interviewed. MSF clinical guidelines were reportedly used by 96.6% of inpatient and outpatient HCWs for children under the age of 5. However, perception of guideline adherence varied between sites. 41.2% of inpatient HCWs reported that routine investigations were not conducted within their facility, highlighting a reliance

on clinical diagnosis within these resource-limited settings. 90% of outpatient HCWs cited amoxicillin as a first-line drug used for patients with non-severe pneumonia. Oxygen concentrators were available in all health facilities, but the number of patients who could be provided with oxygen varied between sites. Four themes around the challenges and barriers experienced by MSF HCWs were identified from the qualitative data: geopolitical and organisational structures, time constraints and workload, resource limitations, and need for improved clinical knowledge and acumen.

### Conclusion

We found key gaps in pneumonia practices within MSF operations. Whilst some of these were consistent across all sites, many findings were not homogenous across facilities, suggesting variation in the factors underpinning each site's practices. Improved resource allocation, strengthening Ministry of Health (MoH) collaboration and increasing training in key areas are among measures which could improve quality of care. This study will inform recommendations for MSF's overall approach to pneumonia services.

# Patrick Yi Hinh

## Non-acid and Bile Reflux Following Bariatric Surgery

### Supervisor Names and Institute Affiliations:

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Professor Wendy Brown. Department of Surgery, Central Clinical School, Monash University, The Alfred Hospital, Melbourne, Australia. Bariatric Surgical Unit, Department of General Surgery, The Alfred Hospital, Melbourne, Australia.



Hi, my name is Patrick and I had the pleasure of undertaking my BMedSc(Hons) year with the Department of Surgery at The Alfred Hospital. I had developed a keen interest in surgery throughout my clinical placements and this project allowed me to explore a different aspect of the specialty not often seen in the hospital. Not only were the clinical experiences invaluable, but the research skills I developed under the guidance of my supervisors will undoubtedly be an aspect of this Honours year that I take with me into the future. Despite the challenges that research may bring, along with less expected pandemic ones, I believe that the Honours program is a deeply enriching experience that serves to complement medical education.

## ABSTRACT

### Background

Bariatric surgery is an increasingly selected option for the management of obesity globally and in Australia. However, reflux of injurious non-acidic stomach contents, in particular bile, is suspected of complicating surgeries, with potential risk of reoperation and cancerous development. Presently, there is limited understanding of the nature of non-acid reflux following bariatric surgery, with descriptive studies identifying whether non-acid and bile reflux are genuine entities following bariatric surgery having not yet been performed.

We aimed to describe key pathophysiological mechanisms involved in the development of bile reflux following bariatric surgery, characterise these reflux events, and identify potential corrective procedures for this disease.

### Method

A total of four studies were conducted. Post-bariatric surgical patients ( $n=23$ ) were identified from a prospectively maintained database of bariatric surgical patients from The Alfred, The Avenue and Cabrini. Protocolised hepatobiliary iminodiacetic acid scintigraphy (HIDA), nuclear scintigraphy, high-resolution oesophageal manometry, and 24-hour ambulatory pH and impedance monitoring data was collected from these patients. The first study compared our postoperative group to a cohort of 10 obese controls. The second trial examined the physiological impact of sleeve gastrectomy (SG) on biliary circulation in a separate prospective group of 7 patients. For the third study, detailed physiological examination of the mechanisms underlying patterns of bile reflux was investigated in 8 post-bariatric surgery patients. In the fourth trial, 10 separate SG patients underwent one anastomosis gastric bypass (OAGB) revision as a potential corrective procedure for their reflux symptoms.

### Results

Bile reflux was significantly increased in the postoperative cohort ( $n=13$ , 56.52%)

compared to the anatomically normal obese controls ( $n=0$ , 0.0%),  $p=0.0022$ . A greater proportion of radioactivity was observed in the gastric pouch in patients with bile reflux compared to the control group (8.18% (5.24-16.64) vs 5.34% (2.26-7.26),  $p=0.0249$ ). Non-acid reflux followed a pattern of post-prandial predominance with an increase in number of events in the post-prandial phase compared to the fasting phase (4 (3-5) vs 0 (0-2),  $p=0.0469$ ). These non-acid reflux events were associated with elevated intragastric pressure (IGP) with a median pressure of 12.13 (5.270-18.71)mmHg.

Gastrointestinal transit time was decreased by OAGB conversion with proportions of radiolabelled food retained in the oesophagus and stomach immediately after eating significantly lower following OAGB than before (1.55% (1.30-2.08) vs 3.02% (1.98-5.60), and 31.38% (24.42-48.54) vs 62.01% (54.70-71.61),  $p=0.0273$  and  $p=0.0117$ ). A conversely increased proportion of radiotracer was identified in the post-OAGB small bowel compared to pre-conversion SG anatomy (68.19% (48.84-71.94) vs 28.80% (15.55-39.02),  $p=0.0078$ ). Reflux frequency tended to be lower following OAGB conversion compared to pre-conversion but was not statistically significant (0 (0-0) vs 2 (0-8),  $p=0.0625$ ).

### Conclusion

We found that bile reflux was significantly increased following bariatric surgery with greater portions of radioactivity in the gastric pouch. Novel patterns of non-acid reflux have been identified, with significantly more reflux episodes in the post-prandial period, along with key association with an increased IGP. Reflux tended to be improved following OAGB conversion, likely due to reduced gastrointestinal transit time and a subsequent reduction in IGP.



# Fransesco Bernado Hubert Jonathan

## The Role of Complementary Medicine in Type 2 Diabetes: An Evidence-Based Study on the Clinical Efficacy of Chromium Picolinate

Supervisor Names and Institute Affiliations:

A/Professor Basia Diug and Professor Jane Banaszak-Holl

School of Public Health and Preventive Medicine,

Faculty of Medicine, Nursing and Health Sciences



Hello! My name is Hubert, and I am a 4th year medical student from Jakarta, Indonesia. I made the decision to do my honours year in 2021 to practice and enhance my research skills before I enter clinical rotations the following year. Metabolic disease, especially diabetes, has been a large interest of mine besides paediatrics. My project sought to evaluate the effectiveness of a complementary medicine that is targeted towards type 2 diabetic patients. It is an interesting topic as there are many marketed products that lack high-quality evidence to back them up. As a future healthcare professional, I believe it is important for patients to get the best out of their medications and not be deceived by false or misleading advertising claims.

I have gained so much new knowledge and learnt new techniques throughout my honours year and this experience has opened me to better ways of thinking and problem-solving. I am grateful for my time and experience learning under Monash University and for future students, I believe that you can learn a lot during your honours year. Honours can be challenging but it is better to maintain good and active communication with your supervisors and research peers than being helpless.

### ABSTRACT

#### Background

Type 2 Diabetes mellitus (DM) is a chronic non-communicable disease that has been increasingly prevalent over the past decade, characterised by abnormally high levels of blood glucose due to insulin resistance. As a result, diabetic patients are faced with the risk of life-threatening complications that may affect their quality of life. Therefore, the management of diabetes, both lifestyle modifications and pharmacological interventions, plays an important role in controlling their blood glucose levels.

Complementary medicines have a large market, and many products are sold with claims of controlling blood glucose levels. One of the popular active ingredients is chromium picolinate, which is claimed to enhance insulin sensitivity and maintain healthy blood glucose levels.

#### Aim

This study aims to evaluate the evidence on the clinical efficacy of chromium picolinate supplementation for controlling blood glucose levels in adults with type 2 DM.

#### Method

A systematic review based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was conducted by identifying records from OVID Medline, Cochrane Central, and SCOPUS databases. Studies were included based on the eligibility criteria on the effectiveness of chromium picolinate supplementation as a complementary medicine in controlling blood glucose levels in adults with type 2 DM. Studies were included if they are RCTs with type 2 diabetic participants taking chromium picolinate as the intervention and have blood glucose level outcomes (either fasting, or postprandial, or both). The risk of bias was also assessed according to the Cochrane Collaboration's tool for assessing risk of bias in randomised trials.

#### Results

8 randomized controlled trials (RCT) were included after satisfying the eligibility criteria. 3 studies reported both fasting and postprandial blood glucose levels while the remaining 5 only reported fasting blood glucose levels. 7 studies reported significant reduction in fasting blood glucose levels and 3 studies reported significant reduction in postprandial blood glucose levels after the intervention. 1 study did not report any significant impact of the chromium picolinate supplementation towards the fasting blood glucose levels. Based on the included studies, chromium picolinate is efficacious in controlling the blood glucose levels of type 2 diabetic patients.

#### Conclusion

Chromium picolinate may be effective in controlling the blood glucose levels of diabetic patients. However, the optimal dose and safety profile, both in short term and long-term use, are yet to be investigated further.

# Muhammad Ikhsan Nur Karim

## Shape Changes in the Dentate Nucleus in Individuals with Friedreich Ataxia Assessed Using Quantitative Susceptibility Mapping

Supervisor Names and Institute Affiliations:

Dr Ian Harding, Dr Louisa Selvadurai, Dr Will Khan

Department of Neuroscience, Central Clinical School, Monash University



Hello! I am a medical student from Universitas Indonesia who is taking the Monash BMedSc(Hons) program in 2020. It was a wonderful experience doing my research project in the Department of Neuroscience in the Central Clinical School, even though I spent the whole program doing research remotely from Jakarta. I learned a lot about conducting excellent research in this program, starting from constructing a research design and proposal until finalising a research paper for publication.

I am beyond grateful to have a fantastic supervisor and co-supervisors who guide me through my honours year, taught me some neuroimaging techniques, and gave me valuable lessons on academic writing and presentation. Thank you for the remarkable opportunity!

### ABSTRACT

#### Background

Friedreich ataxia (FRDA) is a progressive movement disorder and the most common inherited spinocerebellar disease, caused by an abnormal GAA trinucleotide multiplication in the FXN gene. Individuals with FRDA have nervous system pathology, which in the brain primarily impacts the dentate nucleus, leading to several clinical symptoms, including poor balance and uncoordinated movement. Currently, there is no validated treatment and measurement of the disease progression relies on clinical assessment. More sensitive and specific biomarkers of disease expression and progression of FRDA are required to improve treatment monitoring.

Volume reduction of the dentate nucleus has been previously examined using a neuroimaging approach called quantitative susceptibility mapping (QSM). Investigations of the dentate nucleus in FRDA undertaken so far have only looked at the structure as a whole, but there is preliminary evidence that atrophy may be non-uniform. Shape analysis provides a novel examination of dentate nucleus structure by measuring regionally-specific changes.

This study aimed to evaluate the regional shape changes in the dentate nucleus in individuals with FRDA relative to healthy controls. This study also aims to investigate the correlation between shape changes in the dentate nucleus and the clinical severity, disease duration, age at onset, and GAA repeat length among individuals with FRDA.

#### Method

This study uses a cross-sectional study design. The dentate nuclei were manually traced using QSM images from 51 people with FRDA and 47 healthy controls. Shape analysis of the dentate nucleus was conducted using a validated approach implemented in a publicly available toolbox (SPHARM-PDM). Between-group comparisons and correlational analyses of

the shape changes with clinical data (clinical severity, disease duration, age at onset, and GAA repeat length) were performed, with false-discovery rate (FDR) corrections.

#### Results

Statistically significant shape changes relative to controls were found in the rostral and caudal portions in both the left and right dentate nuclei in the FRDA cohort ( $pFDR < 0.05$ ). Atrophy in the dentate nucleus correlated significantly with clinical severity and disease duration in a more limited area of the dorsal surface on the left dentate nucleus ( $pFDR < 0.05$ ). No statistically significant correlations with age at onset and GAA repeat length were found ( $pFDR > 0.05$ ).

#### Conclusion

Individuals with FRDA showed a heterogeneous pattern of regional shape changes in the dentate nucleus, which were associated with measures of disease progression. These regionally-specific changes in the dentate nucleus might provide a basis for disease progression markers that are able to more precisely monitor neurodegeneration in people with FRDA.

# Shaveen Kariyawasam

## Quality of Life of Patients with Primary Aldosteronism treated with Mineralocorticoid Receptor Antagonists and Epithelial Sodium Channel Inhibitors

Supervisor Names and Institute Affiliations:

Dr Jun Yang, Hudson Institute of Medical Research

A/Professor Morag Young, Baker Heart and Diabetes Institute

Professor Michael Stowasser, University of Queensland Diamantina Institute



I undertook my research project at the Hudson Institute Centre for Endocrinology and Metabolism. I chose to complete a BMedSc(Hons) year as I wanted to experience what proper research was like before joining the medical workforce as a junior doctor. This year has been a very productive and fulfilling year for me, and I've learnt a lot about the ins and outs of medical research. Dedication to solely focus on research really gave me the time to develop new skills with the guidance of leading research clinicians and scientists. Research is rarely a straightforward process, and throughout the year, I had to navigate my way across newly arising challenges and learnt to be very adaptive in the process. This year has definitely shown me that research is something I want to continue to be involved in and has only further piqued my interest in the area. Some advice I would give to future students is to speak about the feasibility of your project with your supervisor(s), to begin your ethics application as soon as possible, and to use this year to further explore other aspects of your life you might not have time for in a few years.

Feel free to contact me about my project, or my experiences in research as a medical student.

### ABSTRACT

#### Background

Primary Aldosteronism (PA) refers to a collection of disorders caused by the excessive production of the hormone aldosterone. Untreated, hypertension caused by PA may lead to cardiovascular complications and a significantly impaired Quality of Life (QOL). Measurement of QOL therefore forms an integral part in assessing the impact of treatment and disease from the perspective of the patient. While prior studies compared the QOL of patients with primary aldosteronism who have undergone surgical treatment and those on pharmacological treatment, there is little published data comparing patients on different pharmacological agents and their effect on QOL. The varying mechanisms of action, side effect profiles and efficacy of different medications may contribute to different QOL outcomes.

#### Method

This study aimed to assess and compare QOL outcomes among patients treated with mineralocorticoid receptor antagonists (MR antagonist, spironolactone or eplerenone) and those treated with epithelial sodium channel inhibitors (ENaC inhibitor, amiloride). This study also compared QOL outcomes among patients treated with spironolactone and eplerenone.

An online survey was distributed through international PA patient support groups to assess patient demographics, baseline health status and QOL. Using the validated 36-Item Short-Form Health Survey (SF-36), as well as a PA-specific questionnaire, we compared the QOL outcomes of patients with PA treated with MR antagonists and ENaC inhibitors, in addition to comparing the two MR antagonists, spironolactone and eplerenone.

#### Results

Seventy-nine patients with medically managed PA (45 taking spironolactone,

mean age  $36.3 \pm 12.1$ ; 28 taking eplerenone, mean age  $36.1 \pm 12.4$ ; 6 taking ENaC inhibitor, mean age  $35.3 \pm 6.6$  years) completed the survey.

There were no statistically significant differences in the body mass index, blood pressure, total number of medications and total number of comorbidities between the treatment groups.

SF-36 scale scores of patients taking MR antagonists tended to be higher in the domains of Role-Emotional (role limitations due to emotional problems) and Mental Health compared to those taking ENaC inhibitor (62.1 vs 44.4, 61.6 vs 53.3) but lower in the domain of General Health (37.5 vs 52.5). However, none of these differences reached statistical significance.

The PA-specific QOL questionnaire demonstrated a tendency to higher QOL in the domain of "Fluid balance" in patients taking MR antagonists, but without being statistically significant.

No significant differences were observed in SF-36 domains or results of the PA-specific questionnaire between patients taking spironolactone versus eplerenone. After controlling for confounders however, spironolactone was associated with a significantly poorer Mental Component Score than eplerenone.

#### Conclusion

The results of this study reflected that treatment with MR antagonist leads to comparable QOL outcomes with ENaC inhibitor, with trends observed that need to be further explored with a larger sample size. Despite leading to comparable SF-36 domain scores, treatment with eplerenone was associated with a higher mental health summary score when compared to treatment with spironolactone, following adjustment for confounding factors.



# Donna Lei

## Temperature monitoring device to decrease hypothermia-related escalation of care in low birth weight babies: a randomised controlled trial

Supervisor Names and Institute Affiliations:

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<sup>2</sup>Monash Newborn, Monash Children's Hospital, Melbourne, Australia

<sup>3</sup>The Ritchie Centre, Hudson Institute of Medical Research, Melbourne, Australia



I did my BMedSc(Hons) after 4th year as an opportunity to take a break from clinical placement and to learn more about research. I have always been interested in pursuing paediatrics as a future specialty and therefore chose a project in neonatology, within the Department of Paediatrics at Monash Medical Centre. Despite the many challenges along the way, I thoroughly enjoyed my year and found it to be very rewarding. I would highly recommend the Department of Paediatrics for future BMedSc(Hons) students, as the support provided by staff and fellow students made the year much more enjoyable.

I chose to do a randomised controlled trial to challenge myself and because I was more interested in clinical projects than lab-based projects due to the patient interaction involved. Conducting an RCT (and any other prospective study) comes with many ups and downs, especially with recruiting and following up participants. However, this year has taught me that these challenges are an innate part of research, and even the most experienced researchers face setbacks. I am happy to be contacted about any questions regarding conducting an RCT or BMedSc(Hons) in general.

### ABSTRACT

#### Background

Low birth weight (LBW) and small for gestational age (SGA) babies are at a high risk of hypothermia during the neonatal period, which is associated with significant morbidities and mortality. Hence, accurate methods for detecting hypothermia are vital to addressing this issue. The BEMPU TempWatch allows for continuous temperature monitoring of neonates for the first month of life. Existing studies on the utility of the TempWatch have all been conducted in low- and middle-income countries. Its utility in a high-income setting has not been evaluated. The aim of our study was to determine whether incorporating the BEMPU TempWatch into the care of LBW / SGA neonates for continuous temperature monitoring decreases the rate of hypothermia requiring escalation of care. Escalation of care was defined as requiring special care nursery (SCN) admission or use of a heated mattress, radiant warmer or incubator.

#### Method

This was a randomised controlled trial consisting of LBW / SGA neonates. Eligible participants were recruited on the postnatal wards within 48 hours after delivery and randomly allocated to receive either the TempWatch in addition to standard care, or standard care alone. The primary outcome was the rate of hypothermia requiring escalation of care during their initial hospital stay. Secondary outcomes included other neonatal outcomes and parental feedback regarding the TempWatch. An interim analysis was planned after 60 neonates were recruited to determine the feasibility of the study.

#### Results

Interim analysis revealed a very low rate of hypothermia requiring escalation of care and hence, it was not feasible to continue the study. All 75 neonates recruited to that point were included in the final analyses, with 39

randomised to the control group and 36 to the TempWatch group. The TempWatch and control group infants had a mean (SD) gestational age of 38.1 (1.5) and 38.0 (1.7) weeks, respectively. The rate of hypothermia requiring escalation of care was similar between the TempWatch and control group (2/36 (5.56%) vs. 1/39 (2.56%), respectively; relative risk (RR) 2.17, 95% CI 0.21 to 22.89,  $p = 0.61$ ). The TempWatch group had a higher rate of exclusive breastfeeding at discharge compared to the control group (22/36 (61.11%) vs. 13/39 (33.33%), RR 1.83, 95% CI 1.10 to 3.07,  $p = 0.02$ ). There were no other significant differences between the groups. The watch had a general good acceptance (mean (SD) satisfaction score of 3.4 (1.2)), with 45.7% of parents stating that the device was "useful". There were some parental concerns about the device, which included potential inaccuracy (48.6%), inconvenience due to its large size (40.0%), and causing their baby discomfort (25.7%).

#### Conclusion

Low rates of hypothermia requiring escalation of care meant it was not feasible to study the effects of the TempWatch on these rates. The TempWatch may have a role in promoting exclusive breastfeeding, which needs to be explored further. Addressing parental concerns and implementing suggested improvements into future models of the BEMPU TempWatch may help to increase its uptake in a high-income setting.

# Yingtong Li

## First seizure clinics in the evaluation and management of first seizures

Supervisor Names and Institute Affiliations:

Dr Zhibin (Ben) Chen<sup>1,2</sup>, Dr Emma Foster<sup>1,3</sup>, Professor Patrick Kwan<sup>1,3</sup>

<sup>1</sup>Department of Neuroscience, Central Clinical School, Monash University

<sup>2</sup>School of Public Health and Preventive Medicine, Monash University

<sup>3</sup>Department of Neurology, Alfred Hospital



Having been fascinated throughout medical school by neurology, and epileptology in particular, it was a pleasure to undertake my BMedSc(Hons) at the Central Clinical School Department of Neuroscience. I have always been interested in biostatistics and epidemiology, and so to be able to work on a large-scale data-driven quantitative research project was an invaluable opportunity.

Guided by the incredible support of my supervisors, I have developed not only both theoretic and practical skills in data extraction, biostatistics and academic communication, but also a keen appreciation of the close connection between research and clinical practice, and how each influences the other. I hope to continue developing my relationship with scientific inquiry and clinical practice, as I look towards my future and a career as a clinician-researcher.

My BMedSc(Hons) has broadened my horizons, and given me skills and experiences to enable me to be a better doctor. If you are on the fence, I would encourage you to give a BMedSc(Hons) year a go! I'm happy to be contacted to chat about my project or any other aspect of my BMedSc(Hons) experience.  
<https://twitter.com/RunasSudo>  
<https://yingtongli.me/>

## ABSTRACT

### Background

Seizures are a common neurological presentation, with significant associated health burden. First seizure assessment and management are accordingly of great importance; however, our understanding of the comorbidities and associated management needs of first seizure patients is limited.

International guidelines recommend prompt assessment of first seizures, and to this end, specialised first seizure clinics (FSCs) have been established in Australia and abroad. There is limited evidence, however, on how well these clinics support diverse patient groups, and their effect on long-term outcomes.

We sought to understand if record linkage with administrative datasets could yield insights into these knowledge gaps.

### Methods

We conducted a retrospective observational study of patients with first seizures attending four Melbourne emergency departments (EDs) over January 2008–December 2017. Two of these hospitals offered dedicated FSCs for follow-up. Patients' records were linked with the Victorian Admitted Episodes Dataset (VAED) and Victorian Emergency Minimum Dataset (VEMD) from inception to 2018. Patients subsequently found to have a pre-existing epilepsy diagnostic code from linkage data were excluded.

We compared the comorbidities of study patients with age-sex-location-matched controls drawn from the population-wide VAED/VEMD. For patients who were referred to the FSCs, we used regression models to identify: (a) whether attendance at FSC varied with clinico-demographic factors, and (b) whether attendance at FSC, and time between referral and attendance, influenced the rate of subsequent hospital presentations.

### Results

8351 patients with apparent first seizures were analysed. The median age was 45 years

(interquartile range 25–65), and 58.2% ( $n = 4863$ ) were male.

Notable comorbidities found to be more common in study patients compared with matched controls included dementia (odds ratio [OR] 3.92, 95% CI: 2.83–5.44), mood, psychotic and stress-related disorders (OR 2.14, 95% CI: 1.89–2.43), substance use disorders (OR 2.82, 95% CI: 2.44–3.25) and migraine (OR 1.80, 95% CI: 1.40–2.31).

1134 patients were referred to FSC, of which 840 attended, with a median 44 days between referral and attendance. FSC nonattendance was associated with younger age (adjusted relative risk [aRR] 2.21, 95% CI: 1.53–3.19) and greater relative socioeconomic advantage (aRR 1.47, 95% CI: 1.08–2.01).

FSC nonattendance was in turn associated with increased subsequent all-cause ED attendance (incidence rate ratio [IRR] 2.66, 95% CI: 2.05–3.44), all-cause hospital admission (IRR 2.69, 95% CI: 2.06–3.50) and seizure-related ED attendance or hospital admission (IRR 2.34, 95% CI: 1.63–3.37). Delayed FSC attendance was similarly associated with increased subsequent all-cause ED attendance (IRR 1.07, 95% CI: 1.05–1.08), all-cause hospital admission (IRR 1.05, 95% CI: 1.03–1.06) and seizure-related ED attendance or hospital admission (IRR 1.03, 95% CI: 1.03–1.04).

### Conclusion

Record linkage with administrative datasets yielded significant insights for first seizure management, supporting the position of FSCs as an effective healthcare intervention for reducing subsequent hospital utilisation. Information on patient comorbidities can inform design of integrated multidisciplinary services to best meet patient needs. Understanding factors influencing patient nonattendance can inform projects to support at-risk patients, with a view to improving subsequent outcomes.

# Michael Liu

## Drug-induced liver injury: mechanisms and early prediction

Supervisor Names and Institute Affiliations:

Adjunct Professor Amanda Nicoll, Dr Rohit Sawhney, Dr Pavel Sluka

Department of Gastroenterology, Eastern Health

Eastern Health Clinical School, Monash University



I completed my BMedSc(Hons) project this year with the Department of Gastroenterology at Eastern Health. After completing Year 4C, an Honours year represented an opportunity to both take a short break from clinical medicine, and explore the world of research in a supported and structured environment. Although it's been a challenging year (even more so with COVID around!), I have been able to develop my critical analysis and communication skills, all while exploring an area of medicine that I have a keen interest in. I was also lucky enough to combine both clinical and lab-based research in my project, giving me invaluable skills and experiences that I am sure will help me in my future research career. Overall, this Honours year has been an immensely rewarding experience. Please feel free to get in touch with me at: [mliu0012@student.monash.edu](mailto:mliu0012@student.monash.edu)

## ABSTRACT

### Background

Drug-induced liver injury (DILI) is a serious drug safety issue, with limited tools available to clinicians for diagnosis and prediction of morbidity. Cytochrome P450 autoantibodies, microRNA-192-5p, sCD163, sCD206, IL-4, and IL-13 are novel biomarkers that carry potential utility for DILI evaluation. These biomarkers may also shed further light on the mechanisms of DILI pathophysiology. Therefore, this project aimed to compare levels of these novel biomarkers between patients who develop DILI and healthy controls who are exposed to medications that are known to cause DILI, as well as examine how biomarker levels change with disease to gain insight into DILI mechanisms.

### Method

Prospective cohort study: baseline pre-exposure and follow-up blood samples were collected from patients commencing rituximab, infliximab, and checkpoint inhibitors. Acute DILI inpatients were also recruited with follow-up samples collected during convalescence. Samples were stored at  $-80^{\circ}\text{C}$  for future biomarker assay by our collaborators.

Nested case-control study: 13 DILI cases and 26 matched controls were selected from a previous cohort study completed in 2018 which recruited 157 participants exposed to volatile anaesthetic (VA) during surgery. Controls were matched according to age, sex and VA agent used. IL-4 and IL-13 levels were measured using quantitative enzyme-linked immunosorbent assay (ELISA) techniques.

### Results

Prospective cohort study: 105 patients (39 exposed to rituximab, 29 to infliximab, 37 to checkpoint inhibitors) were recruited. Three checkpoint inhibitor patients developed DILI. Two infliximab patients developed DILI due to agents other than

infliximab, and were reclassified into the acute DILI group. No rituximab patients developed DILI. Twenty-five patients with acute DILI were recruited.

Nested case-control study: there was a statistically significant difference in serum IL-4 in post-VA samples between DILI cases and controls (control: 0.030pg/mL, IQR: 0.030 – 0.030pg/mL vs DILI: 0.044pg/mL, IQR: 0.030 – 0.061pg/mL;  $p=0.039$ ). The area under the receiver operating characteristic curve for post-VA IL-4 was 0.683 (95% CI: 0.517 – 0.850;  $p=0.031$ ). A greater proportion of DILI cases had post-VA IL-4 levels above the assay lower limit of detection compared to controls (control: 23% vs DILI: 69%;  $p=0.013$ ). IL-4 fold change trended towards being higher in DILI compared to control, but this was not significant (control: 1.00 vs DILI: 1.33;  $p=0.194$ ). All DILI cases and controls had IL-13 levels below the assay lower limit of detection.

### Conclusion

IL-4 is a potential biomarker of DILI. Clinical diagnosis and understanding of DILI disease mechanisms may be improved by further investigation of novel biomarkers, and the results of the nested case-control study are important as proof of concept.



# Natalie Liu

## Stillbirth and Maternal Region of Birth: investigating contemporary stillbirth rates, trends and risk factors in migrant women

Supervisor Names and Institute Affiliations:

Dr Miranda Davies-Tuck

The Ritchie Centre, Hudson Institute of Medical Research, Monash Health Department of Obstetrics & Gynaecology



My Honours year was a much-needed break from the fast and furious pace of medical school, and an amazing opportunity to develop myself beyond the hospital wards. Women's health has always been important to me. So, when I first heard of my supervisor's research around the excessive stillbirth rates in migrant women, I knew this project was perfect for me! Although I didn't set foot in a hospital all year, I think I've learnt more about medicine and health in our society than I ever have during my clinical years. Through my project, I learnt how to challenge current practice guidelines, to formulate evidence-based arguments, and present my ideas to a wide variety of audiences. However, when I wasn't waist-deep in statistics and thesis-writing, the flexibility of this year allowed me time to work, travel and pick up a few new hobbies (painting and kick-boxing)! I'm incredibly grateful to my supervisor, Miranda, for all her support and guidance this year, and my research group for our weekly Wednesday zooms throughout lockdown.

My advice for future students would be to choose a project that you'll be excited to work on each day!

Feel free to contact me at  
nliu0004@student.monash.edu.

### ABSTRACT

#### Background

Maternal region of birth is a recognised independent risk factor for stillbirth. With increasing migration and growing awareness of this risk, we sought to determine the contemporary rates and changes to care for stillbirth in migrant women within Victoria.

#### Methods

A retrospective population-based cohort study of all births  $\geq 24$  weeks gestation from 2012–2019 in Victoria, Australia. Maternal regions of birth were defined according to the United Nations classification system of geographical regions. Adjusted logistic regression was used to calculate odds of stillbirth by maternal region of birth, with Australian-born women as the reference group. Rates of stillbirth by maternal region of birth were determined. Analyses were stratified into total, antepartum and intrapartum, preterm and term stillbirths, and examined for interaction with gestation length. Causes of stillbirth by maternal region of birth were tabulated. Rates of intervention (induction of labour) by maternal region of birth were assessed over time. Adverse effects of intervention were measured via neonatal morbidity and mortality metrics. The South Asian population was additionally stratified by maternal country of birth, and the same outcomes determined for each subgroup.

#### Results

A total 629,858 births were analysed. The rate of stillbirth per 1000 births was higher among women from South-Asia (4.23), Oceania (6.46), Africa (5.93) and the Middle East (4.85) than Australian-born women (3.74). Overall, South Asian (aOR 1.36, 95% CI 1.19–1.56), Oceanian (aOR 1.70, 95% CI 1.15–2.52), African (aOR 1.61, 95% CI 1.31–1.97) and Middle Eastern (aOR 1.37, 95% CI 1.06–1.78) born women had significantly higher odds of stillbirth compared to Australian-born women.

However, this differed when stratifying by preterm and term gestations, with significant associations found between African-born women and term stillbirths (aOR 1.81, 95% CI 1.28–2.56), and South Asian-born women and preterm stillbirths (aOR 1.29, 95% CI 1.10–1.50). There were significant increases in the frequency of labour inductions in all maternal birth-region groups ( $p < 0.05$ ). Relative increases were largest in South-East/East Asian (62.4%), Middle Eastern (57.1%) and New Zealand (54.6%) born women. South Asian-born women were induced most frequently out of all migrant groups, and at increasingly earlier gestations throughout the study period. However, we only observed significant decreases in term stillbirths among Middle Eastern-born women, and preterm stillbirths among African-born women. The rates of neonatal harms did not significantly change. Additionally, stillbirth outcomes differed significantly by maternal country of birth within the South Asian population. Women from Afghanistan (aOR 1.91, 95% CI 1.30–2.82), Pakistan (aOR 1.70, 95% CI 1.19–2.42) and India (aOR 1.24, 95% CI 1.06–1.46) were at significantly higher odds of stillbirth. However, Sri Lankan-born women held no significant association.

#### Conclusion

In Victoria, stillbirth rates remain higher among South Asian, Oceanian, African and Middle Eastern migrant women than Australian-born women, despite greater induction rates. However, stillbirth rates in some groups were lower than those of the previous decade, which may indicate increased clinical awareness and intervention. Novel findings also show that stillbirth outcomes vary between individual countries of birth within the South Asian migrant population.

# Calvin Lu

## The Efficacy of Elective Delayed Sternal Closure Following Surgery for Congenital Heart Disease

Supervisor Names and Institute Affiliations:

Professor Warwick Butt (Intensive Care Unit, The Royal Children's Hospital)

A/Professor David Brewster (Intensive Care Unit, Cabrini Health)



After 4 years of clinical medicine, I decided that completing a BMedSc(Hons) would be a great change of pace and a unique opportunity to learn about medical research before graduating. Admittedly, I never seriously considered doing research until about 2 months before the application deadline. However, I was fortunate enough to find an interesting project with supervisors that I got along well with and decided to do it! I had the privilege of working with the RCH PICU research team who were super supportive and a pleasure to be around. Unfortunately, I couldn't go to the hospital that much due to COVID restrictions, but I still enjoyed my year. The opportunity to dedicate a year to studying a particular area of medicine is rare and you end up getting really invested in it. Additionally, learning research skills now while you are a student makes it much easier to pursue research opportunities once you graduate (and it's a great way of seeing if you are actually interested in research in the first place)!

I couldn't recommend a BMedSc(Hons) more – if you have any questions, don't hesitate to contact me at [cluu0003@student.monash.edu](mailto:cluu0003@student.monash.edu)!

### ABSTRACT

#### Background

Congenital Heart Disease (CHD) describes a multitude of heterogeneous defects of the heart and great vessels that are present at birth, many of which require surgical correction. Most surgeries for CHD require a median sternotomy, which involves dividing the sternum in half lengthways to access the heart. At the end of the procedure, the surgeon is faced with a decision: should the chest be closed now (primary sternal closure, PSC) or should the chest be left open for a few days before it is closed (delayed sternal closure, DSC)? Whilst there are benefits to both approaches, there is no clear consensus in the literature about which approach to sternal closure leads to the most favourable patient outcomes.

#### Primary Aim

To evaluate the incidence of various adverse patient outcomes amongst clinically analogous patients following elective DSC and PSC after surgery for CHD.

#### Methods

A retrospective, single-site cohort study was conducted at the Royal Children's Hospital, Melbourne. Surgeries for CHD that occurred between the 1st of January 2010 to the 31st of December 2020 inclusive at the RCH were included in this study. Surgical cases were sorted into the following three comparison groups: elective DSC, emergency DSC, and PSC. Baseline characteristics were assessed and compared between the groups. The elective DSC and PSC groups were subject to propensity score matching (PSM), with multivariable logistic regression being performed on covariates to generate propensity scores. Using the propensity scores, a matched sample of similar elective DSC and PSC groups was created. The outcomes in the matched groups were then compared.

#### Results

5,245 surgical cases were included in the analysis. Statistically significant differences were identified between the baseline characteristics of the elective DSC and emergency DSC groups. Following PSM, a matched sample comprised of 395 pairs of similar surgical cases in the elective DSC and PSC groups was created. On average, patients undergoing elective DSC spent 242.8 more hours in hospital, 161.5 more hours in PICU, and 6.1 more hours on ECLS than similar patients undergoing PSC. Additionally, compared to patients undergoing PSC, mortality was 3.1 times more likely and ECLS was 3.0 times more likely in patients undergoing elective DSC.

#### Conclusion

Sternal closure decisions significantly influence adverse patient outcomes in the post-operative period. Though the theoretic benefits of elective DSC are well-understood, this study revealed that patients that underwent elective DSC had a three-fold increased risk of mortality when compared to patients that underwent PSC. Additionally, significantly protracted stays in hospital and the use of ECLS were more likely following elective DSC than following PSC. Matching processes were employed to ensure that differences in outcomes between the PSC and elective DSC groups could only be attributable to elective DSC and not any confounders. In this way, a causal relationship was identified between elective DSC and increased rates of adverse patient outcomes.

## The Ethical Considerations of Non-Invasive Prenatal Testing for Adult-Onset Conditions

Supervisor Names and Institute Affiliations:

Professor Catherine Mills (Monash Bioethics Centre) and Dr Katrien Devolder (Oxford Uehiro Centre for Practical Ethics)



Having completed year 4C of my medical degree in 2020, I chose to pursue the BMedSc(Hons) year to gain some research experience and potentially travel overseas. My particular interests in paediatrics, global health and ethics led me to apply for the Oxford/Monash Bioethics BMedSc(Hons) program. I was incredibly grateful to be chosen for the program. My project initially appealed to me because it combined a number of my interests; I was fascinated by discussions about the extent of genetic information prospective parents can acceptably access about their fetus, as well as the impacts of novel prenatal testing on the wellbeing of future children. I really enjoyed learning more about philosophical inquiry, as well as the opportunity I had to write freely throughout the year. I found that the BMedSc(Hons) year was more self-directed than my previous medical studies. While the inability to spend the year in Oxford was certainly disappointing, I enjoyed being able to organise and balance my own time working from home. I am happy to be contacted by future students who may have questions about the BMedSc(Hons) year, especially those interested in the Oxford Bioethics Program.

### ABSTRACT

#### Background

Over the past decade, the non-invasive prenatal test (NIPT) has been adopted into routine obstetric care. NIPT consists of a maternal blood test performed from around 10 weeks' gestation. The standard NIPT screens for fetal sex, trisomies 21, 18 and 13, and sex chromosome aneuploidies. It is predicted that the scope of NIPT could be expanded in the future, creating significantly enhanced possibilities for the extent of genetic information prospective parents could access about their fetus. Testing for adult-onset conditions (AOCs) is one ethically controversial possible future application. In this thesis the ethical implications of NIPT screening for AOCs are analysed and empirical research on the relevant views of NIPT users presented.

#### Aims

The overall aim of this thesis is to develop an account of how the ethical intuitions of NIPT consumers relate to existing bioethical debates around NIPT for AOCs. The empirical component aimed to collect and analyse participants' views on how NIPT for AOCs may impact the parent(s) and future child. This includes consumer views on a proposed model to make access to testing conditional on parents' stated intention to terminate in the case of a positive result.

#### Methods

Individuals and partners of individuals who have previously undergone NIPT completed an online quantitative survey on Qualtrics survey software. The survey ascertained support for, and personal interest in, the availability of NIPT for several traits/conditions including AOCs. Participants were then asked about their level of concern about testing implications on the future child and parent(s). They also answered questions about the ethics of pregnancy termination and continuation following diagnosis of an AOC. Descriptive

and comparative data analyses were conducted utilising SPSS software. Data were used to engage in 'public reflective equilibrium', which entailed working back and forth between survey participants' intuitions and relevant philosophical theory to identify points of coherence and divergence among them.

#### Results

One-hundred and nine eligible surveys were received. Of these, the majority expressed overall support for NIPT testing for preventable (70.9%) and non-preventable AOCs (80.8%). Most participants endorsed concerns around possible harmful impacts of NIPT for AOCs, including psychological distress among the future child and parent(s). Despite this, most indicated that continuation of a pregnancy where the fetus has been diagnosed with an AOC was ethically acceptable, particularly for preventable conditions (90.6%), and less strongly endorsed for non-preventable conditions (62.5%). Moreover, most participants did not support a conditional access model for preventable (77.1%) and non-preventable (72.9%) AOCs.

#### Conclusion

This study suggests that NIPT users support the availability of NIPT for AOCs without any conditional access, yet simultaneously hold concerns around its harms. Through ethical analysis, I have outlined the numerous benefits this testing could provide and proposed that hypothetical harms to the future child cannot justify restricting access. I encourage further research to examine these potential harms, which are evidently of concern to NIPT users, particularly psychosocial adversity. This project contributes to continued ethical debate around acceptable applications of NIPT and the allocation of public funding to prenatal screening.



# Keeth Mayakaduwa

## Reducing Stillbirth in Victoria: Early Insights from the Safer Baby Bundle

Supervisor Names and Institute Affiliations:

Dr Miranda Davies-Tuck<sup>1,2,3</sup>, Adjunct Professor Tanya Farrell<sup>2</sup>, Professor Euan Wallace<sup>3,4</sup>

1. Hudson Institute of Medical Research, Melbourne, Australia
2. Safer Care Victoria, Melbourne, Australia
3. Monash University, Melbourne, Australia
4. Department of Health, Melbourne, Victoria, Australia



I had the pleasure of completing my BMedSc(Hons) at the Hudson Institute of Medical Research focusing on stillbirth prevention. During my fourth year of medical school in 2020, I discovered my passion for obstetrics and gynaecology. I decided to complete an Honours year in this field not only to learn more about research in this area, but also to contribute to improving pregnancy outcomes for women in Australia. I have developed many valuable research skills this year, through handling state-level datasets and using complex statistical programs. I was fortunate to have worked with some amazing colleagues and to have been guided by supportive supervisors. This Honours year has ignited my passion for research, and I hope to continue contributing to research in the field of obstetrics and gynaecology. I would advise any future students interested in learning more about research in a particular field to consider completing a BMedSc(Hons). While it is a challenging year, it is a very rewarding experience. I am more than happy to be contacted by any future BMedSc(Hons) students.

Email: keeth.maya@gmail.com

## ABSTRACT

### Background

The importance of reducing stillbirth in Australia is gaining increasing recognition. In 2019, the Australian Safer Baby Bundle (SBB), an evidence-based bundle of care to reduce stillbirth, began across 22 Victorian sites and is being implemented throughout other states. Targeting five antenatal care areas, the SBB aims to decrease the national late gestational stillbirth rate by 20% by 2023. However, the SBB may increase unwarranted obstetric interventions and iatrogenic harms.

### Aim

To assess the obstetric and perinatal outcomes of the SBB in Victoria.

### Methods

A retrospective population-based study was conducted using the Victorian Perinatal Data Collection, a government legislated database. All births delivered at  $\geq 28$  weeks' gestation in Victoria from 2014-2020 were included, excluding congenital anomalies, multiple pregnancies, terminations of pregnancy, and home births. Outcome measures for perinatal mortality, smoking cessation, fetal growth restriction (FGR), decreased fetal movement (DFM), and iatrogenic delivery were computed. The bundle implementation point was defined as July 2019. Unadjusted relative risk (RR) ratios for outcome measures in SBB and non-SBB sites were obtained, comparing the pre- and post-bundle periods. Multiple-group interrupted time series analyses were performed to compare trends in outcome measures in SBB and non-SBB sites, in the pre- and post-bundle periods.

### Results

In SBB sites, the stillbirth rate non-significantly reduced by 9% (RR:0.91|95%CI=0.75-1.11| $p=0.36$ ) from 2.19 to 1.99 per 1000 births, between the pre- and post-bundle periods. The stillbirth rate in SBB sites was decreasing significantly by 0.02 per 1000 births per month (95%CI=-0.03,-0.004| $p<0.01$ ) before bundle implementation. This rate of decline did not significantly change after bundle implementation

( $p=0.9$ ). In non-SBB sites, the stillbirth rate non-significantly increased by 20% (RR:1.20|95%CI=0.95-1.52| $p=0.12$ ) from 1.61 to 1.94 per 1000 births, between the pre- and post-bundle periods. The stillbirth rate in non-SBB sites was decreasing non-significantly by 0.01 per 1000 births per month (95%CI=-0.02,0.003| $p=0.15$ ) before bundle implementation. This trend did not significantly change after bundle implementation ( $p=0.3$ ). In SBB and non-SBB sites, the early term (37+0-38+6 weeks' gestation) iatrogenic delivery percentage was increasing significantly by 0.18% per month (95%CI=0.17,0.20| $p<0.01$ ) and 0.16% per month (95%CI=0.15,0.18| $p<0.01$ ), respectively, before bundle implementation. This trend significantly decreased by 0.11% (95%CI=-0.22,-0.01| $p=0.04$ ) in SBB sites after bundle implementation but did not significantly change in non-SBB sites ( $p=0.57$ ). After bundle implementation, the trend in smoking cessation rate did not significantly change in SBB sites, but significantly increased in non-SBB sites. Trends in undelivered severe FGR, iatrogenic delivery for FGR, DFM antenatal reporting, and iatrogenic delivery for DFM did not significantly change after bundle implementation in all sites.

### Conclusion

The bundle did not significantly impact the trend of stillbirth in all sites. However, since the stillbirth rate continued to decline after implementation in SBB sites but remained unchanged in non-SBB sites, further reductions may still be possible in SBB sites. The trend of early term iatrogenic delivery reduced after implementation in SBB sites but continued unchanged in non-SBB sites, suggesting that concerns of iatrogenic harm may be unwarranted. This early evaluation of the SBB's impacts in Victoria supports the bundle's national rollout.

# Iolanda Miceli

## GILZ and E3-X: Investigating a negative regulator of GILZ protein abundance

Supervisor Names and Institute Affiliations:

Dr Sarah Jones, Dr Wendy Dankers and Professor Eric Morand

School of Clinical Sciences



I undertook a BMedSc(Hons) in 2021 after completing my 4th year of medicine. I was always interested in rheumatology, particularly in the immunological processes underlying rheumatological diseases, so I decided to do a lab-based BMedSc(Hons) in the Rheumatology Research Group at Monash Health. I found myself immersed in an exciting and supportive research environment with a team who supported my transition from full-time clinical studies to full-time lab-based research. It has been a challenging but immensely rewarding year which has kick-started my interest in scientific research, which I now plan to pursue throughout my career.

### ABSTRACT

Despite well-known adverse effects, glucocorticoids (GCs) are still widely used in medicine for their potent immunosuppressive effects. Therefore, the development of a glucocorticoid alternative is a major unmet need. Glucocorticoid-induced leucine zipper (GILZ) is an attractive therapeutic target which mediates many of the beneficial anti-inflammatory actions of GCs but not their adverse effects. A potential strategy for amplifying the anti-inflammatory effects of GILZ is prevention of its degradation through inhibition of E3 ubiquitin ligases. “E3-X” is an E3 ubiquitin ligase of GILZ identified by mass spectrometry, which is a potentially targetable mediator of GILZ degradation. My results show that deficiency of E3-X was associated with increased GILZ protein and slowed degradation. Meanwhile, E3-X deficiency resulted in broad anti-inflammatory effects across various cell types, including reduction in secretion of MCP-1 and TNF and downregulation of the DC costimulatory molecule CD86. E3-X was found to be highly expressed in SLE and regulated by type I interferon. Thus, my results indicate that inhibition of E3-X is an attractive therapeutic strategy for potentiating the anti-inflammatory effects of GILZ.

# Jasmine Moses

## Perivascular Spaces as a Potential Biomarker in Behavioural Variant Frontotemporal Dementia

Supervisor Names and Institute Affiliations:

Dr Lucy Vivash, Professor Terrence O'Brien

Central Clinical School, Alfred Health



I am an undergraduate student that completed my BMedSc(Hons) after 4th year. I chose my project as I wanted something clinical and have an interest in dementia. As it turns out, my project had more of a neuroradiology background and required many technical skills including coding and using imaging software. However, I thoroughly enjoyed my year and learnt many new skills that will help me with future research endeavours. I was extremely fortunate to have supportive supervisors who I could ask for help whenever I needed, which was necessary with my zero experience with imaging software and codes. If I were to do anything different, I would try to understand the requirements of the Honours year and what my expectations of my project were. Overall, I had a very enjoyable year and am extremely glad I made the decision to undertake a BMedSc(Hons). Although it is tough at times and I would ask myself "is it too late to drop out", it all paid off in the end.

If anyone has any questions, feel free to shoot me an email:

jmos0002@student.monash.edu

### ABSTRACT

#### Background

Behavioural Variant Frontotemporal Dementia (bvFTD) is a rapidly progressing neurodegenerative disease characterised by the accumulation of either tau, TDP-43 or FUS protein in the brain. There are currently no treatments available, and the median survival from diagnosis is approximately 7-11 years. Accurate prognosis is difficult due to a lack of clinically available biomarkers. Perivascular spaces (PVS) form a part of the glymphatic system. When enlarged due to poor glymphatic clearance of toxic proteins, such as tau protein, they become visible on Magnetic Resonance Imaging (MRI). This makes PVS a good candidate as a surrogate marker of poor glymphatic drainage.

#### Aims

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.

#### Methods

The multimodal autoidentification of perivascular spaces (MAPS) algorithm identifies PVS using intensity, size, and linearity thresholds. MAPS was optimised to allow accurate measurement of PVS on a T1-weighted MRI scan only. MAPS was then applied to a cohort of patients with bvFTD treated with sodium selenate. Eleven patients were recruited into a phase Ib open label study of the use of sodium selenate as a potential treatment in patients with bvFTD with a duration of 52 weeks. Sodium selenate is a potential disease-modifying drug for the tau pathology of bvFTD. PVS cluster number and volume were extracted from the final PVS mask and used in mixed model analysis

between PVS burden and cognition, disease severity, and various fluid biomarkers.

#### Results

In a dataset of research quality scans, the count correlation between manual segmentations and MAPS segmentations was 0.973. In a dataset of clinical quality scans, the count correlation was 0.348. In a cohort of patients with bvFTD, there was no significant difference for PVS cluster number ( $\beta = -1.5015$ , CI [-3.368 – 0.365],  $p = 0.154$ ) or PVS volume ( $\beta = 0.770$ , CI [-22.6 – 24.19],  $p = 0.950$ ) and time between the progressor and non-progressor groups. Within the whole group analysis, there was evidence of an association between cerebrospinal fluid (CSF) total-tau (t-tau) and PVS burden (PVS cluster  $\beta = 0.638$ , CI [0.108 – 1.17],  $p = 0.034$ , PVS volume  $\beta = 11.2$ , CI [2.74 – 19.7],  $p = 0.019$ ), and between the change in CSF t-tau and the change in PVS cluster number over the trial period ( $\beta = 0.486$ , CI [0.143 – 0.830],  $p = 0.013$ ). An association was found between change in serum t-tau measurements and the change in PVS cluster number over the trial ( $\beta = -70.43$ , CI [-117.7 – 23.1],  $p = 0.009$ ). Within the non-progressor group analysis, there was a significant relationship between the change in CBS and the change in PVS volume over the trial period ( $\beta = 0.00445$ , CI [0.00196 – 0.00695],  $p = 0.005$ ), and evidence of a significant relationship between the change in NfL levels and the change in PVS cluster numbers over the trial period ( $\beta = 0.0492$ , CI [0.00592 – 0.0924],  $p = 0.047$ ).

#### Conclusion

MAPS was shown to accurately detect PVS on research quality T1w MRI scans. It performed worse on a dataset of clinical quality scans from a cohort of bvFTD patients. Nonetheless, longitudinal data demonstrated a relationship between PVS burden and disease severity as measured by the CBS and biomarkers of neurodegeneration. Thus, PVS has the potential to be a clinically useful biomarker to measure disease progression.



# Abhir Nainani

## General practitioners' experiences when screening for primary aldosteronism in hypertensive patients

Supervisor Names and Institute Affiliations:

Professor Grant Russell – Department of General Practice, Monash University

Dr Sanne Peters - Department of General Practice, Monash University

Dr Jun Yang – Hudson Institute for Endocrinology and Metabolism



I completed my Honours year with the Department of General Practice and can't recommend it enough. I had the opportunity to interact with PhD students (and learn from them), present at conferences and learn more about research in general.

### ABSTRACT

#### Background

Primary aldosteronism (PA) is a common cause of hypertension caused by excess production of the adrenal hormone aldosterone. Screening hypertensive patients with an aldosterone renin ratio (ARR) enables early detection and targeted treatment of PA, which can optimise blood pressure and lower cardiovascular risk. Despite these benefits, PA is rarely screened for in general practice. Earlier research has suggested that few general practitioners (GPs) are aware of the implications of PA. A recent study found that, even among Melbourne GPs that were taught to screen for PA, there was significant variation in screening rates. Thus, we sought to understand the factors that influence a GP's experience of screening for PA.

#### Method

We used a qualitative design, framed by phenomenology, to explore the experiences of GPs when screening for PA. Eligible GPs had previously attended a training intervention on PA. We conducted semi-structured interviews with a purposive sample of GPs who varied in terms of practice location, clinical experience, and the number of patients screened for PA. Interviews were face-to-face or online, audio-recorded, transcribed verbatim, and entered into NVivo 12.0 to assist with coding. Analysis was completed by two researchers who independently reviewed transcripts and developed a coding template to understand themes in the data.

#### Results

We collected data from 16 GPs. The data suggested that these GPs were generally positive to the concept of screening once it had been introduced to them, as they recognised the positive impact that detecting PA and initiating treatment could have on patient wellbeing. They found the screening process to be practical,

inexpensive, and by and large, acceptable to their patients. However, GPs were less enthused about screening patients that fitted their clinical conceptualisation of essential hypertension. They were also reluctant to alter antihypertensive medications before screening to allow for easier interpretation of the ARR result.

The GPs' approach to screening was influenced by their perceptions about the cost and convenience of performing the ARR. They commonly based their decision to screen on the perceived risk that PA posed to their hypertensive patients. Knowledge deficits in key areas of the PA diagnostic process influenced their ability to conduct screening within the existing time constraints of primary care. Improving clinical care was a priority for GPs and often under-pinned their motivations to screen for PA.

#### Conclusion

Given the explosion of research into PA, it seems likely that GPs will become increasingly aware of this condition. As GPs become more aware of PA, future interventions should consider the influencing factors identified in our study when attempting to increase the detection of PA in primary care. Our findings revealed that errors in diagnostic reasoning and knowledge deficits deterred GPs from routinely screening for PA. These should be addressed in future GP screening guidelines and training interventions. They also highlighted the practical limitations of the ARR, which made it difficult for GPs to incorporate PA screening into routine clinical practice. Further research is needed to overcome these limitations and improve PA screening rates in general practice.

# Vinitha Narasimhan

## Quality of Care in the Management of Ovarian Cancer

Supervisor Names and Institute Affiliations:

Dr Wentao Li – Department of Obstetrics and Gynaecology, Monash Health

Professor Ben W Mol - Department of Obstetrics and Gynaecology, Monash Health

Dr Sara Yeoh – Department of Obstetrics and Gynaecology, Monash Health



I completed fourth year in 2020 and after the craziness of COVID-19, I decided to undertake BMedSc(Hons) before commencing fifth year. I really enjoyed my women's health rotation and felt supported at Monash Health which is why I wanted to choose a project within the department. There were so many fascinating projects to choose from but I was particularly interested in this project because of the emphasis on quality of care provided to patients who are unfortunately delivered a very poor prognosis. Having minimal research experience, the year came with many challenges but I am grateful for the support of my team. I learnt that it is important to ask questions especially considering most of the work is completed independently. Not understanding everything is very reasonable and the team is always happy to help! I have learnt a lot about research this year and came out realising it really is an ongoing process. I hope to continue learning about research and integrating it with my clinical career in the future. Feel free to contact me for any questions!

## ABSTRACT

### Background

There is an increasing need to ensure adequate Quality of Care (QoC) in the management of ovarian cancer. With the lack of monitoring of standardised ovarian cancer care it is imperative to look into current management strategies and identify areas of improvement. There has been little attempt at monitoring the QoC provided. Therefore, QoC assessment in gynaecological-oncology is urgently needed in Australia.

### Method

Firstly, quality indicators were selected by experts within Monash Health from the results of a systematic scoping review as well as those proposed by the National Gynae-oncology Registry (NGOR). After quality indicators had been selected, an audit using retrospective data from all patients with epithelial ovarian, fallopian tube, or peritoneal cancers diagnosed between July 2015 to September 2019 was performed. We presented the proportion of patients satisfying each quality indicator at Monash Health.

### Results

We selected 16 quality indicators, of which 11 were selected from the 15 NGOR indicators and five additional quality indicators from our systematic review. There were two structural indicators, five institutional process indicators, six treatment process indicators and three treatment interval indicators selected. We assessed the QoC in 335 patients using these 16 quality indicators. Institutional process indicators measuring multidisciplinary team discussion (98.5%), imaging prior to treatment initiation (87.1%) and tissue diagnosis before neoadjuvant chemotherapy (NACT) commencement (98.9%) were the best adhered to. Monash had low rates of significant intra-operative events (7.1%) and 30-day postoperative adverse events classified as Clavien-Dindo > III (2.5%). The

current data-set was complete for 11/16 indicators, additional data retrieval was required for 2/5 indicators whilst 3/5 were completely absent.

### Conclusion

This audit confirms that quality indicators can be measured with routinely-collected clinical data. The current clinical data-set can partly meet the need for quality improvement measurement but optimisation of data collection is still warranted. Ovarian cancer management at Monash health can be improved by detailing residual disease in operation reports, holding regular morbidity and mortality meetings, and continuous monitoring of selected quality indicators.

# Sophie Nunn

## How have Aboriginal and Torres Strait Islander characteristics changed over time, and how might these changes have impacted data trends and outcomes?

Supervisor Names and Institute Affiliations:

Dr Mary-Ann Davey<sup>1,2</sup>

Adjunct Professor Tanya Farrell<sup>2</sup>

1. Department of Obstetrics and Gynaecology,  
School of Clinical Sciences, Monash University

2. Safer Care Victoria,

Department of Health and Human Services



I completed my BMedSc(Hons) in the year between 4C and 5D. I chose to undertake my project with Safer Care Victoria as I am extremely passionate about women's health and I was then especially fortunate to be able to focus on another area of interest, Aboriginal and Torres Strait Islander health. One lesson I learnt from my year was that sometimes your study design needs to be adapted in response to the data or new questions that arise and that is not only okay but also an exciting (and at times stressful) aspect of research. I am happy to be contacted by future students.

## ABSTRACT

### Background

Babies of Aboriginal and Torres Strait Islander mothers remain at greater risk than their non-Aboriginal counterparts of the tragedy that is perinatal death (PND). However, there has been a reduction in PND rates within the Aboriginal and Torres Strait Islander community over time. Moreover, 2014-2016 provided a short-lived triennium of promise, where disparity in PND and Stillbirth (SB) rates was eliminated.

Factors potentially influencing these improvements are data volatility, efficacy of targeted healthcare services and evolution in the socio-demographics of Aboriginal and Torres Strait Islander mothers. Several key maternal characteristics are cemented in literature as risk or protective factors for perinatal outcomes. Changes to these in the Aboriginal and Torres Strait Islander maternal population may have influenced perinatal outcome trends.

### Aims

To explore trends in perinatal outcomes and maternal characteristic rates for Victorian mothers between 2000 and 2019 and assess how relationships between them may have influenced trends, particularly in 2014-2016.

### Methods

We undertook a retrospective population-based study utilising data from the Victorian Perinatal Data Collection (VPDC), assessing all births in Victoria from 2000 to 2019, excluding terminations of pregnancy and babies with a birthweight below 150 grams. Primary outcomes of interest were PND, including Neonatal death and Stillbirth, with secondary outcomes of pre-term birth and small for gestational age. Maternal characteristics of interest were maternal socio-economic status, living location, smoking during pregnancy, BMI, age, pre-existing DM, GDM, gestation at first antenatal visit, gestation at birth and KMS access. We performed standard descriptive statistics to calculate outcome rates and characteristic proportions, graphing trends over time and calculating p for trend to assess significance.

Relationships between outcomes and characteristics were determined by relative risk ratios with 95% confidence intervals. Univariate logistic regression and multivariate regression for crude and adjusted odds ratios demonstrated the adjusted relationship between outcomes and Aboriginal and Torres Strait Islander status.

### Results

Within the Aboriginal and Torres Strait Islander population all outcomes decreased over the study period (all p for trend = <0.05), excepting PTB which showed no significant change (p for trend = 0.80). Over this period, we observed increases in the proportion of Aboriginal and Torres Strait Islander mothers with characteristics associated with lower risks of PND and decreases in those associated with increased PND risk (all p for trend = <0.05). However, there was contemporaneous stagnancy (p for trend = >0.05) and increases (p for trend = <0.05) in rates of characteristics associated with increased PND risk. In 2014-2016 we observed parity in PND and lower SB rates in the Aboriginal and Torres Strait Islander population compared to the non-Aboriginal population, accompanied by a peak in the number of Aboriginal and Torres Strait Islander mothers and deviations from overall characteristic trends.

### Conclusion

Trends in maternal characteristics may have contributed to improvements in perinatal outcomes for the Aboriginal and Torres Strait Islander population over the study period. However, several characteristics displaying concerning trends may have simultaneously hindered further improvements. Finally, 2014-2016 may not reflect meaningful improvements in Aboriginal and Torres Strait Islander perinatal outcomes.



# Ibukun Oloruntoba

## Assessing Generalisability of deep learning models trained on Standardised and Non-standardised images and their performance against tele-dermatologists.

Supervisor Names and Institute Affiliations:

Name: Victoria Mar

Degree: PhD

Affiliation: Monash University

Name: Zongyuan Ge

Degree: PhD

Affiliation: Monash University



My name is Ibukun, and I did a BMedSc(Hons) this year. I chose my project because I am interested in dermatology and believe it is something I could possibly pursue in the future. Personally, this year was a great year for me, I learnt a lot about research and dermatology and highly recommend a BMedSc(Hons) to anyone who is interested in delving deeper into a speciality they enjoy. If you have any questions, feel free to email me at aolo0001@student.monash.edu.

## ABSTRACT

### Background

Convolutional neural networks (CNNs) are a type of artificial intelligence (AI) which show promise as a diagnostic aid for skin cancer. However, the majority are trained using retrospective image datasets of varying quality and image capture standardisation. The objective of our study was to use CNN models with the same architecture, but different training image sets, and test variability in performance when classifying skin cancer images in different populations, acquired with different devices. Additionally, we wanted to assess the performance of the models against Danish tele-dermatologists, when tested on images acquired from Denmark.

### Method

Three CNNs with the same architecture were trained. CNN-NS was trained on 25,331 non-standardised images taken from the International Skin Imaging Collaboration using different image capture devices. CNN-S was trained on 235,268 standardised images and CNN-S2 was trained on 25,331 standardised images (matched for number and classes of training images to CNN-NS). Both standardised datasets (CNN-S and CNN-S2) were provided by Molemap using the same image capture device. 495 Danish patients with 569 images of skin lesions predominantly involving Fitzpatrick's skin types II and III were used to test the performance of the models. 4 tele-dermatologists independently diagnosed and assessed the images taken of the lesions. Primary outcome measures were sensitivity, specificity and area under the curve of the receiver operating characteristic (AUROC).

### Results

569 images were taken from 495 patients (280 women [57%], 215 men [43%]; mean age 55 years [17 SD]) for this study. On these images, CNN-S achieved an AUROC

of 0.861 (CI 0.830 – 0.889;  $P < 0.001$ ) and CNN-S2 achieved an AUROC of 0.831 (CI 0.798 – 0.861;  $P = 0.009$ ), with both outperforming CNN-NS, which achieved an AUROC of 0.759 (CI 0.722 – 0.794;  $P < 0.001$ ,  $P = 0.009$ ) (Figure 1). When the CNNs were matched to the mean sensitivity and specificity of the tele-dermatologists, the model's resultant sensitivities and specificities were surpassed by the tele-dermatologists (Table 1). However, when compared to CNN-S, the differences were not statistically significant ( $P = 0.100$ ,  $P = 0.053$ ). Performance across all CNN models as well as tele-dermatologists was influenced by image quality.

### Conclusion

CNNs trained on standardised images had improved performance and therefore greater generalisability in skin cancer classification when applied to an unseen dataset. This is an important consideration for future algorithm development, regulation and approval. Further, when tested on these unseen test images, the tele-dermatologists 'clinically' outperformed all the CNN models; however, the difference was deemed to be statistically insignificant when compared to CNN-S.

# Morgan Peel

## Using individual patient data meta-analyses to compare mechanical and pharmacological methods of inducing labour

Supervisor Names and Institute Affiliations:

Professor Ben Mol, Dr Kirsten Palmer, Dr Wentao Li

Department of Obstetrics and Gynaecology, Monash Health



During my fourth year I developed a keen interest in women's health. Therefore, pursuing a research project that compares various labour induction methods for both their efficacy and safety was a natural and exciting progression. I loved every moment of working on this project from collaborating with authors to extracting and checking data to running the statistical analysis with a lot of assistance and guidance along the way. Through this year I developed skills in scientific writing, working in a research team, cleaning, coding, and analysing data and most terrifyingly in public speaking. I have acquired so many skills and achieved things I couldn't possibly have fathomed; whether it be writing an actual minor thesis to getting through an oral presentation without hiccupping and stuttering. This year has been the most incredible blessing and if there is any advice I'd give to future students it would be to do a research year, it's an amazing experience.

I am happy to be contacted by future students, my email is [morg0001@student.monash.edu](mailto:morg0001@student.monash.edu).

### ABSTRACT

#### Background

Labour induction is the process of artificially causing regular uterine contractions resulting in delivery of the foetus and is an increasingly common procedure in obstetrics across the globe. Methods for induction of labour include mechanical methods such as the single balloon catheter or double balloon catheter. Balloon catheters create a stretching effect on the cervix that produces release of local prostaglandins to induce labour. Labour can also be induced through pharmacological methods such as the prostaglandin misoprostol which encourages both cervical effacement but also induces uterine contractions.

#### Method

Two separate individual patient data meta-analyses were performed. We identified randomised controlled trials (RCTs) were identified from their inclusion in the Cochrane Review on Mechanical Methods for Induction of Labour. To identify any RCTs published since the Cochrane Review a further search of Ovid MEDLINE, Embase via Ovid, Ovid Emcare, CINAHL Plus, Scopus and clinicaltrials.gov was conducted for trials published until 13th April 2021. All RCTs comparing low dose misoprostol and mechanical methods versus low dose misoprostol alone or double balloon catheter versus single balloon catheter for labour induction were eligible to contribute data.

Our primary outcomes were rates of vaginal birth achieved, a composite measure of adverse maternal outcomes and a composite measure of adverse perinatal outcomes.

#### Results

From the 12 trials eligible for participation in the low dose misoprostol and foley catheter versus low dose misoprostol alone meta-analysis, authors of five RCTs shared their data. We included three trials in the final

analysis as two trials were excluded after data sharing due to data integrity concerns. A total of 562 participants were analysed. No significant difference was found between the two groups for vaginal delivery rates (RR, 1.04 (95%CI, 0.91-1.18); I<sup>2</sup>, 0%) and a statistically non-significant trend was identified that the combined group improved perinatal composite outcomes (RR, 1.25 (95%CI, 0.79-1.98); I<sup>2</sup>, 66.124%). Difference in maternal composite outcomes were comparable between the two groups (RR, 1.18 (95%CI, 0.57-2.43); I<sup>2</sup>, 0%).

Data of three RCTs participated in the double balloon catheter versus single balloon catheter meta-analysis, resulting in 689 participants. Vaginal delivery rates were significantly higher in the single balloon catheter group (RR, 0.92 (95%CI, 0.86-1.00); I<sup>2</sup>, 0%). Both perinatal (RR, 1.02 (95%CI, 0.71-1.48); I<sup>2</sup>, 0%) and maternal composite outcomes (RR, 0.88 (95%CI, 0.42-1.85); I<sup>2</sup>, 10.925%) were comparable across the two groups.

#### Conclusion

In labour induction at term, low dose misoprostol and mechanical methods result in equal outcomes as low dose misoprostol alone.

Single balloon catheter significantly increases vaginal delivery rate compared to double balloon catheter with no detriment to either maternal or perinatal outcomes.

# Vinsensia Maharani Kanya Dhira Pradipta

## Actions to Manage Mental Health Concerns during the COVID-19 Pandemic

Supervisor Names and Institute Affiliations:

Dr Daniel Griffiths, Professor Alex Collie

School of Public Health and Preventive Medicine (SPHPM), Monash University



Hi everybody! I am Kanya, a 4th-year medical student from the University of Indonesia. I developed an interest in mental health and wanted to make my year of research an opportunity to explore my interests. Since pandemics don't happen every year, this topic is of great interest to me. I found out about this topic after being contacted by my supervisor, and I ended up doing my research project in the COVID Work and Health Study. This team works to study the impacts of the COVID-19 pandemic on Australians' physical and mental health who have lost work or lost their jobs. My study specifically analysed the actions that are more and less commonly done by people regarding managing their mental health. This team is also very warm, welcoming and passionate about what they do. They gave me valuable experience during this research year. I am also very grateful for the extraordinary support from my supervisors and all the skills I have learned this year. I would thoroughly recommend doing BMedSc(Hons) degree and encourage others interested in mental health research to contact my supervisors.

### ABSTRACT

#### Background

The COVID-19 pandemic has disrupted the way we live. Restrictions on gatherings and physically distancing from others have helped to reduce viral transmission, but these measures also result in many negative consequences. Changes in the nature of work have caused many people to either lose their jobs, be temporarily stood down from work, or adapt to remote-working arrangements. These changes can result in a deterioration in mental health, as work is an important determinant of health. Poor employment opportunities, increased uncertainty, and restrictions on everyday life may leave some people feeling helpless and unsettled, leading to increasing levels of anxiety and depression. This study explored the approaches people were taking to manage their mental health concerns throughout the COVID-19 pandemic, and sought to identify the characteristics of people who performed specific actions.

#### Method

This project is part of a larger national longitudinal cohort study that surveyed 2603 Australians who lost their jobs during the early stages of the pandemic. A control group was included consisting of people who remained working. Across three survey timepoints, between 27 April and 28 December 2020, summary statistics were calculated to summarise the prevalence of actions taken by people to manage mental health concerns. Actions were grouped into five higher order categories describing changes to diet and exercise, lifestyle, medications, alcohol consumption and drug use, and use of online resourced or telephone support lines. Binary regression models were calculated for each action category to determine the characteristics of the particular people who conducted the actions. Several demographic, employment, and pre-existing health covariates were included

in models, in addition to current levels of distress, assessed using the 6-item Kessler psychological distress scale.

#### Results

During 27 April to 26 July 2020, 78% of people reported making lifestyle changes during the prior months and 52% spoke to family or friends about their mental health concerns. Only 20% reported speaking to a health professional. Most people took multiple actions to manage their mental health during the pandemic, though the nature of actions taken depended on an individuals' demographics, employment status and personal health. Overall, actions were more commonly taken by women, people who were out of work, those with pre-existing depression or people experiencing distress.

#### Conclusion

Behavioural actions to manage mental health concerns during the COVID-19 pandemic were common, as were conversations with friends or family members. Interventions to encourage the use of formal mental health supports are encouraged such as promoting accessible mental health supports in the workplace, and increasing mental health education for all workers. Supports and services should focus on reducing barriers to health care, particularly for people associated with commonly taking less help-seeking behaviour in general, and those experiencing high levels of distress.



# Mutiara Reka Ananda Putri

## Parenting on the spectrum: A systematic scoping review of parenting experiences and the mental health of parents with ASD or autistic traits

Supervisor Names and Institute Affiliations:

Katrina Williams<sup>a,b</sup>, Georgina Cox<sup>a,c</sup>

<sup>a</sup> Department of Paediatrics & Education Research, Monash University, Melbourne, Australia

<sup>b</sup> Monash Children's Hospital, Melbourne, Australia

<sup>c</sup> Department of Neurodevelopment and Disability, The Royal Children's Hospital, Melbourne, Australia



Mental health has always been one of my interests. When I read the project description, I knew I'm going to love learning about this. As a person who sometimes can get a bit distracted, having supportive supervisors has been very helpful to keep me motivated. Maintain a good relationship and communication with your supervisors! They have lots of experience and you can learn a lot from them. And don't hesitate to ask for help when you need it.

### ABSTRACT

#### Background

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder with main characteristics of impaired social and communication skill and restricted repetitive behaviours. They can also present with sensory sensitivity and other co-occurring conditions. The high heritability of ASD has been frequently observed and relatives of autistic individuals may present milder autistic traits referred as Broader Autism Phenotype (BAP). Recent studies show that the prevalence of autism is increasing. This suggests that there will be a higher number of adults with ASD and BAP, both diagnosed and undiagnosed. If adults with ASD and BAP become parents, their autistic traits may influence their parenting ability, family functioning, their child development, and mental health of the parent. The aim of this study is to systematically map and summarise findings from studies on effect of parental ASD or BAP on parenting experience, mental wellbeing of parents, and the way the family functions / the functioning of the family. The secondary aim is to locate knowledge gap for possible future research.

#### Methods

This scoping review followed PRISMA Extension for Scoping Reviews (PRISMA-ScR). Databases used in this study were MEDLINE, PsycINFO, Cochrane Library, EMBASE, and SCOPUS. Studies obtained were inputted into COVIDENCE software for title and abstract screening, followed by a full text screening. The findings were summarized in a narrative form.

#### Results

28 articles were included in this review. 5 broad outcome themes were found associated with parental ASD and BAP: parent's mental wellbeing, early parenthood experience, later parenthood

experience, family dynamic and parent-child relationship. There were gaps in knowledge regarding the effect of parental ASD and the effect of ASD and BAP on fathers, due to the limited number of articles that include parent with ASD and lower involvement of fathers with ASD or BAP compared to mothers.

#### Conclusion

ASD and BAP in parents has been reported have affected parents and their family in various ways, generally increasing the difficulty of parenting. There was limited father involvement compared to mother in the studies and a few studies had parents with ASD. Further research is needed to address the gaps in knowledge.

# Natasha Rasaratnam

## Assessing the within-individual variability of urine albumin/creatinine ratio in people with type 2 diabetes

Supervisor Names and Institute Affiliations:

Dr Julian Sacre, Professor Jonathan Shaw

Baker Heart and Diabetes Institute

School of Public Health and Preventive Medicine, Monash University



My decision to undertake a BMedSc(Hons) following fourth year was a result of many factors: wanting a change of pace and environment before graduating, an opportunity to develop new skills, and finding a project that I was interested in with an experienced team that I was keen to learn from.

This year was both extremely rewarding and challenging. The year requires a lot of independent learning and initiative, but I was lucky to have supervisors who always took the time to answer my questions. Whenever we met a hurdle in the project, my supervisors provided guidance so that I never felt like I had to solve an issue all by myself. I was also able to sit in on some diabetes clinics and appreciate the impact of research in clinical practice.

My advice for future students is to find supervisors who can give you the time and support needed for the year. I would also recommend finding a project that sparks your curiosity. It's a long year and you need to keep yourself motivated, so if you can find meaning in your work, it goes a long way.

Please feel free to contact me with any questions ([nras0001@student.monash.edu](mailto:nras0001@student.monash.edu))

## ABSTRACT

### Background

Measurement of the urine albumin/creatinine ratio (UACR) from a random spot sample is commonly used for the assessment of diabetic chronic kidney disease (CKD). High within-individual variability presents a challenge for both monitoring and diagnosis. Multiple tests may better characterise clinical status based on albuminuria.

### Aims

To quantify the within-individual variability of the random spot UACR in people with type 2 diabetes, its implications for the number of samples required for diagnosis and monitoring of diabetic CKD and assessing the factors that influence variability.

### Methods

People with type 2 diabetes ( $n = 544$ ; median 67 years, 69% male) participating in the Progression of Diabetic Complications (PREDICT) prospective cohort study provided four random spot urine samples within a four-week period. Absolute reliability (the extent by which an individual's repeated measurements vary over time) was characterised by the coefficient of variation (CV) and 95% limits of random variation (range encompassing 95% of differences between any two samples). Relative reliability (within-individual variation as a proportion of total study population variation) was based on the intraclass correlation coefficient (ICC). These metrics of variability were used to compare between sample collection factors (clinic vs home; same day vs different day). The influence of clinical characteristics was assessed through multiple linear regression. We estimated the number of samples needed for monitoring (using 95% limits of agreement with the mean) and for diagnosis (using area under receiver operating characteristic [AUROC] curve analyses). Log-transformation was used due to skewness and heteroscedasticity.

### Results

Most participants (69%) were classified as normoalbuminuric ( $\text{UACR} < 3 \text{ mg/mmol}$ ). We observed a high CV of 48.1% and wide

limits of random variation, by which a second sample may be as small as 0.24 times or as large as 3.35 times the first sample, due to within-individual variability. The 95% limits of agreement with the mean suggested a single sample could be expected to be between 0.44 and 2.34 times the four-sample mean. Although agreement with the four-sample mean increased as sample number increased, the three-sample mean remained 20-30% different to the four-sample mean.

Relative reliability was more favourable ( $\text{ICC} = 0.86$ ). The AUROC (representing agreement with four-sample classification) was  $> 0.96$  for a single sample, marginally increasing to  $> 0.98$  when two and three samples were averaged. Sensitivity was  $> 90\%$  for two-sample and three-sample means.

There were significant correlations of lower within-individual UACR variability with both SGLT2 inhibitor use and  $\text{eGFR} < 60$ , but these associations were modest (beta-coefficient:  $< -0.2$ ). Same-day samples differed significantly less from each other than samples collected on different days ( $\text{CV } 36.2\% \text{ vs } 49.0\%$ ;  $p = 0.001$ ). Variability of home-collected and clinic-collected samples were not significantly different.

### Conclusion

Our study provides greater insight into the extent by which the random spot UACR may vary within a person. Our results suggest multiple samples are necessary to quantitatively monitor UACR. However, this within-individual variability has only a modest impact on diagnosis. Same-day samples may underestimate within-individual variability and obscure characterisation of UACR. Overall, fewer samples are required for diagnosing diabetic CKD compared to monitoring.

# Yvette Raymond

## The predictive accuracy of cell-free fetal DNA screening in the detection of clinically significant rare autosomal trisomies and segmental copy number variants

Supervisor Names and Institute Affiliations:

Dr Daniel Lorber Rolnik (Monash University, Monash Health)

Dr Shavi Fernando (Monash University, Monash, Monash Obstetrics)



I chose to pursue a BMedSc(Hons) after my 4C rotation in Women's health. I loved Obstetrics and was very fortunate to meet my future supervisors who both have an infectious passion for research, who presented a research opportunity in the field of prenatal genetic science which was one of my areas of keen interest. The BMedSc(Hons) year has easily been my favourite year of medical school to date. The completion of my thesis is one of my proudest accomplishments, and I was privileged to work with an incredible team of mentors from whom I learnt more than I could have possibly anticipated. This year lead me to discover a love of research which has prompted me to now pursue the MD/ PhD pathway, something I never would have foreseen myself doing prior.

My advice for future BMedSc(Hons) students would be to jump in! Take every opportunity afforded to you, ask as many questions as you can think to, cherish the connections you make with your fellow research students, and enjoy every moment because the year will be over in the blink of an eye!

### ABSTRACT

#### Background

Non-invasive prenatal testing (NIPT) is a prenatal screening test which analyses cell-free DNA from placental cells for indication of fetal chromosomal anomalies. While NIPT is accurate for the detection of common aneuploidies such as Trisomy 21, concerns have arisen over a recently introduced expansion of NIPT in which the entire genome is analysed, termed genome-wide NIPT. Particular anomalies of interest in relation to genome-wide NIPT include rare autosomal trisomies, and segmental copy number variants. While there is limited evidence available in this field, the predictive accuracy of genome-wide NIPT appears low, and the clinical implications of both true-positive results, as well as false-positive results which may indicate anomalies of the placenta, are poorly understood.

In this study we aimed to investigate the predictive accuracy of genome-wide NIPT for rare autosomal trisomies and segmental copy number variants, and any prenatal factors which could influence this accuracy. We also sought to investigate outcomes of these pregnancies, particularly those pertaining to fetal growth outcomes given they are at increased risk of placental genetic mosaicism.

#### Method

We conducted a retrospective cohort study beginning with a clinical audit of records of high-risk genome-wide NIPT results obtained from one of Melbourne's major genome-wide NIPT providers. Participants were contacted for missing outcomes, pertaining to diagnostic testing results, birth outcomes and postnatal development. Additional participants were also acquired from interstate collaborating genome-wide NIPT providers. Participants for whom no outcomes were attainable post-screening were excluded from the final cohort. Positive predictive values

were calculated from cases with karyotype confirmation. Various analyses were used to assess for significance between screening accuracy and prenatal variables such as maternal age, fetal fraction and presence of uterine fibroids. Finally, birthweight and birthweight percentiles were compared to the expected values in the general population.

#### Results

The final cohort included 86 rare autosomal trisomies and 77 segmental copy number variants. This study showed that the positive predictive value of genome-wide NIPT is 3.9% for rare autosomal trisomies, and 18.8% for segmental copy number variants. The positive predictive value increases in the presence of ultrasound anomalies. Pregnancies which receive a false-positive gwNIPT result for a rare autosomal trisomy are at increased risk of having an infant below both the tenth and third percentile for birthweight, but there is no apparent association between these results and other adverse obstetric outcomes such as prematurity or miscarriage. No complications of pregnancy were found to be associated with false-positive segmental copy number variant results.

#### Conclusion

Genome-wide NIPT has poor positive predictive values for rare aneuploidies, generating an undesirably high rate of false positive results. Women who screen high risk for a rare autosomal trisomy or segmental copy number variant with genome-wide NIPT should be carefully counselled about the low likelihood of fetal involvement before progressing to further invasive diagnostic testing. Further research is required to better ascertain the implications of these results, including the impact of placental involvement, in order to guide appropriate management for these patients.



# Tianrui (Ray) Ren

## Health Burden of Deferred and No Treatment for Newly Diagnosed Epilepsy

Supervisor Names and Institute Affiliations:

Professor Patrick Kwan, MB, BChir, PhD, FRCP, FRACP, FAHMS

Professor of Neurology, Monash University

Director of Epilepsy, Alfred Health

Dr Zhibin Chen, PhD, MBiostat, Bsc(Hons)

Research Fellow, Central Clinical School, Monash University.



Wow - where do I even begin. These past 10 months have been some of the most rewarding, albeit challenging, parts of my medical school journey.

My research investigated the health outcomes of epilepsy patients using large state-wide databases. This taught me essential biostatistics and data analysis skills. Simultaneously, my project helped me establish important networks in neurology, whilst providing ample opportunity for publication.

A major highlight of my year was obtaining clinical exposure in parallel to research. Through attending weekly epilepsy clinics, I met some incredible mentors at The Alfred who encouraged and guided me. As I gained confidence, I even got the chance to parallel consult 1 or 2 patients in my own room. In theatre, I also saw the frontiers of epilepsy treatment in the form of neurologist-guided epilepsy surgery. These experiences not only cemented my passion for medicine, but demonstrated to me the real-world impact that research has on improving patient care. Finally, my year would not be the same without the friends I made along the way. From break-rooms to clinics, they supported me through my ups and downs and greatly enriched my journey. Ultimately, I cannot recommend BMedSc(Hons) highly enough to future students.

## ABSTRACT

### Background

Though medications help many epilepsy patients achieve seizure freedom, 30% of newly diagnosed epilepsy patients in Australia are not initially treated at diagnosis. Whilst this may partially reflect conservative clinical decision-making, current Australian Therapeutic Guidelines strongly recommend immediate treatment to prevent further seizures. Assessment of the health consequences of deferred and no treatment, therefore, can determine if current practice is justified and guide health service delivery.

This project aimed to assess the health consequences of deferred and no treatment among newly diagnosed epilepsy patients in Australia. As a secondary aim, we also examined the health burden of newly diagnosed epilepsy compared to the general population.

### Methods

We performed linkage analysis of patients with newly diagnosed epilepsy between 1999 and 2016 with state-wide healthcare databases to extract hospital admission, ambulatory psychiatric care, and mortality data from 1970 to 2019. Data were compared between epilepsy patients with immediate, delayed and no treatment. For each epilepsy patient, seven population controls were matched, with the latter extracted from a 1% random sample of the Western Australia electoral roll from 1999-2016. Analyses were performed at up to 10 years post-diagnosis, adjusted for seizure type, age at onset, sex, baseline comorbidity, and relevant follow-up times.

### Results

603 patients (61% male; median age 40 years) with newly diagnosed epilepsy were studied. 422 (70%) were treated immediately, 110 (18%) received delayed treatment, and 71 (12%) were untreated at the end of clinical follow-up (median 6.8 years, interquartile range: 4.0–10.0).

At five years post-diagnosis, the rate of all-cause admissions or emergency department presentations was higher in the immediate

treatment group than the untreated group (incidence rate ratio [IRR]=2.3; 95% confidence interval [CI]: 1.5–3.6) or delayed treatment group (IRR=1.7; 95%CI: 1.0–2.8).

However, there were no differences in overall mortality at five years (n=70) between immediate treatment and delayed treatment (hazard ratio [HR]=1.18; 95%CI: 0.55–2.48) or untreated groups (HR=1.59; 95%CI: 0.48–5.25). Immediately treated patients also had similar risks of developing new physical comorbidities and psychiatric comorbidities compared with the delayed (p=0.74; p=0.15, respectively) and untreated groups (p=0.63; p=0.39, respectively) at five years.

Finally, when compared to 4,824 matched population controls, epilepsy patients had 2.5 (95%CI: 2.06–3.06) times more physical comorbidities and 3.6 (95%CI: 2.4–5.3) times the rate of psychiatric comorbidities at ten years. The mortality rate was also 2.6 (95%CI: 2.1–3.3) times higher in the latter. Furthermore, epilepsy patients had 2.3 (95%CI: 1.6–3.3) times the rate of hospitalisations and 3.2 (95%CI: 2.7–3.7) times the rate of emergency presentations, compared to the general population in Australia.

### Conclusion

Newly diagnosed epilepsy patients with deferred or no treatment did not have worse prognostic outcomes, compared to those with immediate treatment. Instead, patients requiring immediate treatment have a high rate of healthcare utilisation, which may reflect a more severe underlying epilepsy condition.

Compared to the general population in Australia, newly diagnosed epilepsy patients have excess mortality, comorbidities and healthcare utilisation. Through targeted intervention of the comorbidities identified, the health burden of newly diagnosed epilepsy can be mitigated.

# Nicholas Sean

## Mapping Gender Differences in Internet Gaming Disorder and Mental Health among University Students in Indonesia

Supervisor Names and Institute Affiliations:

Dr Shalini Arunogiri, Central Clinical School, Monash Alfred Psychiatry Research Centre.



Greetings, I'm Sean, a fourth-year medical student from Indonesia. I was fortunate enough to take part in this year's Honours program despite having to conduct the entire research project online due to the global pandemic situation. Although I was unable to experience campus life in Melbourne, I was grateful to have encountered many lecturers from the MAPrc department, including my supervisor Dr Shalini Arunogiri, who have contributed greatly to my knowledge of statistical research. Being a gamer myself, the topic of online game addiction caught my attention despite being a niche topic in the medical field. To my surprise, I was able to gain a fresh understanding about non-substance, behavioural addictions that at first seemed unimportant. With that being said, I would encourage future students to take risks in exploring new, emerging topics as the reward is well worth it. Always keep good relations with your supervisors and don't be afraid to initiate questions when confused. I would also advise for good time management to acquire a substantial amount of time to work on feedback. Overall, I was happy with how the year went and I hope that others would have a fruitful learning experience as well.

### ABSTRACT

#### Background

Internet gaming disorder (IGD) is the recurrent and persistent use of online games as indicated by symptoms of preoccupation, withdrawal, tolerance, uncontrollable behaviour, loss of interests in previous hobbies, and psychosocial problems. There were limited studies in South East Asia despite a growing trend towards more online gaming among young adults in that region. The purpose of this study was to explore gender differences in IGD among Indonesian university students and determine its association with mental health and motivations for playing online games.

#### Method

The study utilized a cross-sectional design on 432 Indonesians through the use of an online survey that consisted of the Internet Gaming Disorder Short-Form Questionnaire (IGDS9), the Problematic Online Gaming Questionnaire (POGQ), the Indonesian Online Game Addiction Questionnaire (IOGAQ), the Depression, Anxiety, and Stress Scale (DASS-21), and the Motives for Online Gaming Questionnaire (MOGQ). The inclusion criteria were Indonesian young adults. The exclusion criteria were non-Indonesians and Indonesians without informed consent. Chi-square and bivariate logistic regression tests were used to analyse the data.

#### Results

From 432 respondents, a majority of 302 (69.9%) respondents were male at the age of 25. Half of the respondents (50.5%) participated in some form of gaming daily and had an average playing time of three hours. The most played online game genre based on 374 respondents was First-person shooter (FPS) (30.2%) with the second most

popular being Multiplayer online battle arena (MOBA) (24.6%). IGD was more prevalent among males (6.29%) than females (1.54%) based on the Chinese context IGDS9. Problematic gaming and online game addiction with mild addiction were also more prevalent among men as seen by the 83 (27.5%) and 324 (75%) respondents respectively. Bivariate analysis demonstrated that depression and stress were strongly associated with the IOGAQ ( $p < 0.05$ ) while stress was only strongly associated with the POGQ ( $p < 0.05$ ) and the IGDS9 had no strong associations with the DASS-21 variables. Gender was not strongly associated with depression, anxiety, or stress ( $p > 0.05$ ). Men had a higher mean score for all MOGQ motives compared to women but only escape, competition, and recreation ( $p < 0.05$ ) were statistically significant. MMORPG had the highest mean score for the social, escape, coping, skill, fantasy and recreation motives while MOBA had the highest mean score for competition. Bivariate analysis established that the POGQ, IGDS9 had a strong association with the escape and competition motives ( $p < 0.05$ ) while the IOGAQ was strongly associated with escape and recreation ( $p < 0.05$ ).

#### Conclusion

Gender differences included a higher prevalence of IGD among males than females for this sample of Indonesian young adults. Men were more motivated to play online games compared to women who preferred casual games. There were no gender differences in terms of mental health, although IGD had a strong association with stress. The escape and competition motives were strong indicators of IGD.

# Uvin Seneviratne

## The analgesic management and healthcare utilisation of patients presenting with low back or radicular pain for four weeks following discharge from a tertiary hospital emergency department: An observational cohort study

Supervisor Names and Institute Affiliations:

Supervisor: Dr Kerry McLaughlin

Co-Supervisor: Professor Paul Myles

Institute: Department of Anaesthesiology and Perioperative Medicine, Alfred Health



Hi, I am a BMedSc(Hons) student in the Department of Anaesthesiology at the Alfred Health.

This year, I have furthered my interests in anaesthesia and gained more clinical training in theatres. I would like to thank the various anaesthetic consultants and registrars who were instrumental in this rewarding year. As my project was conducted in the emergency department, we also developed a close partnership with the ED clinicians and musculoskeletal physiotherapists.

During the year, I was given the opportunity to present at the ACEM Research Network Symposium. This allowed me to connect with like-minded clinicians, with plans to liaise with other major metropolitan hospitals to conduct future multicentre, randomised controlled trials.

My main advice for future students would be to choose the right supervisor for you. This year would not have been possible without my wonderful supervisors. Setting clear expectations with your supervisor will also be pivotal in maximising the year. I would also advise that submission timelines are set around supervisors and co-authors, so they have 2-4 weeks to review major assignments or manuscripts.

I will be continuing my research commitments next year and am more than happy to be contacted by future students (usen0002@student.monash.edu).

### ABSTRACT

#### Background

Literature surrounding low back and radicular pain in the emergency department (ED) focuses mainly on pharmacological management. There is a current gap in literature regarding ED non-pharmacological management and management changes due to post-discharge healthcare utilisation. The aim of this observational, cohort study was to obtain data on the analgesic management, discharge planning and further healthcare utilisation of adults presenting to the Alfred Health ED with low back or radicular pain, in the four-week period following discharge from the ED.

#### Method

The primary outcome is the pharmacological and non-pharmacological management prescribed in ED. The secondary outcomes include post-discharge management, pain and functional status, and healthcare utilisation. The management participants received within ED and upon discharge were obtained from the Alfred Health EMR. Participants were followed-up via weekly telephone questionnaires over four weeks post-discharge to observe their use of discharge management, pain and functional capacity, and healthcare utilisation (in particular focusing on changes to prescribed discharge management plans resulting from post-discharge healthcare utilisation).

#### Results

The thesis data set included 37 patients. Data collection is ongoing. Of the 37 participants, 34 completed follow up, resulting in an 8% lost-to-follow-up rate. It was observed that 78% (n=29) received non-pharmacological management and 84% (n=31) received pharmacological management within ED. Of pharmacological management, 59% (n=22) received NSAIDs and 62% (n=23) received opioids. Opioid delivery was not influenced by opioid tolerance as 63% (n=5) of opioid-

dependent and 62% (n=18) of opioid-naïve patients received opioids. Patients who presented out-of-hours (18.00 to 9.30) were 1.3 times more likely to receive pharmacological management within ED than those who presented in hours (09.30 to 18.00). Although there were similar rates of discharge pharmacological management prescribed to groups presenting in and out-of-hours, the patients who presented in hours were 1.8 times more likely to receive non-pharmacological management upon discharge compared to out-of-hours. All patients (n=19) who received discharge exercise prescription, presented in hours. General practitioners were the most utilised avenue for healthcare utilisation with 57% (n=21) patients presenting within the first week post-discharge. On the final week of follow-up, only 22% (n=7) used discharge pharmacological management, compared to the 45% (n=13) who continued to use non-pharmacological interventions.

#### Conclusion

This study found that patients presenting to the ED with low back pain out-of-hours received less non-pharmacological treatment, largely because of the lack of physiotherapy input available in the out-of-hours period. NSAIDs were under-utilised. Concerningly, 4% of patients in the opioid-naïve group remained on opioids 4 weeks post-discharge, which if representative of the Australian LBP population signifies a potential 'gateway' towards unintentional long-term opioid use. The full study is ongoing (sample size 100 participants), providing further sub-group data to better inform future interventional trials in this field.



# Anna Shalit

## Are Australian clinical practice guideline panels gender balanced? An analysis of the gender of members of Australian clinical practice guideline development panels from 2015 to 2021.

Supervisor Names and Institute Affiliations:

A/Professor Joshua Vogel, Burnet Institute and School of Public Health and Preventative Medicine; Professor Caroline Homer, Burnet Institute



I completed my Honours project at Burnet Institute this year after finishing fourth year in 2020. I chose to do my project in public health because I am very passionate about equity, and this project seemed the perfect fit. Having the opportunity to learn from such fantastic researchers and being part of an engaged and prolific team was invaluable. Being able to fully immerse myself in the project helped me strengthen my understandings of the broad principles of research and gain specific, transferrable skills. If research is something you're even vaguely considering, I strongly recommend doing an Honours year and giving it a proper chance! Feel free to get in touch with any questions.

### ABSTRACT

#### Background

Gender equality is a critical component of ensuring health services are effective, equitable and get the best health outcomes for all people. However, gender equity in Australian health leadership has not yet been achieved, with persistent gender bias, pay discrepancies and under-acknowledgment of women's contributions. Development of national clinical practice guidelines is one important aspect of health leadership. However, gender balance on Australian guideline development panels has not previously been assessed. I conducted an analysis of the gender of individuals on clinical practice guideline development panels in Australia to determine whether equity is being achieved.

#### Methods

The aims were:

1. To identify high-quality Australian clinical practice guidelines published between 2015 and 2021
2. To determine the gender composition overall, the proportion of women on each guideline panel, and to examine differences in gender distribution between guideline panel roles
3. To explore the relationship between gender balance and guideline factors including NHMRC approval, source of funding, type of methodology and subject area

A systematic analysis of publicly available data from published clinical practice guidelines was conducted. The search strategy consisted of receiving data from the National Health and Medical Research Council as well as searching PubMed, the Guidelines International Network Library, and the Trip Database. I searched for high-quality guidelines that were produced in Australia for national use between 2015 and 2021. These results were screened by two independent reviewers against a set of eligibility criteria. Characteristics of eligible guidelines and the individuals involved in their development were extracted into Microsoft Excel. I calculated

descriptive statistics and measured associations between guideline features and gender balance using Stata.

#### Results

The combined searches identified 4382 documents, from which 142 high-quality guidelines were included. Overall, there were more male (48.8%) than female (46.1%) guideline developers, though almost half of all guidelines (47%) had a guideline panel with less than 40% women on it. There was no significant difference in the proportions of men and women who were guideline development group chairpersons, when compared to guideline development group members. A significant association between the source of a guidelines funding and the proportion of women on development panels was found, with NHMRC and Government funded guidelines demonstrating better gender balance. NHMRC approval was also associated with fewer guidelines that had very low proportions of women. Australian cardiovascular disease and cancer guidelines were both predominantly authored by men.

#### Conclusion

This is the first study to assess the gender composition of Australian clinical practice guideline panels. A significant gender imbalance was found, with men holding more than half the positions on the majority of guideline panels. Though gender inequity clearly remains in Australian healthcare leadership, including in clinical practice guideline development, efforts to improve the gender balance appear effective. Findings from this study present a baseline from which future changes can be measured. Ultimately, measuring gender gaps in Australian health care leadership represents the first step towards managing disparities and reaching gender equality.



# Henry Shen

## Potential prognostic biomarkers in pancreatic ductal adenocarcinoma: KRAS and BMP4

Supervisor Names and Institute Affiliations:

Mr Daniel Croagh, Monash Department of Surgery, School of Clinical Sciences

Professor Brendan Jenkins, Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research



I committed to a BMedSc(Hons) year after 4th year for a number of reasons. These included exploring a field of interest (pancreatic cancer and general surgery/gastroenterology), learning new skills such as statistics, scientific writing and lab work, and having the freedom to manage an extremely self-guided year. Instead, I also came away with an appreciation for deadline desperation, weeks of waiting around, and the self-realisation of the necessity of organisation. Nevertheless, I had an extremely memorable year, and have learnt so much about the research process and myself. I had the chance to take ownership of a project from start to finish, and fill in the gaps with self-teaching and mistakes. Most importantly, I have developed a genuine passion for research, which would not have been possible without the endless support from my supervisors Dan and Brendan.

I definitely recommend the BMedSc(Hons) year if you are interested in developing a solid, lasting foundation in research skills. Make sure to talk to as many supervisors as possible before you decide your Honours project, taking into consideration both your supervisor's goals as well as the merit of the project itself. Feel free to contact me at [hshe0005@student.monash.edu](mailto:hshe0005@student.monash.edu) if you have any questions!

## ABSTRACT

### Background

Pancreatic ductal adenocarcinoma (PDAC) is one of the leading causes of cancer death in Australia and the world. The majority of patients present with unresectable disease at diagnosis. There is no clinically available biomarker to assess prognosis in PDAC. However, KRAS mutation is present in over 90% of PDAC cases. Furthermore, bone morphogenetic protein 4 (BMP4) is involved in various oncogenic cellular processes in PDAC. This project aims to investigate the role of detecting the KRAS mutation and subtype in PDAC patients to determine prognosis across all stages of disease. This project also aims to investigate the association between BMP4 expression and survival in PDAC.

### Method

We reviewed the records of 231 patients presenting with PDAC to Monash Health from 2012 to 2020. We recorded age, sex, date of diagnosis, date of death, National Comprehensive Cancer Network (NCCN) clinical stage, KRAS status, KRAS detection method, type of treatment received, and surgery details such as lymph node status and resection margin status. We also conducted immunohistochemistry on 12 PDAC and 4 non-PDAC resection specimens, and semi-quantitatively scored BMP4 expression. We compared survival using the Kaplan Meier method, log-rank test and Cox proportional hazards regression model.

### Results

The 3 most frequently occurring KRAS mutation subtypes were G12D (40.3%), G12V (27.7%) and G12R (10.4%). KRAS mutation was not significantly associated with poorer survival (420 days) compared to KRAS wild-type (296 days) (HR 1.050, 95% CI 0.646 - 1.709;

$p=0.843$ ) and G12D mutation subtype was not significantly associated with poorer survival compared to all other PDAC patients (HR 1.293, 95% CI 0.946 - 1.767;  $p=0.107$ ). Within the operable group, G12D patients had a significantly shorter median survival time of 356 days compared to non-G12D patients (median survival 810 days) (HR 1.991, 95% CI 1.121 - 3.537;  $p=0.019$ ). There was no significant correlation between KRAS mutation and clinical stage at diagnosis ( $p=0.1627$ ). There were no statistically significant differences in BMP4 expression between the PDAC and non-PDAC groups ( $p=0.3874$ ). High BMP4 expression was not significantly associated with poorer survival compared to low BMP4 expression (HR 0.425, 95% CI 0.050 - 3.637;  $p=0.435$ ).

### Conclusion

Although there was a trend in correlation between KRAS mutation and survival across all NCCN stages, this was not statistically significant. G12D patients who were operable had significantly shorter survival compared to all other PDAC patients. The data suggests that KRAS G12D may be a clinically useful prognostic biomarker in the future for operable PDAC patients. There was no association between BMP4 expression and survival in PDAC patients, however, this represents the first time BMP4 expression has been characterised in human PDAC samples. A larger sample size is required to confirm this.

# Tymon Shih

## The Role of BRCA1 and BARD1 in Alternative Lengthening of Telomeres

Supervisor Names and Institute Affiliations:

A/Professor Tony Cesare, CMRI

Dr Sam Rogers, CMRI

Traude Beilharz, Monash Biomedicine Discovery Institute



I chose to do my project straight after my 3rd year of the BMedSc/MD degree, after a very enjoyable research stint at the CMRI lab in Sydney during the 2019/2020 summer break. During that time, I was introduced to a new domain of cancer-related biochemistry, and worked on a fun coding-based project to design a browser for ALT-related cancer proteins. Piqued by research, I decided to return to the lab for my Honours. This year has left me more acquainted with laboratory-based research after learning a variety of commonly used wet-lab techniques. It has also greatly increased my appreciation for molecular biology that forms the foundation of many aspects of medicine. I was also incredibly lucky to have great supervisors who kept me motivated during a challenging year fraught with lockdowns, and am so grateful to everyone who supported me throughout the year. I am sure that the skills and knowledge I have gained this year will be valuable for years to come!

Please feel free to contact me through:  
tymon135@gmail.com

### ABSTRACT

#### Background

Telomeres are DNA sequences found at the ends of eukaryotic chromosomes. Telomere shortening places a key limitation on cell proliferation in untransformed cells, acting as a tumour suppressive barrier. However, telomere maintenance through alternative lengthening of telomeres (ALT) enables unlimited proliferation in found in tumours. Current research indicates ALT utilises homologous recombination (HR) - a pathway that repairs double-stranded DNA breaks (DSBs). However, mechanisms driving ALT in cancer remain unclear.

Emerging evidence supports the notion that BRCA1 – a regulator HR and stalled fork repair – and its obligate binding partner BARD1 play roles in regulation replication stress at ALT telomeres. BRCA1 complexes with BARD1 to enhance activity of DNA recombinase Rad51, which catalyses strand invasion in HR. Similarly, phosphorylation of BRCA1 at serine 114 (S114) enhances Rad51 binding to the complex. The aim of this project was to mechanistically determine the role of BRCA1 and BARD1 in signalling pathways at the ALT telomeres.

#### Method

This study utilises an immunofluorescence (IF) approach to investigate protein distributions in ALT cells. We depleted both BRCA1 and BARD1 in ALT+ U2OS cells using siRNA transient siRNA transfection (including a non-targeting control). 48 h after transfection we fixed and stained depleted cells for combined IF and telomere fluorescent in situ hybridisation (FISH). We then stained cells to assess four DNA damage markers: 53BP1, RPA32, Rad51 and Rad52. Using the Zeiss Axiolmager system we quantified fluorescent colocalisations between proteins of interest and the telomere-FISH PNA probe.

#### Results

We also found that depleting BRCA1 and BARD1 accumulated Rad51 and Rad52 to

telomere, consistent with inducing replication stress. Compared to our control group, siBARD1 increased Rad51 foci per cell (1.550, 95% CI [0.631, 2.470],  $p=0.0003$ ) and at the telomere (1.488, 95% CI [0.503, 1.927],  $p=0.0003$ ). For Rad52, knocking down BRCA1 accumulated foci across the cell (9.972, 95% CI [6.602, 13.340],  $p<0.0001$ ) whilst both siBRCA1 (6.366, 95% CI [3.651, 9.081],  $p<0.001$ ) and siBARD1 (4.484, 95% CI [1.646, 7.321],  $p=0.0008$ ) increased its localisation to the telomere. Rad51 and Rad52 are strong markers for HR; this suggests that BRCA1- and BARD1- deficient cells feature high replication stress and BRCA1-independent pathways for Rad51-mediated HR repair. In contrast, we saw a decrease in RPA32 foci when knocking down BARD1 (1.550, 95% CI [0.6309, 2.470],  $p<0.0003$ ), supporting the notion that the signalling repair cascade may not follow canonical HR. Unexpectedly, there were no significant differences in 53BP1 foci.

#### Conclusion

This study characterises the effect of BRCA1 and BARD1 knockdown in cells actively undergoing ALT. Our results suggest that knockdown of either gene induces replication stress across the nucleus and at the telomere, priming the cell for DNA damage repair. Moreover, Rad51 may be recruited to the telomere to resolve DSBs through BRCA1-independent pathways. Overall, BRCA1 and BARD1 potentially play a role in telomere maintenance by suppressing replication at the ALT telomere.

# Rhea Singh

## General practitioner perspectives and experiences in delivering early medical abortion services to women from culturally and linguistically diverse backgrounds

Supervisor Names and Institute Affiliations:

Dr Asvini K. Subasinghe, Professor Danielle Mazza and Dr Mridula Shankar

SPHERE (NHMRC Centre of Research Excellence in Sexual and Reproductive Health for Women in Primary Care)

Department of General Practice, Monash University



My name is Rhea, and I chose to undertake a BMedSc(Hons) after completing Year 4C with the hope to develop my skills in research and explore my interest in women's sexual and reproductive health. I chose my project as I have a strong interest in both general practice and women's health, with a particular interest in addressing health inequalities in priority populations. I was interested in qualitative research as it was an area that I have not had much exposure to, and I thought it would be a valuable way to gain insight into the experiences and perspectives of GPs. Although challenging at times, I have really enjoyed my year and have had a lot of support from my supervisors and the Department who have provided me with multiple learning and professional development opportunities. I have gained many new skills around designing a qualitative study, recruiting participants, conducting interviews, analysing qualitative data, and academic writing. My advice for future students would be to try and stay organised and on top of deadlines so you can give your supervisors plenty of time to review. I am more than happy to be contacted by any future BMedSc(Hons) students: [rsin0008@student.monash.edu](mailto:rsin0008@student.monash.edu).

### ABSTRACT

#### Background

Women from culturally and linguistically diverse (CALD) backgrounds have higher unintended pregnancy rates than Australian-born women and underutilise sexual and reproductive health (SRH) services. Consequently, the National Women's Health Strategy has identified women from CALD backgrounds as a priority group for improving access to SRH services, including early medical abortion (EMA). Women commonly seek the counsel of general practitioners (GPs) for sexual and reproductive health concerns, making GPs ideally placed to deliver EMA services. However, little is known about how GPs should best deliver this care to women from CALD backgrounds. Our aim was to explore GP perspectives and experiences in relation to providing EMA services to women from CALD backgrounds and how to improve the delivery of such care.

#### Methods

We undertook a qualitative-descriptive study involving semi-structured, audio-recorded telephone interviews with 18 GPs who provide EMA to women from CALD backgrounds in the general practice setting. GPs were purposively sampled nationwide using three strategies: email invitations to publicly listed medical abortion providers, social media posts on a special interest Facebook group, and participant referral. The interview guide was informed by the Capability-Opportunity-Motivation Behaviour (COM-B) model and explored the challenges and strategies GPs encountered when delivering EMA to women from CALD backgrounds. Following verbatim transcription, data were managed in NVivo software. Reflexive thematic analysis by two coders was used to develop themes and subthemes, categorised according to the capability, opportunity, and motivation domains of the COM-B model.

#### Results

Four key themes reveal the complexities of and best practice approaches to delivering EMA to women from CALD backgrounds.

These are summarised as: (1) sociocultural influences; (2) structural barriers and disincentives; (3) poor provider preparedness; and (4) GPs conceptualisation of their professional role. Sociocultural influences, including culturally prescribed gender roles and stigma surrounding premarital sex and abortion, were integral for GPs to acknowledge as they impacted the provision of women-centred care. Additionally, inadequate government reimbursement for EMA consultations, which contributes to high out-of-pocket costs for women, was identified as a financial impediment to care because women from CALD backgrounds tend to be more socioeconomically disadvantaged than the general population. Lack of cultural competency training and communication challenges due to language differences, lack of multilingual resources, and complexities in effectively using interpreter services also decreased GPs' capability to provide culturally appropriate EMA services. Despite these challenges, GPs believed they were ideally positioned to provide EMA to women from CALD backgrounds since their embeddedness within CALD communities facilitates the building of trusting relationships with their patients.

#### Conclusion

Up-skilling of GPs in the provision of culturally competent care and cross-cultural communication, multilingual EMA patient education resources, and efficient systems for interpreter use are required to optimise EMA delivery by GPs to women from CALD backgrounds. Further exploration of incentivising service provision is required to offset financial barriers to patients. Our findings may be transferable to other services Australian GPs deliver to women from CALD backgrounds and other high-income countries similarly working towards improving the delivery of women's healthcare in migrant and refugee populations.



# Lucy Standish

## Assessment of the Microcirculation with the Cytocam

Supervisor Names and Institute Affiliations:

A/Professor Roderic Phillips, Professor Tony Penington, Professor Andrew Heggie



I decided to enrol in an Honours year partly because of the positive experience echoed by previous years and partly to ensure I had a year of stability (i.e. no moving around for placements). I chose a project that crossed multiple disciplines, including plastic and maxillofacial surgery and dermatology. My experience in these fields was amazing and reaffirmed my goal of becoming a surgeon one day. Completing my Honours year has been very interesting and has given me a great insight into both the challenging and fulfilling aspects of applying for, performing, writing, and publishing medical research. I had the privilege of interacting with patients and their families to complete my research project. This has given me a new perspective on patient treatment and the willingness of my patients to participate in the continuation of medical research is greatly appreciated. I would strongly recommend applying for an Honours year and advise potential students to consider the specialties or aspects of medicine that they enjoy and to pursue research in those areas.

## ABSTRACT

### Background

The microcirculation is the communicating link between major blood vessels and body tissue, responsible for oxygen and nutrient transfer via capillaries and small arterioles. Imaging of the microcirculation can be performed with handheld microscope cameras, such as the Cytocam. In generalised pathologies such as sepsis and haemorrhagic shock, this technology has been used to assess the global microcirculation, based on a representative area of the body. However, research into the microcirculation with such devices where there is a local pathology has not been carried out.

### Aims

The primary aim is to investigate whether the Cytocam has potential as a tool for the evaluation of local changes to the microcirculation in two distinct clinical scenarios. Secondary aims include assessment of whether the Cytocam can be used as a diagnostic aid in vascular anomalies and whether it can be used to monitor skin and mucosal circulation in maxillary orthognathic surgery.

### Methods

Patients with vascular anomalies and those undergoing maxillary orthognathic surgery were selected for two arms of research. Patients were recruited from various clinics at the Royal Children's Hospital. Measurements were performed at a single timepoint for those with vascular anomalies, with videos taken at multiple sites on the one lesion. For surgical patients, measurements were taken five time points: prior to anaesthetic induction (T1), seven minutes after infiltration with local anaesthetic (T2), after mobilisation of the maxilla (T3), after completion of surgery prior to extubation (T4) and finally, at a follow-up appointment between 7 and 10 days after surgery (T5). These measurements were taken at the labial gingival mucosa of the left and right upper lateral incisors at each timepoint.

### Results

Infantile haemangiomas demonstrated identifiable microcirculatory architecture, including high vessel density, vessel dilation and vessel tortuosity. These features were present in 71% of lesions assessed. Proliferative or plateau phase lesions were more likely to exhibit high vessel density (79%) compared to involuting lesions (50%). Topical beta blocker treatment led to reduced vessel density in a lesion assessed before and after its initiation.

Mobilisation of the maxilla resulted in a 23% (95% CI 4 to 41,  $p=0.017$ ) and 26% (95% CI 6 to 47,  $p=0.013$ ) decrease in the proportion of perfused vessels from baseline and post-local anaesthetic administration respectively. All patients had reduced proportion of perfused vessels and perfused vessel density between T2 and T3. No statistically significant changes to total vessel density occurred across the timepoints. No patients developed infection, tissue devitalisation or osteonecrosis.

### Conclusion

Use of the Cytocam in local pathologies demonstrated altered microcirculatory architecture and reduced proportion of perfused vessels and perfused vessel density after blood flow alterations. Haemangiomas demonstrated unique microcirculatory patterns that were most prevalent in the proliferative phase of their pathogenesis. Beta blocker therapy was demonstrated to decrease the vessel density in a proliferating lesion using this technology. More research is required to validate this finding. For orthognathic patients, a reduction in the proportion of perfused vessels following maxillary mobilisation did not result in adverse outcomes such as infection, tissue devitalisation or osteonecrosis. This result provides a potential method for monitoring tissue viability in the mouth.



# Naura Syafira

## Development of Liver Injury Despite Early Acetylcysteine Treatment in Paracetamol Overdose

Supervisor Names and Institute Affiliations:

- A/Professor Anselm Wong

- Professor Andis Graudins

Department of Medicine, School of Clinical Science at Monash Health, Monash University, Victoria, Australia



Hi, I'm Naura. I'm a fourth-year medical student from Universitas Indonesia. Our cohort was the first to be conducted remotely from Indonesia. Hence, there were only limited types of research offered. Despite that, I enjoyed doing my research project with an interesting topic and resourceful supervisors who are experts in their fields. This research involved collaboration throughout Australia and Canada. Additionally, paracetamol overdose is not as common and well-studied in Indonesia as in Australia or Canada, so I was intrigued to explore the topic. I believe the skills I have obtained during the Honours year will help me to become a better physician one day. I would highly recommend choosing a topic that you are passionate about. The research project would need a great deal of work but would also be rewarding at the end.

### ABSTRACT

#### Background

Paracetamol is a commonly used over-the-counter analgesic. Paracetamol overdose is a growing health concern world-wide. Early administration of acetylcysteine, a paracetamol antidote, offers greater protection from liver injury than late administration. However, recent studies have revealed that early administration of acetylcysteine may fail to prevent the development of liver injury in some patients. This study sought to compare the incidence of acute liver injury (ALI) in patients receiving acetylcysteine early with a two-bag acetylcysteine regimen (200 mg/kg over four hours, 100 mg/kg over 16 hours) compared to patients receiving three-bag regimen (150 mg/kg over one hour, 50 mg/kg over four hours, 100 mg/kg over 16 hours).

#### Methods

Retrospective cohort study comparing the two-bag and three-bag acetylcysteine regimens in Australia (2009 – 2020) and Canada (1980–2005). The two-bag and three-bag regimen data were obtained from patient records at Monash Health and compared to the three-bag regimen data from the Canadian Acetaminophen Overdose Study (CAOS). We included patients with acute single ingestion of paracetamol; normal alanine aminotransferase (ALT) on presentation, acetylcysteine administered  $\leq 8$  hours post-overdose, and treatment decision based upon the adapted Rumack-Matthew nomogram. Primary outcome: development of ALI (peak ALT  $>150$  IU/L). Secondary outcome: development of hepatotoxicity (peak ALT  $>1,000$  IU/L).

#### Results

At Monash Health, 191 patients were treated with the two-bag acetylcysteine regimen and 180 patients were treated with the three-bag regimen. The CAOS cohort provided 515 patients treated with the three-bag regimen. ALI developed in 1.6% (3/191) of the two-bag

Monash Health group, 2.2% (4/180) of the three-bag Monash Health group (Difference -0.6%,  $p$  0.7), and 2.9% (15 / 515) of the three-bag CAOS group (difference compared to two-bag -1.3%,  $p$  0.4). Hepatotoxicity developed in 0.5% (1 / 191) of patients treated with the two-bag regimen, 1.7% (3/180) three-bag regimen in the Monash Health, and 1% (5/515) of the three-bag CAOS group. There were no statistically significant differences between groups.

#### Conclusion

ALI and hepatotoxicity were observed in small percentage of patients receiving early acetylcysteine using the two-bag and three-bag acetylcysteine regimens. Repeating blood tests at the end of acetylcysteine treatment will identify these patients and indicate those requiring extended therapy.

# Kaven Tannardi

## Continuation of Antithrombotic Use in Hand Surgery: An Analysis of Risks and Benefits

Supervisor Names and Institute Affiliations:

Professor Warren Rozen (Peninsula Health), Professor David-Hunter Smith (Peninsula Health)



My name is Kaven Tannardi, doing my research year at Monash University remotely from Indonesia. A project that I wished to undertake was the effects of ceasing antiplatelet and anticoagulants during hand surgery. The reason why I chose this specific project was because of my interest in the subject. I found many challenges during writing this systematic review but fortunately, kind supervisors and instructors were staunch supporters, helping me get past one difficulty after another. Especially friends and family that emotionally supported me through it all. While I gained valuable experiences in writing scientific papers, their process, and intricacies, to be frank, it was a lot different than what I imagined. COVID brought many unavoidable changes to everybody and several great opportunities were lost. I sincerely hope that future students could enjoy the full advantage of the research year at Monash University as I know that it will be invaluable in your research journey.

### ABSTRACT

#### Background

Antithrombotic medication continuation during surgery continues to be the subject of debate. The risk of bleeding complications must be weighed against the risk of thromboembolic events for each patient. The bleeding complications of antithrombotic patients undergoing surgery are discussed at length in many studies. However, few studies compare the effects of continuing vs discontinuing antithrombotic medication during hand surgery. As hand surgeries are considered to have relatively few bleeding complications compared to other surgeries, clinicians should consider whether to stop their patient's antithrombotic medication. In essence, is the increased risk of bleeding complications preferable to the increased risk of thromboembolic episodes?

#### Method

PRISMA method was used to conduct this systematic review, which resulted in the selection of 9 studies for data extraction. The extracted data were then arranged into a set of tables to compare the rate and severity of bleeding complications when antithrombotic medication was continued or not in hand surgery and reported in these studies. No statistical assessment of the combined studies was possible at this time.

#### Results

There was no apparent difference between the bleeding complication rates when antithrombotic medication was continued or not in hand surgery.

#### Conclusion

The continuation of antithrombotic medication does not pose a significant increase in bleeding complication risk in hand surgery. Furthermore, tourniquet and WALANT technique could be used to mitigate the risk of

bleeding complications. However, the effectiveness of WALANT in comparison to tourniquet cannot be reliably determined due to the low number of studies which included the WALANT technique. The results of this study can be used to aid a physician's decision to continue antithrombotic medication or not during hand surgery.

# Kieran Taylor

## Prediction of postoperative opioid requirements by anaesthetists: a prospective cohort study

Supervisor Names and Institute Affiliations:

Professor Kate Leslie AO and A/Professor Jai Darvall, School of Public Health and Preventive Medicine, Monash University and The Royal Melbourne Hospital



I decided to complete a BMedSc(Hons) year between Year 4C and 5D. I was definitely hesitant at first as I never intended to spend an entire year doing honours, but I was curious when the time came to decide which direction I should take. After looking through some potential supervisors and projects on Monash Supervisor Connect, I found a supervisor with an interesting trial who I wanted to work with. I was also interested in spending some time in a hospital outside of the Monash system so this project at the Royal Melbourne Hospital was perfect for that. I had an amazing year with the Department of Anaesthesia and Pain Management at the Royal Melbourne Hospital in conjunction with the School of Public Health and Preventive Medicine. I'd encourage anyone who has an area that they are interested in, to consider taking an honours year. Not only was I able to complete my own research project and connect with people in the field of anaesthetics, but I was also able to spend some time doing clinical work with my supervisors. I am happy to be contacted by future students if they have any questions.

## ABSTRACT

### Background

Postoperative nausea and vomiting (PONV) is one of the most frequent side effects experienced by patients after anaesthesia. Its occurrence negatively impacts patient experience, has clinical complications, and increases healthcare costs. The Apfel simplified risk score is the most common tool used by anaesthetists to estimate PONV risk and guides antiemetic prophylaxis. The Apfel score includes four risk factors: female sex, non-smoking status, history of PONV or motion sickness and postoperative opioid use.

Importantly, the Apfel score is used in the preoperative setting and at this time 'postoperative opioid use' must be predicted by anaesthetists. Postoperative opioid use is multifactorial and uncertain preoperatively. Additionally, there is currently no literature describing whether anaesthetists can accurately predict their patient's opioid requirements after surgery. Thus, it is unclear as to whether this component of the Apfel score is clinically accurate.

### Aims

Primary aims included:

1. To determine if anaesthetists can predict opioid administration and opioid dose in the post anaesthesia care unit (PACU)
1. To determine if anaesthetists can predict opioid administration and opioid dose during the first 24 hours postoperatively or until hospital discharge.

Secondary aims were to observe preoperative documentation of PONV risk factors and to identify possible predictors of accurate prediction of postoperative opioid use.

### Methods

Consultant anaesthetists were recruited from the Royal Melbourne Hospital's operating suites between May and September 2021. Anaesthetists were asked preoperatively to predict postoperative opioid administration and exact dose requirements for their patients. Medical records were accessed postoperatively and data pertaining to patient

baseline characteristics, Apfel score, and intraoperative and postoperative medication usage were collected. Postoperative opioid use was then compared to each anaesthetists' predictions.

Percent agreement (with 95% confidence intervals) was used to represent accuracy of prediction of both postoperative opioid administration and opioid dose. Predicted opioid dose and actual opioid dose were displayed using Bland Altman plots.

### Results

We recruited 100 anaesthetists across 14 different surgical specialties. The anaesthetists had a median of 11 (IQR 4-20) years of consultant experience. The median age of the patients included was 53 (IQR 38-66) years. Males and female patients were equally represented.

Percent agreement for opioid administration was determined to be 66% (56%-75%) for the PACU and 82% (73%-89%) for 24 hours postoperatively. Percent agreement for opioid dose within 20% of the actual dose used was 38% (28%-48%) for the PACU and 18% (11%-27%) for 24 hours postoperatively.

Documentation of PONV risk factors were found to be inconsistent. Significant predictors of accurate prediction of postoperative opioid use included patient age and weight.

### Conclusion

To our knowledge, this is the first study to describe how well anaesthetists can predict their patient's postoperative opioid requirements. Our findings show that anaesthetists cannot reliably predict postoperative opioid administration nor dose. This has implications for the use of the Apfel score and its accuracy in determining PONV risk.

Our findings regarding predictors of agreement between predicted and actual opioid administration and dose are hypothesis-generating and highlight the need for further research into the Apfel score, opioid utilisation, and PONV.

# Kaarthikayinie (Kaarthy) Thirugnanasundralingam

## Telehealth Integrated Antenatal Care

Supervisor Names and Institute Affiliations:

Dr Kirsten Palmer<sup>1,2</sup>

A/Professor Ryan Hodges<sup>1,2</sup>

1: Department of Obstetrics & Gynaecology, School of Clinical Sciences, Monash University

2: Monash Women's and Newborn, Monash Health, Melbourne, Victoria



I undertook a desk-based project with the Department of Obstetrics. We looked at the implementation of a hybrid antenatal care model propelled into the spotlight by COVID-19. I have always been interested in medical research, so I decided the best way to develop analytic skills would be through undertaking a dedicated year under the guidance of experienced clinician-scientists. It has by far been the most rewarding opportunity in medical school. I was able to learn so much about the ins and outs of research from statistical analysis all the way to concise scientific writing. This year has also left me with skills I did not anticipate (think: learning how to schedule emails!) To prospective students: Select a supervisor who is happy to mentor you, or whose values align closely with your own. Often the conversations we shared beyond research were the ones which left me truly thinking about how to be a good clinician, and a good human.

If you are on the fence, take the plunge! It may be challenging but you will come out glittering with shiny new skills and newfound curiosity about the world of medicine - you absolutely will not regret it.

More than happy to be contacted:  
kthi0002@student.monash.edu

## ABSTRACT

### Background

Pregnant women are vulnerable to serious adverse outcome following viral infection due to physiological adaptations which occur during pregnancy. With maternal and fetal consequences of COVID-19 initially unknown, Telehealth integrated antenatal care (THIANC) was rapidly implemented at Victoria's largest maternity service to minimise unnecessary exposure of pregnant women and their dedicated healthcare workers to SARS-CoV-2. The Telehealth integrated schedule sought to convert 50% of in-person appointments in both low and high-risk care models to a virtual platform, without compromising pregnancy outcomes. To support detection of complications through THIANC, remote blood pressure monitoring and self-measured symphyseal fundal height protocol were introduced.

Aim: To evaluate the implementation, uptake, safety and efficacy of Telehealth integrated antenatal care compared to conventional in-person delivered care. Additionally, we sought to evaluate the influence of population characteristics on engagement with THIANC.

### Method

Routinely collected data on all women who received public antenatal care for a singleton pregnancy and birthed at Monash Health during the conventional-care (1/1/2018–22/3/2020) and Telehealth-integrated (20/4/2020–25/4/2021) periods was retrospectively analysed. Baseline demographics, attendance at clinic appointments and outcomes relating to pregnancy complications including pre-eclampsia, gestational diabetes (GDM), fetal growth restriction (FGR), stillbirth and perinatal morbidity, were evaluated. Pooled outcomes were compared using Chi-squared, Mann-Whitney-U and T-tests. Additionally, interrupted time-series analysis was performed to track evolution in pregnancy outcomes over time (STATA-SE v17.0). For all outcomes, statistical significance was defined at  $p < 0.05$ .

### Results

Overall, 18,917 and 8,495 women birthed in the conventional and integrated care periods respectively. Following Telehealth integration 45.9% (34,444/74,982) of consultations that occurred during the integrated period were delivered through Telehealth, compared to 0.08% (107/129,514) in the conventional period. No significant difference in median gestation at diagnosis of pre-eclampsia was seen following Telehealth-integration in low- (37.1 vs 37.3;  $p = 0.17$ ) or high-risk models (35.6 vs 34.6;  $p = 0.37$ ) compared to conventional-care. Likewise, no significant differences in FGR in low- (1.81% vs 1.69%;  $p = 0.54$ ) or high-risk models (4.50% vs 4.29%), preterm birth in low-risk (10.6% vs 10.3%;  $p = 0.503$ ) or high-risk models (17.58% vs 19.73%;  $p = 0.051$ ) or stillbirth in low-risk (0.78% vs 0.67%;  $p = 0.36$ ) or high-risk models (1.61 vs 1.81;  $p = 0.52$ ) were observed following widespread implementation of Telehealth. Interestingly, a statistically significant decrease in the proportion of induction of labour for suspected FGR was observed following introduction of THIANC (3.02% vs 3.68%;  $p = 0.015$ ) in low-risk care models. The majority of women birthing in the integrated period had good uptake of Telehealth in low- (69.4%) and high-risk care models (87.0%). Comparatively poorer engagement with Telehealth was observed in women of non-Australian origin, low socioeconomic background, and in women who required an interpreter.

### Conclusion

Telehealth integrated care reduced in-person consultations by 45.9% without compromising pregnancy outcomes. It may also be associated with a reduction in labour induction for suspected FGR, particularly for women in low-risk care models without compromising detection of FGR perinatal morbidity. These findings support the ongoing use of Telehealth in providing personalised, agile antenatal care.



# Lauren Vallely

## Defining intrapartum care measures for WHO recommendations for a positive childbirth experience: a scoping review

Supervisor Names and Institute Affiliations:

Supervisor – Associate Professor Joshua P Vogel

Co-Supervisor – Professor Caroline SE Homer

Institute – Burnet Institute, Global Women's and Newborn's Group

School – Monash University School of Public Health and Preventative Medicine



Hi, I'm Lauren, a BMedSc/MD student who undertook an Honours year at the Burnet Institute in Melbourne. After completing Year 4 in 2020, amidst a year of global pandemic, I decided to take a break from clinical medicine to pursue a BMedSc(Hons).

I developed a keen interest in global health through my medical degree and knew I wanted to incorporate it into my BMedSc(Hons). Further, during my fourth year, I thoroughly enjoyed both my paediatric and obstetric placements, so the Global Women's and Newborn's group at the Burnet Institute was a perfect fit.

Undertaking this Honours year has been immensely valuable. It has been a challenging and rewarding experience and has encouraged me to grow personally and professionally.

To future students, I advise you to seek out a motivated supervisor who strives to ensure that you enjoy the experience alongside supporting your academic goals. A BMedSc(Hons) is a fantastic opportunity to experience the diversity that a career in research can offer and one that I cannot recommend more highly.

If you would like to know more about my experiences, please feel free to contact me at lhval1@student.monash.edu.

## ABSTRACT

### Background

The intrapartum period is a time of particular risk for maternal complications that contribute to a significant proportion of pregnancy-related deaths. The publication of recommendations from the World Health Organization (WHO) – Intrapartum care for a positive pregnancy experience in 2018 elevated the importance of developing a comprehensive approach to the measurement and monitoring of intrapartum care quality to improve maternal health outcomes with respect to the intrapartum period.

It is recognised that strong maternal health monitoring systems lead to more effective and population-specific actions that will improve the health of women and newborns. However, a wide disparity in the availability of reliable health information monitoring systems globally is reported, especially in low- and middle-income countries.

The aim of this project was to collate available literature on measures or indicators used to monitor the provision, scope and quality of intrapartum care, and identify if these measures or indicators can be mapped to the WHO recommendations.

### Method

A scoping review was performed according to the Joanna Briggs Institute (JBI) Methodology for Scoping Reviews and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) standards. Database searching was performed in MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCO), Cochrane Library (Wiley), the Maternity and Infant Care Database (Ovid), and Global Index Medicus (WHO), to identify studies reporting measures or indicators of intrapartum care.

Relevant websites were searched for articles, publications or reports discussing measures or indicators of intrapartum care, as part of grey literature searching. All citations were independently screened for eligibility by two reviewers. Data was extracted on study

and measure characteristics. Results were presented tabularly, with accompanying diagrams and descriptive summaries.

### Results

Database searching returned 12,376 unique studies for screening, of which 69 were eventually included in the review. Grey literature searching contributed one additional source. From these sources, a total of 577 measures of intrapartum care were identified.

All 9 WHO intrapartum care domains ("care throughout labour and birth", "first stage of labour", "second stage of labour", "third stage of labour") were represented within the identified measures. However, measures were only identified for 30 of the 41 included WHO recommendations. Further, measures relating to one WHO recommendation – Respectful maternity care, accounted for more than half of all 577 measures identified by the scoping review. With respect to the country of origin of the identified measures, low-middle income countries were well represented. The majority of measures were recorded at the patient level, emphasising that most existing measures of intrapartum care focus on the woman's experience.

### Conclusion

This scoping review of intrapartum care measures and indicators has provided a database of measures and indicators identified as being used to monitor the provision and quality of intrapartum care. The review team was able to map the measures to the WHO recommendations to identify which components of intrapartum care measurement are currently under-represented in the relevant literature. This project will inform future research opportunities.

# Carine Wessels

## What do women undergoing IVF understand about their treatment?

Supervisor Names and Institute Affiliations:

Professor Beverley Vollenhoven, Professor Ben Mol and Dr Karin Hammarberg

Monash University Department of Obstetrics and Gynaecology, School of Clinical Sciences at Monash Health



I completed my BMedSc(Hons) year in women's health after discovering a passion for this important field of medicine during my 4th year. I chose my project because it was nothing more than an idea at the time, which meant I could be involved in the entirety of its development, including writing the protocol and designing the survey. Initially, I was overwhelmed by the size and complexity of the project, and unsure of where to begin. However, through this challenge, I have gained an invaluable understanding of the research process, as well as skills that I hope will make me a more critical clinician in the future.

I enjoyed the change of pace from clinical placement, and the flexibility of completing my project from home. I valued being able to learn and grow by attempting to solve problems that arose in my research, but also having the support of my supervisors for the (many) times I got really stuck. The experience has been incredibly worthwhile, and I would recommend it to anyone who is interested in broadening their skillset and taking on something different.

## ABSTRACT

### Background

Infertility affects around one in six couples who want to conceive, and the number of women using assisted reproductive technology (ART) to conceive is increasing. High quality treatment information is important to patients, but a review into ART practice has highlighted a deficiency in adequate information-provision. Little is known about the level of knowledge of ART in women undergoing the treatment.

### Aim

This study aimed to assess the level of understanding that women undergoing IVF have of their treatment and particularly their chance of success.

### Methods

An anonymous online survey of women who had started IVF treatment since 2018 asked questions about what they understood about different aspects of their treatment, including their chance of having a baby from one IVF treatment cycle. Participants' beliefs about their chance of success were then compared with the chance as calculated by the Society for Assisted Reproductive Technology's (SART) online calculator, which is based on the data from 320,000 women in the United States. Data were analysed using descriptive statistics and inductive thematic analysis for free-text responses.

### Results

The survey was completed by 225 women. Only about a quarter (25.8%) of participants accurately estimated their chance of success within 20% relative to their SART calculated chance, and more than half (52.4%) overestimated their chance. Among women who rated their understanding of their chance of success as 'high' (7-10/10), less than one third (31.6%) accurately estimated their

chance of success. Increased age and having undergone several cycles were associated with women being more likely to overestimate their chance of success (OR 3.16 and OR 2.48, respectively). Despite feeling that, on average, doctors only explained the different aspects of their treatment moderately well, women indicated that their preferred source of treatment information was a consultation with their doctor. Women also said that they wish they had been given a more realistic expectation of ART and their chance of success.

### Conclusion

We found a poor understanding of personal chance of success amongst women undergoing ART. This highlights the need for systematic and evidence-based improvement in the way clinics provide this information.

# Kate Wilcox

## Using Machine Learning to Create a Multivariate Model to Predict Platelet Transfusion Based on Patient Characteristics

Supervisor Names and Institute Affiliations:

Dr Alisa Higgins a, b, Dr Adam Irving b, c, A/Professor Zoe McQuilten c

a Australian and New Zealand Intensive Care Research Centre, School of Public Health and Preventative Medicine, Monash University, Melbourne, Australia

b Centre for Health Economics, Monash University, Melbourne, Australia

c Transfusion Research Unit, School of Public Health and Preventative Medicine, Monash University, Melbourne, Australia



I undertook my BMedSc(Hons) after completing my fourth year of medicine. It was an excellent learning opportunity and I was privileged enough to work with Monash University's Transfusion Research Unit and the Australian and New Zealand Intensive Care Research Centre team in a number of roles throughout the year. My project was the groundwork for the health economic evaluation of the distribution of cryopreserved platelets and spanned across haematology, transfusion medicine, intensive care and health economics. These are all areas that interest me greatly and even more so after working with the two excellent teams that I outlined above. I am very happy to be contacted by any prospective students looking to undertake research in this sector.

### ABSTRACT

#### Background

Platelets are a valuable, altruistically donated resource with a short shelf life. Distribution of platelets to hospitals must balance adequate supply with the potential for wastage. It is currently not feasible to routinely stock platelets in rural hospitals where inconsistent demand would result in unacceptable levels of wastage. In such locations, novel treatments such as cryopreserved platelets – which have a shelf life of up to two years – could be utilised in the management of active bleeding. To assess demand for cryopreserved platelets in locations without routine access to liquid platelets, a model for predicting platelet transfusion was developed based on patient characteristics. In the future, this model could be applied to hospital data to determine which hospitals have sufficient demand to stock cryopreserved platelets.

#### Aim

To develop a model that predicts platelet transfusion using patient data from a large transfusion database of adult in-patients who received any blood product transfusion during their hospital admission.

#### Methods

This was a retrospective analysis of the National Transfusion Dataset (NTD). The NTD is a database of electronic clinical records of adult patients who were transfused with any blood product during hospital admission. It records patient demographics, admission details, transfusion of blood products, diagnoses, procedures and laboratory values. At the time of this study, data from two Australian metropolitan hospitals for the period of 2017 to 2019 was available for model development. To determine the demand for acute, therapeutic platelet transfusions, the model was developed excluding planned day-only admissions (patients with single-day admissions that did not result in death). For patients with multiple admissions, only the first admission data were used. There were 69 variables analysed for relevance to platelet transfusion.

To develop the predictive model, the data

were partitioned with 80% for training and 20% for testing of the model. Four supervised machine learning algorithms were run on the training data using five-fold cross-validation. The model accuracy was assessed by applying each model to the testing dataset.

#### Results

There were 7,183 admissions included in the analysis. The model with the greatest accuracy was the Random Forest model including laboratory values. This model included 68 variables. The most significant predictors were age, hospital length of stay, ventilation time, haematological cancer, chemotherapy, FFP, cryoprecipitate or red blood cell transfusion, international normalised ratio (INR) > 3.5 and platelet count between 50 – 100 x 10<sup>9</sup>/L. The area under the receiver operating characteristic (AUROC) was 0.9314, the sensitivity was 95.22% and the specificity was 66.56%. When the algorithms were run without laboratory values, the Random Forest model still outperformed the others with an AUROC of 0.8949, sensitivity of 94.74% and specificity of 59.09%.

#### Conclusion

Models both with and without laboratory values had a high accuracy for predicting platelet transfusion in patients who had received a blood product transfusion. Prediction of platelet transfusion using one of these models could assist in informing the distribution of cryopreserved platelets to rural hospitals. Further refinement of the models on a larger dataset of more diverse hospitals is recommended.

# Sarah Woodward

## The influence of coping strategies during COVID-19 on the development of PTSD symptoms

Supervisor Names and Institute Affiliations:

A/Professor Caroline Gurvich, Dr Shalini Arunogiri

Monash Alfred Psychiatric Research Centre (MAPrc)



My name is Sarah, and this year I completed my Honours year at MAPrc after four years of undergraduate medical studies. I have always had a special interest in psychiatry, particularly after my fourth year placement at Monash Medical Centre in Clayton. After seeing and personally experiencing the mental health effects of the COVID-19 pandemic in 2020, I was interested in pursuing a project exploring the psychosocial repercussions of being exposed to such an unprecedented event in this day and age. With the help of my supervisors, I was able to develop research skills which were crucial to explore both the short- and long-term effects of the pandemic, and hopefully provide advice regarding psychoeducation, therapy and public health initiatives to combat COVID-induced PTSD symptoms.

### ABSTRACT

#### Background

The emergence of COVID-19 rapidly generated widespread psychological distress. Given its classification as a traumatic stressor, we sought not to investigate its physical complications, but instead the acute and long-standing psychological ramifications of this global pandemic.

Psychosocial disturbances prompted various emotional and problem-solving responses. Proactive efforts prompted some to seek pandemic-related information and advice, whilst others remained passive in the face of COVID-19. Despite relevant research during previous health crises, we had a limited understanding of how coping strategies may exacerbate or attenuate avoidance, intrusion, and hyperarousal symptoms in the context of the unprecedented COVID-19 crisis.

#### Method

This longitudinal sub-study was conducted using an online survey initially designed for a broader study tracking the mental health of the Australian public following the initial outbreak. Between April 2020 and September 2021, we disseminated an online survey to monitor PTSD symptomology and the use of coping strategies among the Australian public. Use of the Revised Impact of Event Scale and Brief COPE Inventory as screening tools was validated by extensive research during prior epidemics like severe acute respiratory syndrome.

We selected fourteen coping strategies as our independent variables, whose relationships with Intrusion, Avoidance and Hyperarousal symptoms were modelled via multiple regression analysis. By running several models comparing 1,124 baseline and 250 twelve-month respondents, we obtained cross-sectional and longitudinal data indicating the correlations between coping strategies, our covariates, and PTSD symptoms.

#### Results

In line with our hypotheses, cross-sectional analysis indicated significant correlations between maladaptive coping strategies and

PTSD symptomology during COVID-19. High beta coefficient values revealed the strong association of Behavioural disengagement with Intrusion ( $\beta=1.08$ ) and Hyperarousal ( $\beta=1.05$ ) at baseline. Additionally, a coefficient of 1.26 implied the sizable effect of Self-distraction on Avoidance symptoms.

With respect to our covariates, gender surpassed age in its significant correlations with Intrusion ( $\beta=2.24$ ), Avoidance ( $\beta=1.62$ ) and Hyperarousal (1.57) symptom scores. A similarly strong correlation between current psychiatric diagnosis and Hyperarousal at baseline was denoted by a beta value of 1.73.

We also modelled the longitudinal relationship between prior and current psychological state by including baseline IES-R scores as predictors of their corresponding IES-R subcategory scores at the 12-month timepoint. Significant coefficients of .28 for Intrusion and Hyperarousal, and .26 for Avoidance, revealed the importance of baseline IES-R scores on predicting future PTSD symptomology. Meanwhile, baseline coping scores appeared to have relatively weaker predictive capacity than 12-month scores on 12-month PTSD symptoms.

Longitudinal analyses provided insight into the fluctuant strength and directionality of the correlations between coping and PTSD symptoms. Although coping strategies are classifiable as 'adaptive' or 'maladaptive', unexpected findings such as the reversal of the beta coefficient for Self-blame over time reinforced the inaccuracy of grouping strategies.

#### Conclusions

Cross-sectional analyses revealed the unique relationships of coping strategies with PTSD symptoms. Longitudinal findings suggesting the changeability of certain strategies emphasised the urgent need for personalised psychotherapy to equip patients with necessary skills to cope effectively throughout the pandemic. We forecast that teaching adaptive coping and amending dysfunctional strategies may minimise PTSD symptoms as COVID-19 progresses, and in the event of future health crises.



# Wentong Mary Xu

## Menstrual Fluid: Diagnostic Potential and Disease Modelling Applications for Endometriosis and Adenomyosis

Supervisor Names and Institute Affiliations:

Dr Caitlin Filby<sup>1,2</sup>

Professor Caroline Gargett<sup>1,2</sup>

<sup>1</sup>The Ritchie Centre, Hudson Institute of Medical Research

<sup>2</sup>School of Clinical Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University



I chose to complete my BMedSc(Hons) between Year 4C and 5D because I wanted to gain research experience and expand my experience outside of clinical medicine. I chose a lab-based project working with primary human endometrial cells, which was a huge learning curve but highly rewarding. I learnt many new skills, including 2D and 3D tissue culture, flow cytometry, as well as data analysis and scientific communication. I've also gained a newfound appreciation for translational research and the basic sciences that underpin medical advancements.

The Ritchie Centre undertakes a diverse range of research in Women's and Children's Health and is a really supportive environment for students. I made many new friends as a result of working here, as well as developed professional relationships with leading clinicians and scientists.

I highly recommend undertaking a BMedSc(Hons) year to any prospective students. While it can be a challenging year, you will experience both personal and professional growth as a result and can be really proud of the research you generate!

I would love to be contacted about my research, lab-based projects or the BMedSc(Hons) year in general at: [wxxu0007@student.monash.edu](mailto:wxxu0007@student.monash.edu)

### ABSTRACT

#### Background

Cyclical regeneration of the endometrium is likely controlled by endometrial stem/progenitor cells found in menstrual fluid (MF) and endometrial tissue. These cells can be identified by surface markers SSEA-1/N-cadherin and SUSD2 and may behave aberrantly to cause endometriosis/adenomyosis. MF is a non-invasively obtained, endometrium-specific medium containing these cells and related proteins, which could be harnessed as diagnostic biomarkers or used to model mechanisms of disease. This study compared endometrial stem/progenitor cell proportions, cell clonogenicity, and organoid behaviour in MF between women with and without endometriosis/adenomyosis. Secondly, the study compared MF to eutopic endometrial tissue in women with endometriosis.

#### Method

MF (Day 2) from a menstrual cup (case n=6, control n=6; age: 33.1±9.6years, mean±SD) and surgical endometrial tissue (case n=5, control n=0; age: 33.2±9.3years) were collected. Samples were dissociated to single cells or cell clusters for different assays. Red blood cells and leukocytes (MF only) were depleted. Endometrial stem/progenitor cell proportions were determined by flow cytometry (N-cadherin+ or SSEA-1+ cells from CD45-CD31-EpCAM+/EpCAMhigh endometrial epithelial cells or SUSD2+/SUSD2high cells from CD45-CD31- endometrial cells) and clonogenicity determined by colony forming assay. Organoids were derived from epithelial glandular cells and compared between groups. SUSD2+ cells were prospectively isolated for future disease modelling applications and supernatant was isolated for future protein analysis.

#### Results

There was no difference between endometrial epithelial (EpCAM+ or EpCAMhigh) cells in MF groups but EpCAMhigh was significantly lower in tissue than MF (tissue: 4.7±0.4%, mean±SEM; MF: 21.0±1.5%, p=0.04).

Epithelial progenitor cells (SSEA-1+ and/or N-cadherin+) and mesenchymal stem cells (SUSD2+) cells were not different between MF groups, although subgroups (high vs. low) were revealed for SSEA-1+ and/or N-cadherin+. N-cadherin+ proportions from EpCAM+ cells were significantly higher in tissue compared to MF cases (tissue: 70.8±17.3%; MF: 9.2±3.3%, p=0.04), while SSEA-1+ proportions were significantly lower (tissue: 0.3±0.1%; MF: 2.6±1.0%, p=0.04). These trends were not significant in the EPCAMhigh population. SUSD2+ proportions were higher in tissue than MF (tissue SUSD2+: 37.9±4.6%; MF SUSD2+: 10.0±2.8%, p=0.04), which was also seen for SUSD2high proportions (tissue SUSD2high: 10.2±1.1%; MF SUSD2high: 3.4±1.2%, p=0.04). A higher proportion of viable CD45-CD31- endometrial cells was found after beading in MF cases (case: 69.5±6.1%; control: 23.2±9.3%, p=0.02).

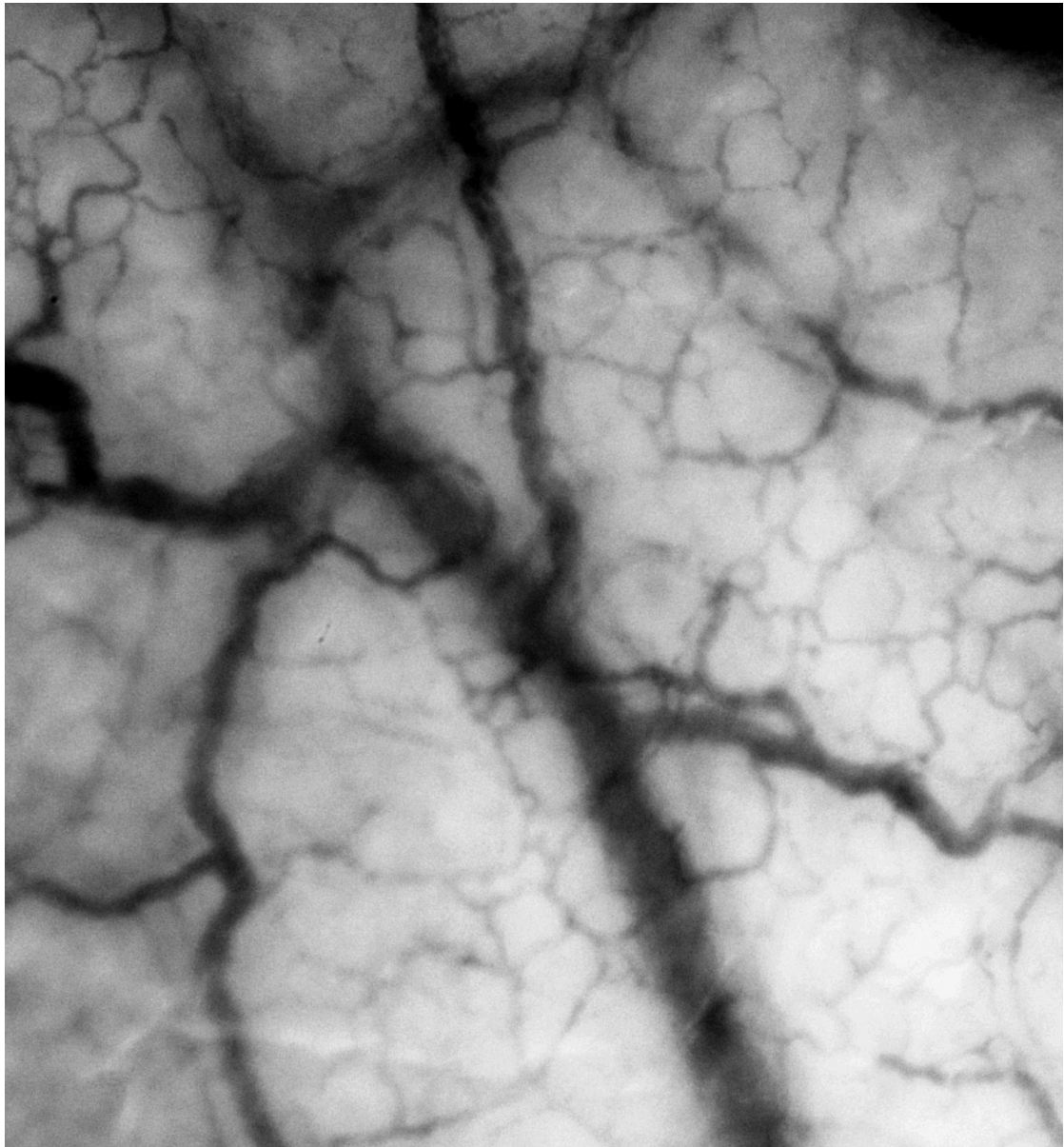
Epithelial and stromal clonal efficiency were not significantly different between case and control MF, or between MF and tissue cases.

Single cell derived MF organoids from cases showed greater proliferation (organoid count and total surface area per 5000cells/well) than controls (n=1 per group). MF organoids had greater proliferation than tissue organoids when derived from single cells.

#### Conclusions

MF contains shed endometrial stem/progenitor cells in endometriosis/adenomyosis and healthy controls. Subgroups in SSEA-1+ or N-cadherin+ parameters need further investigation. Increased epithelial proliferation in a single cell derived organoid model in endometriosis also warrants investigation. Matched MF and tissue samples may reveal the predictive value of MF compared to eutopic endometrium across each parameter. MF is demonstrated to be a robust resource for the study of endometriosis/adenomyosis, and increased power may reveal differences of diagnostic or disease modelling potential.





## **INSIDE BACK COVER**

### **Lucy Standish - Cytocam Image of a Rapidly Involuting Congenital Haemangioma**

The cytocam takes images of the microcirculation that are compiled to create video sequences. This still image was taken of an area of a rapidly involuting congenital haemangioma in a two day old neonate. This is the first time that this technology has been used to image vascular anomalies, or birthmarks. The patient consented to use of the image.

## **BACK COVER**

### **Rayscha Farah – 3D Segmentation of a Mouse Brain MRI**

A stunning axial (top), sagittal (2nd from top), coronal (2nd from bottom) and 3D (bottom) view of a mouse brain MRI on a black background. The mouse brain MRI was segmented using bright colors to highlight distinct brain regions. In-vivo DCE-MRI was performed using 9.4T/20 MRI with T1-w acquired utilizing the 3D FLASH sequence in the TDP-43 transgenic and littermate controls.



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