

**MHTP PhD Student Showcase**  
**Symposium Wed 6 Oct 2021**  
**12:45 – 3:30PM via Zoom**

Showcasing the best of clinical and basic research by 2nd and 3rd year Monash University PhD students.

MHTP Monash Health Translation Precinct  
 MONASH University  
 HUDSON INSTITUTE OF MEDICAL RESEARCH

| Timing  | Title/Speaker   |
|---|---|
| 12.45pm – 12.59pm   | Official opening Prof Kate Loveland, with The Chairs (HISS reps) & entertainment  |
| <b>Research Presentations – Session 1, chaired by HISS President (Shaye Game)</b> |   |
| 1:00pm – 1:15pm   | <b>Preventing Schizophrenia Before it Begins</b><br>Brendan Gillespie, Psychiatry   |
| 1:15pm – 1:30pm   | <b>Activin A impacts on germ cell development: new insights into male infertility</b><br>Penny Whiley, Molecular Translational Science/Hudson Institute         |
| 1:30pm – 1:45pm   | <b>Leveraging routinely-collected health data to examine medication adherence and survival in the real-world setting post-stroke</b><br>Lachlan Dalli, Medicine |
| 1:45pm – 2:00pm   | <b>Preeclampsia: what's in a diagnosis?</b><br>Michael Tanner, Obstetrics & Gynaecology   |
| <b>Research Presentations – Session 2, chaired by HISS rep (Ashlyn Pascoe)</b>    |   |
| 2:05pm – 2:20pm   | <b><math>\alpha</math>-Amylase inhibition by (poly)phenols: direct effect and/or starch complexation</b><br>Rizliya Visvanathan, Nutrition, Dietetics and Food  |
| 2:20pm – 2:35pm   | <b>Advancing Women in Healthcare Leadership</b><br>Mariam Mousa, Monash Centre for Health Research and Implementation (MCHRI)                                   |
| 2:35pm – 2:50pm   | <b>Causes and long-term consequences of respiratory instability on neurodevelopment outcomes in preterm infants.</b><br>Alica Yee, Paediatrics                  |
| 2:50pm – 3:05pm   | <b>Paying attention to cardiac surgical risk</b><br>Dr Jahan Penny-Dimri, Surgery   |
| 3:06 PM   | Official closing Prof Kate Loveland, with The Chairs (HISS reps)  |

# Speaker Bio and Abstracts

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## Brendan Gillespie, Psychiatry



### Biography

Brendan is passionate about improving the supports available for those managing mental ill-health. After obtaining BSc with majors in biochemistry and pharmacology, he then undertook an honours year under Rachel Hill, where he applied his molecular knowledge to the field of translational neuroscience. He then secured a role as a clinical trials co-coordinator, where he managed the day-to-day operations of two phase II clinical trials. After the conclusion of this role, Brendan returned to Rachel's group to commence a PhD, where he continues research related to his honours project. When not working on his PhD, Brendan provides auxiliary support for two clinical trials within the psychiatry department, which investigate new treatments for schizophrenia.

### Preventing Schizophrenia Before it Begins

#### Abstract:

Schizophrenia is a chronic and often devastating condition which carries significant long-term implications for both patients and their families. While current antipsychotic medications are often effective at managing the hallucinations and delusions associated with this condition, schizophrenia remains associated with a 15-year mortality gap, an unemployment rate of 70-90%, and estimated economic cost of \$60,000 per patient per year. My PhD is focused on understanding how infections during pregnancy impact foetal brain development, and place the unborn child at risk of developing schizophrenia once they reach adulthood. In fact, it has been estimated that up to a third of schizophrenia cases may be prevented if the effects of maternal infection were eliminated. This research is achieved through injecting pregnant mice with a virus-like substance, assessing their offspring across a range of behavioural assessments relevant to schizophrenia, and then investigating neurological changes that may underpin these deficits. My PhD also aims to investigate if two lost cost pregnancy supplements may be able to prevent these behavioural and neurological changes from developing in the first place. If these supplements prove beneficial, my project will provide supporting evidence for their use as prophylactics during pregnancy. The first supplement my project is investigating is 7-8 DHF. 7-8 DHF is an orally bioavailable and naturally occurring compound that readily crosses the blood brain barrier. Once within the brain, it activates a range of neurotrophic pathways via the TrkB receptor. The second supplement my project investigates is Sodium selenate, which provides an additional source of dietary selenium. Selenium is an essential trace nutrient that is vital for the function of many antioxidant enzymes. As oxidative stress has been implicated in both maternal infections and schizophrenia, supporting the capacity of endogenous antioxidant enzymes may reduce the impact of maternal infection on foetal brain development.

## Penny Whiley, Molecular & Translational Science/Hudson Institute



### Biography

Penny Whiley is a 2<sup>nd</sup> year PhD candidate in the Centre for Reproductive Health (CRH). After completing her undergraduate studies in England, Penny moved to Australia and worked as a research assistant for over 10 years. Her ongoing enthusiasm for medical research and male reproductive health led her to enrol in a PhD where she exercises her passion for learning how cells in the testis communicate to produce healthy sperm. Her long-term goal is to identify factors that contribute to male infertility and testicular germ cell tumours.

### Activin A impacts on germ cell development: new insights into male infertility

Penny A F Whiley<sup>1,2</sup>, Robin M Hobbs<sup>1</sup>, Kate L Loveland<sup>1,2</sup>.

<sup>1</sup> Centre for Reproductive Health, Hudson Institute of Medical Research, Clayton, Australia

<sup>2</sup> Department of Molecular and Translational Sciences, School of Clinical Sciences, Monash University, Clayton, Australia

Male infertility and testicular cancer are significant health issues thought to result from disruptions to testis development that occur *in utero*. Physiological events during human pregnancy such as preeclampsia, infection or ingestion of certain medications may be associated with high activin A levels. My PhD research is investigating the hypothesis that elevated activin A during pregnancy can affect the precursor germ cells (gonocytes) in the testis destined to form sperm. My work focuses on the transformation of gonocytes that occurs shortly after birth, as they transition into either differentiating spermatogonia that initiate the first round of spermatogenesis, or into spermatogonial stem cells (SSCs) that sustain spermatogenesis in adults. Using a mouse model with elevated activin A bioactivity (*Inha* KO; lacks inhibin  $\beta$  subunit), I investigated how this condition affects establishment of the two spermatogonial populations (spermatogonia and SSCs) after birth. Immunofluorescent analysis was used to score germ cell populations; RNAseq was used to examine their transcriptional profiles, and testis fragment cultures were used to manipulate activin signalling and further explore the mechanisms that control the developmental maturation of germ cells. I discovered that elevated activin leads to gonocyte loss during fetal life, alters the developmental trajectory of germ cells after birth, and favours formation of SSCs. My work also investigates the importin protein, IPO5, that selectively transports cargo into the nucleus. I am testing the hypothesis that the balance between activin A and BMP4 signalling, controlled by IPO5, influences this critical stage of spermatogonial maturation. Primary mouse spermatogonial cells are in use to manipulate IPO5 levels and identify IPO5 transport cargo. My data, showing systemic activin A levels determine the pace of germ cell development and stem cell establishment, suggests that human pregnancy conditions with elevated activin A can influence the male germline and consequently may affect adult fertility.

## Lachlan Dalli, Medicine



### Biography

Lachlan Dalli is a PhD Candidate and Research Assistant from the Stroke and Ageing Research Group, Monash University. He has a background in Biomedical Science and more recent experience in epidemiology, statistics and health services research. Lachlan completed his Honours degree in 2018 using linked data from the Australian Stroke Clinical Registry to identify health inequities in the prescription of evidence-based medications after stroke. Currently, Lachlan is involved with the analysis of linked pharmaceutical data to determine outcomes associated with medication adherence after stroke to inform policy and practice within Australia, and internationally.

### Leveraging routinely-collected health data to examine medication adherence and survival in the real-world setting post-stroke

Lachlan L. Dalli<sup>1</sup>; Joosup Kim<sup>1,2</sup>; Dominique A. Cadilhac<sup>1,2</sup>; Monique F. Kilkenny<sup>1,2</sup>

**Background:** Recent advances in data linkage capabilities have provided unique opportunities to explore person-centered care and health outcomes. Within Australia, use of data linkage is currently limited for examining medication adherence and health outcomes post-stroke. We aimed to investigate associations between medication adherence during the first year and mortality up to 3 years post-discharge.

**Methods:** A cohort of 1-year survivors of first-ever stroke or transient ischemic attack (TIA) was selected from the Australian Stroke Clinical Registry (July 2010–June 2014). Data were individually linked with the Pharmaceutical Benefits Scheme, Medicare Benefits Schedule, and National Death Index. Adherence to antihypertensive, antithrombotic, and lipid-lowering medications was assessed in pharmaceutical claims using the proportion of days covered (PDC) method up to 1 year post-discharge. Continuous associations between one-year medication adherence and long-term survival (between 1-3 years) were examined using restricted cubic spline analyses, adjusted for patient, clinical (e.g. stroke severity), and healthcare utilisation factors (e.g. primary-care visits).

**Results:** Among 8363 survivors of first-ever stroke/TIA, 75% were dispensed antihypertensive medications within 1-year post-discharge. Excluding patients with intracerebral hemorrhage (N=7446), 84% were dispensed statins, and 65% were dispensed non-aspirin antithrombotic medications. Users of medication were older, had more regular primary-care visits, and were more commonly discharged to aged care than non-users. During the first-year post-discharge, approximately half of all users of medication had a PDC  $\geq 85\%$  (i.e. access to medication for  $>310$  days). For survivors with PDC  $\geq 60\%$ , each 10% increase in adherence was associated with a 13-15% reduced risk of all-cause mortality between 1-3 years post-discharge.

**Conclusions:** We provide important insights on the uptake and real-world effectiveness of medications post-stroke and show that greater levels of medication adherence are associated with improved survival. Therefore, an arbitrary adherence target of 80% may be inappropriate as additional survival benefits were observed closer to 100%.

### Affiliations

1. Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia
2. Stroke Theme, the Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Heidelberg, VIC, Australia

## Michael Tanner, Obstetrics & Gynaecology



### Biography

Michael is undertaking the dual MD/PhD program in the Department of Obstetrics and Gynaecology. His research passions revolve around evaluating the utility of a diagnosis in medicine, trying to ensure they serve their ultimate purpose of improving health outcomes. He takes this passion beyond research by writing about the intersection of public health and public policy, and has had articles published in *The Sunday Age* and independent media.

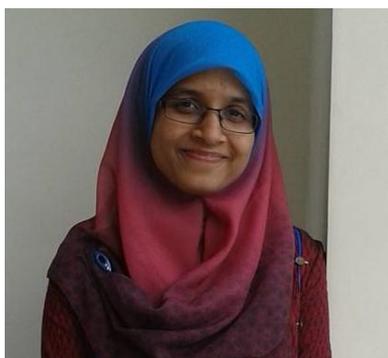
### Preeclampsia: what's in a diagnosis?

#### Abstract

Preeclampsia, characterised by the onset of hypertension and organ dysfunction in pregnancy, is a major cause of maternal and perinatal morbidity and mortality. The understanding of its pathophysiology has evolved significantly in recent decades, but this has not yet led to a diagnostic test. This leaves clinical evaluation as the mainstay of diagnosis. My PhD revolves around studying the effectiveness of the current diagnostic criteria in identifying women at risk of complications. We reviewed how the criteria for diagnosing preeclampsia has evolved, particularly over the past 70 or so years. We found that simplicity, convenience, and statistical limits have often been used to determine thresholds for diagnosing preeclampsia – particularly for defining hypertension in pregnancy. The rest of my PhD looks at how the clinical course and outcomes of preeclampsia vary across different groups of women. We first looked at women with comorbidities that increase the risk of developing preeclampsia – hypertension, diabetes, or obesity – and make accurate clinical diagnosis challenging. We began with a study exploring biomarkers that have in recent years been increasingly studied to rule preeclampsia in or out. We found that among women diagnosed with preeclampsia, the presence of comorbidities was potentially associated with less dysregulation in these biomarkers. Subsequent projects found a milder course of disease for women with comorbidities. They generally suffered fewer complications, largely as a result of earlier intervention. Our final studies involve evaluating how maternal characteristics – chiefly age, body mass index and early pregnancy blood pressure – and the subsequent development of complications – such as preeclampsia – influence the trajectory of blood pressure throughout pregnancy. Our early findings suggest that these characteristics have a significant influence. This has implications for the prediction and diagnosis of preeclampsia. Overall, our research demonstrates that different groups of women have significantly different outcomes from preeclampsia, and that diagnosing preeclampsia should move away from a “one-size-fits-all” approach.

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## Rizliya Visvanathan, Nutrition, Dietetics and Food



### Biography

Rizliya Visvanathan is a PhD student working with Professor Gary Williamson at the Department of Nutrition, Dietetics and Food, Monash University. She completed her Bachelor's in Food Science and Master's in Clinical biochemistry in Sri Lanka and moved to Melbourne in 2019 to start her PhD. Her research interests are focused on studying the association between biologically active dietary components, especially the (poly)phenols, metabolism and chronic disease. In her PhD, she is looking at how the interaction of (poly)phenols with the gut and digestive processes aid in reducing the risk of Type 2 Diabetes and associated comorbidities.

### **$\alpha$ -Amylase inhibition by (poly)phenols: direct effect and/or starch complexation**

Rizliya Visvanathan, Michael J. Houghton, Elizabeth Barber, Gary Williamson

High postprandial glycaemic excursions are an important factor contributing to the development of insulin resistance and type 2 diabetes (T2D). Reducing the glycaemic load from constant intake of high glycaemic index foods could reduce the risk of T2D. One possible way to achieve this goal is through reducing starch digestion and absorption in the gut using natural inhibitors, such as (poly)phenols. (Poly)phenol consumption is strongly associated with a reduced risk of T2D, partly attributed to  $\alpha$ -amylase inhibition and reduced starch digestion. In this work, we present a new sensitive method to determine human  $\alpha$ -amylase inhibition using maltoheptaoside (Mal-7) as substrate with direct chromatographic product quantification, compared with amylose/amylopectin hydrolytic products estimated using 3,5-dinitrosalicylic acid (DNSA). The pharmaceutical drug acarbose exhibited similar  $IC_{50}$  values with Mal-7, amylopectin or amylose as substrates, whilst varied results were observed for the polyphenols (epigallocatechin gallate (EGCG), quercetagenin and punicalagin). The polyphenols weakly inhibited Mal-7 (<50% inhibition) hydrolysis compared to amylose ( $IC_{50}$ : EGCG =  $20.41 \pm 0.25 \mu\text{M}$ , quercetagenin =  $30.15 \pm 2.05 \mu\text{M}$ ) or amylopectin. All three (poly)phenols interfered with the DNSA method, with minimal interference using Mal-7 as substrate. (Poly)phenols may inhibit  $\alpha$ -amylase through (1) direct action on the enzyme and/or (2) starch-(poly)phenol complexation. The main inhibition mechanism of EGCG and punicalagin was through starch complexation, especially amylose, whereas quercetagenin additionally binds to the  $\alpha$ -amylase active site. The new method using Mal-7 as substrate is superior for determining direct  $\alpha$ -amylase inhibition, whilst the conventional DNSA method, using native starch as substrate, detects both inhibitory mechanisms. Accurate identification of (poly)phenols and their  $\alpha$ -amylase inhibitory mechanism could aid in developing dietary strategies focused at reducing postprandial glycaemia.

## Mariam Mousa, Monash Centre for Health Research and Implementation (MCHRI)



### Biography

Organisational Psychologist, Graduate Research and Industry Partnership Scholarship funded PhD candidate in the final year at Monash Centre for Health Research and Translation, School of Public Health and Preventive Medicine  
Twitter @MariamMousa\_

### Advancing women in healthcare leadership: an evidence based organisational change approach

#### Abstract:

Women in Australia play a pivotal role in the delivery of health services, yet they remain the minority decision makers, occupying less than 25% of the most influential leadership positions. In the health sector, a disparity persists between what is considered effective leadership performance, and the actual work-life capacity of women. While many organisations in the sector have catalysed action to enable gender equity for women, they have also struggled to address the deeply vexing issue of systemic inequality built into concepts of career advancement and outcomes related to leadership. Understanding how career paths are modelled within organisational structures is fundamentally tied to how decisions on critical career factors are made, from cultivating leadership potential, training and development of talent, and the provision of resources and role advancement opportunities within an organisational setting.

The scale and complexity of this endeavor has proved difficult for organisations to facilitate, and with good reason. Research is needed to synthesise and understand evidence on organisational interventions that work to advance women, and how they can be materially adapted into realistic career models for healthcare, acknowledging and incorporating the reality of women's experiences across the span of their working lives. Accelerating the rate of progress for women requires organisational approaches to adapting workplace culture, policy and strategies to move beyond a focus on the individual, with measurement and reporting that actively addresses performance indicators associated with achieving gender equity. This PhD project aims to make a meaningful contribution to the healthcare community by conducting a systematic, translational, and evidence-based methodology to generate insights and identify ways in which organisations can remove long standing, often overlooked barriers and biases and facilitate action specific to the organisational context. This work informs the co-design priorities for a large-scale, national health and medical research council funded project that aims to improve career outcomes for women in healthcare leadership within Australia and beyond.

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## Alicia Yee, Paediatrics



### Biography

Alicia Yee is a third year PhD student. She started her PhD in 2019 with the Infant and Child Health group at the Ritchie Centre and Department of Paediatrics, with Prof. Rosemary Horne and A/Prof. Flora Wong, following the completion of her Bachelor of Medical Science (Honours) at Monash Malaysia.

### **Causes and long-term consequences of respiratory instability on neurodevelopment outcomes in preterm infants.**

#### **Abstract:**

Almost 27,000 babies are born early (< 37 weeks of gestational age) each year in Australia, and globally this number is over 15 million. Despite the significant advances in medical care which have dramatically increased survival in these fragile infants, developmental morbidity has not improved. Infants born moderately or late preterm (> 32 weeks of gestation) are at double the risk for neurodevelopmental disability at 2 years of age compared to term born peers. Preterm infants are born with immature cardio-respiratory control, which often manifests as pauses of breathing in the form of short central apnoeas and periodic breathing (a cyclical pattern of short repetitive central apnoeas). These breathing patterns that occur during sleep are currently undetected in the nursery because the apnoeas are short and they are deemed to be not life threatening. Our group have shown that these short apnoeas and periodic breathing are associated with hypoxia and reduced cerebral oxygenation in preterm infants after hospital discharge. Given that preterm infants are already at a higher risk for adverse neurodevelopmental outcomes, the associated hypoxia may contribute to adverse neurocognitive outcomes.

My research follows preterm infants longitudinally, before and up to 6 months after hospital discharge, to explore the relationship between changes in cerebral oxygenation, peripheral oxygen saturation, heart rate and blood pressure during apnoea and periodic breathing and neurodevelopmental outcomes. In addition, a number of pre- and postnatal clinical factors may affect respiratory control in preterm infants, therefore, we also aim to identify maternal or infant factors, which increase the risk of preterm infants having increased sleep time in apnoea and periodic breathing in the nursery and over the first 6 months after hospital discharge. My findings will inform a trial of treatment, with the potential to change clinical practice, improve outcomes and reduce long-term health care burdens.

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## Dr Jahan Penny-Dimri, Surgery



### Biography

Jahan is a part time current surgical registrar and PhD candidate. His area of research focuses on expanding the latest developments in machine learning into the sphere of surgical risk prediction

Jahan is a junior doctor working in surgery, and an early career researcher in applying emerging data science techniques to improve healthcare outcomes.

### Paying attention to cardiac surgical risk

Abstract:

Machine learning (ML) is increasingly being applied to risk stratification and prediction of postoperative outcomes in cardiac surgery. Many ML models are limited in practice by producing unexplained predictions or are inflexible to input data availability at inference time. We have developed an interpretable ML model with flexibility in the setting of missing data. Using properties of regularisation in the latent space, we are able to guard against the biases of missingness of an unknown pattern during both training and inference. We have shown state-of-the-art performance when compared to other algorithms that are capable of dealing with missingness.