

# MHTP PHD STUDENT SHOWCASE SYMPOSIUM

WEDNESDAY, 7 OCTOBER 2020

1pm - 4pm via Zoom

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



Timing	Title/Speaker
1.00pm – 1.15pm	<b>Official opening</b> Prof Eric Morand with <i>The Hudcast Duo, Ben and Mikee</i>
<b>Research Presentations – Session 1, chaired by Marina Yakou</b>	
1:15pm – 1:30pm	<b>Transcriptomics as a window into individual variation in weight loss</b> Kaitlin Day, Nutrition, Dietetics and Food
1:30pm – 1:45pm	<b>Targeting Ovarian Cancer Leader Cells</b> Nazanin Karimnia, Molecular Translational Science/Hudson Institute
1:45pm – 2:00pm	<b>Using the Design of Experiment (DoE) approach to maximise research efficiency</b> Anqi Li, Obstetrics and Gynaecology
2:00pm – 2:15pm	<b>Feasibility, safety and effectiveness of a pilot 16-week home-based, impact exercise intervention in post-menopausal women with low bone mineral density</b> Carrie Ng, Medicine
<b>2:15PM – 2:30PM</b>	<b>BREAK AND ENTERTAINMENT</b>
<b>Research Presentations – Session 2, chaired by Rama Ravinthiran</b>	
2:30pm – 2:45pm	<b>Machine Learning in Cardiac Surgery: Predicting Postoperative Outcomes with Explainable AI</b> Dr Jahan Penny-Dimri, Surgery
2:45pm – 3:00pm	<b>Community participation for adults with autism</b> Lauren Cameron, Psychiatry
3:00pm – 3:15pm	<b>Understanding the relationship between ventilatory control instability and sleep disordered breathing from infancy to childhood</b> Leon Siriwardhana, Paediatrics
3:15pm – 3:30pm	<b>Prediction for Risk-Stratified care for women with Gestational Diabetes (PeRSONal GDM)</b> Dr Shamil Cooray, Monash Centre for Health Research and Implementation
<b>3:30 – 4:00PM</b>	<b>CLOSING ENTERTAINMENT AND PRIZE AWARDS</b>

# Speaker Bio and Abstracts

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## Kaitlin Day, Nutrition, Dietetics & Food (1:15pm – 1:30pm)



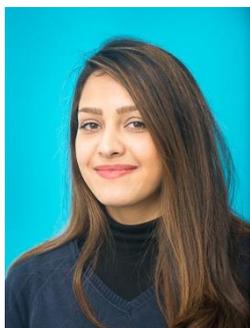
Kaitlin is a final year PhD Student in the Department of Nutrition, Dietetics and Food at Monash University. She has a background in Biomedical Sciences and completed her Bachelor's Degree at the University of Surrey in the UK. Her research interests include personalised nutrition and bioinformatics approaches for obesity.

### **Transcriptomics as a window into individual variation in weight loss**

Obesity rates have tripled in the last 40 years globally and is an independent risk factor for a host of non-communicable disease. The World Health Organisation reports that globally, obesity causes 15 million pre-mature deaths annually. Current strategies to reduce obesity rates employ a “one size fits all” approach that has not mitigated the rise in obesity rates. Both weight gain and weight loss are influenced by a host of environmental and physiological factors and it is anticipated that a more personalised approach will have more success. However, our current lack of understanding about how subtle and intertwined the differences in physiology are and how this could play a role in treatment response is a barrier to personalising weight loss strategies. Transcriptomics is the capture of global gene expression levels in a given tissue at a given time. Transcriptomics enable the capture of a global picture of the molecular adaptations occurring during weight loss and as such offers a window into individual differences in treatment response. Through a comprehensive review and re-analysis of the literature in conjunction with primary data, my PhD research explores the extent of individualisation at the transcriptomic level in weight loss response, the drivers of potential differences and key pathways underpinning those responses. My findings suggest that there are subtle and highly variable transcriptomic changes occurring during weight loss and the impact on health outcomes is yet to be fully elucidated. Open source and standardised -omics research is needed in the future to fully understand individual variation and the benefit of personalised nutrition.

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## Nazanin Karimnia, Molecular & Translational Science/Hudson Institute (1:30pm – 1:45pm)



Nazanin is a final-year Ph.D. student in the Ovarian Cancer Biomarkers group based at Hudson institute of medical research. I completed both of my bachelor's and master's degree in molecular genetics in Iran. During this time, I also worked in a molecular pathology focussing on prenatal genetic tests and collaborated as a research assistant in a project working on driver mutations of thrombophilia. I started my Ph.D. in the ovarian cancer biomarkers group in 2017. My project focuses on the "Leader cells" (LCs), a specialised sub-

population of ovarian cancer cells that are the key mediators of invasion and metastatic disease. During my project, we have established a novel drug screening pipeline enabling us to repurpose FDA-approved drugs for effectively targeting the LCs and potentially upgrade the treatment regimen for ovarian cancer patients who are getting the same treatments that were established three decades ago.

### **Targeting Ovarian Cancer Leader Cells**

Over the past two decades, the overall survival rate for ovarian cancer patients has remained as low as 30%, making ovarian cancer the most lethal gynaecological malignancy. As symptoms of ovarian cancer are vague at early stages, about 70% of the patients are diagnosed with extensive metastatic disease. For over 20 years platinum-based chemotherapy has remained the gold-standard first-line treatment and despite promising initial response, 80% of the patients will relapse with cancer resistant to the available treatment regimens.

Recently, we identified a subpopulation of "Leader Cells" (LCs) that control invasion, progression and acquired chemoresistance in ovarian cancer. Therapies targeting leader cells are likely to be pivotal to improve prognosis, particularly in patients who are refractory to standard-of-care. Using a high content-high throughput drug screening approach we have identified FDA-approved compounds with a great repurposing potential to impede the LCs function in vitro.

Through secondary interrogations of the identified hits, we could confirm that low doses of omipalisib, a PI3K/mTOR dual inhibitor, can effectively inhibit LC-mediated invasion and migration without cytotoxicity effects. Furthermore, low-dose omipalisib synergises with cisplatin and paclitaxel treatment, reducing the effective dose of these chemotherapeutics by ~4-5 folds.

The data demonstrate that our developed high-throughput screen pipeline is a viable approach to identify opportunities for drug repurposing in ovarian cancer. Moreover, the PI3K signalling pathway appears to be important in LC function and inhibiting this pathway results in increased sensitivity to

chemotherapy in vitro. Ongoing work will evaluate the applicability of our pipeline for clinical screening programs, and further, validate existing drugs for potential repurposing.

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## Anqi Li, Obstetrics and Gynaecology (1:45pm – 2:00pm)



Anqi is a PhD candidate in the Amnion Cell Biology research group at The Ritchie Centre. Her project involves close collaboration with Scinogy Pty Ltd and Thermo Fisher to develop processes using a novel cell processing device for the cell and gene therapy industry. The findings from her research has provided critical support for device development.

### **Using the Design of Experiment (DoE) approach to maximise research efficiency**

Traditionally, scientists assess the impact of variables on an outcome using one-factor-at-a-time experiments (OFAT). However, the OFAT approach is incredibly time-consuming when multiple factors are of interest. The outcomes of OFAT experiments also fail to identify interactions between factors, which may lead to incorrect conclusions. Instead, a more effective method using multivariate statistical analysis called Design of Experiments (DoE), can be applied. Each set of DoE experiments is comprised of multiple experiments so that each experimental run will test a combination of high or low values of four or more parameters. The data are then used to establish a mathematical model, which then captures the multi-dimensional relationship between the testing factors (including any interactions) to the testing outcomes.

The DoE method can also be applied to the manufacturing of cell and gene therapy products. The successful commercialisation of any given cell and gene therapy product is greatly dependent on the ability to transition from a manual, operator-dependent process to one that is suitable for scalable manufacturing. A common route is through the onboarding of automated solutions where multiple physical parameters may significantly impact cell quality. Using the DoE method, we identified critical processing factors that influence cell quality when applying an automated device, as well as the interactions between these factors.

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## Carrie Ng, Medicine (2:00pm – 2:15pm)



Carrie-Anne is a 2nd year PhD candidate in the Department of Medicine at Monash Health. Her doctoral research investigates the effects of impact osteogenic exercise on skeletal health over the lifespan, with added focus on reducing falls and fracture risk later in life. She is also interested in the utilisation of tools used to assess the mechanical loading of everyday physical activity and their association with bone health.

### **Feasibility, safety and effectiveness of a pilot 16-week home-based, impact exercise intervention in post-menopausal women with low bone mineral density**

**PURPOSE:** The feasibility and efficacy of impact exercise in postmenopausal women with low bone mineral density (BMD) are unclear. We aimed to determine adherence, safety and changes in BMD, bone microarchitecture and physical function following a pilot home-based, impact exercise intervention in postmenopausal women with low BMD.

**METHODS:** 50 community-dwelling postmenopausal women with BMD T-scores < -1.0 participated in 16-weeks of home-based impact exercise progressively increasing to 50 multi-directional unilateral hops on each leg daily. Bone density and structure were assessed by lumbar spine and hip dual-energy X-ray absorptiometry (DXA), 3D modelling (3D-SHAPER) of hip DXA scans, and distal tibial high-resolution peripheral quantitative computed-tomography scans. Physical performance was assessed by repeated chair stand time and stair climb time.

**RESULTS:** 44 women (mean±SD age 64.5±7.5 years) completed the intervention, with adherence of 84.7±18.0%. Reasons for withdrawal were related soreness (n=2), unrelated injury (n=1) and loss of interest (n=3). Femoral neck areal BMD increased by 1.13±3.76% (p=0.048). Trabecular volumetric BMD (vBMD) increased at the total hip (2.27±7.03%; p=0.038) and femoral neck increased (3.20±5.39%; p<0.001). Distal tibia total vBMD increased by 0.32±0.88% (p=0.032) and cortical cross-sectional area increased by 0.55±1.54% (p=0.034). Chair stand and stair climb time improved by 2.3±1.88s (p<0.001) and 0.27±0.49s (p<0.001), respectively.

**CONCLUSION:** A 16-week home-based, impact exercise was feasible and may be effective in improving femoral neck areal BMD, total hip and distal tibial vBMD, and physical function in postmenopausal women. Appropriately designed randomised controlled trials are now required to determine whether such interventions can reduce fracture risk in older populations.

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## Dr Jahan Penny-Dimri, Surgery (2:30pm – 2:45pm)



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

### **Machine Learning in Cardiac Surgery: Predicting Postoperative Outcomes with Explainable AI**

Cardiac surgery is one of the most physiologically demanding stressors for the human body. Predicting and preventing the onset of postoperative complications is an important goal for improving patient outcomes. We have applied modern machine learning techniques to predict cardiac surgery-associated acute kidney injury, and leverage model complexity to create individualised patient risk profiles. We are now extending this work to create deep learning models with intrinsic interpretability for multiple postoperative outcomes.

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## Lauren Cameron, Psychiatry (2:45pm – 3:00pm)



Lauren is in the final year of her PhD with the Centre for Developmental Psychiatry and Psychology, working under the supervision of Professor Kylie Gray and Emeritus Professor Bruce Tonge. Her research interests include intellectual and developmental disabilities, particularly autism, across the lifespan, and the ways in which we look at and define positive outcomes and quality of life for individuals with developmental disabilities. Lauren's PhD is exploring outcomes for adults with autism who have been involved in a longitudinal study since they were children.

### **Community participation for adults with autism**

**Background:** Regular participation in community activities is an important contributor to better quality of life for adults with autism. Research suggests that community participation is limited for children and adolescents with autism, however, less is known about community participation in adulthood, the benefits of community participation on quality of life and wellbeing, and the barriers and facilitators to community participation.

**Method:** A systematic review was conducted to synthesise the available literature on community participation, the benefits for adults with autism, and the factors that support adults with autism to participate in the community. Next, information on community participation (including employment, recreation, and leisure activities) and living arrangements was collected from N = 84 participants (80% male). Participants age ranged from 26.80 to 44.10 years (M = 34.10 years, SD = 4.49).

**Results:** A summary of the themes identified in the systematic review will be presented, followed by preliminary results of the cross-sectional element of the research study.

**Implications:** Results will be discussed by identifying which groups of individuals are at greatest risk for reduced community involvement, highlighting those individuals in which supports and programs to improve community participation should be targeted.

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## Leon Siriwardhana, Paediatrics (3:00pm – 3:15pm)



Leon is a fourth year medical student undertaking the MD/PhD pathway. He commenced his PhD in 2019 with the Infant and Child Health group at The Ritchie Centre and Department of Paediatrics, following the completion of his Bachelor of Medical Science (Honours) in 2018.

### **Understanding the relationship between ventilatory control instability and sleep disordered breathing from infancy to childhood**

During infancy and childhood, sleep is at a lifetime maximum. Disruption to sleep in these early years, through conditions such as sleep disordered breathing, can adversely affect the developing brain and other body systems. In preterm infants, patterns of unstable breathing, termed periodic breathing are common. Periodic breathing in preterm infants have been attributed to immature ventilatory control and are currently deemed benign. However, as emerging evidence points to associations between periodic breathing and adverse neurodevelopmental outcomes, there is an urgent need to understand the postnatal development of ventilatory control, and how it relates to periodic breathing. In addition, in older children, longer pauses in breathing associated with airway collapse are termed obstructive sleep apnoea (OSA). OSA is clinically recognised as a condition that requires timely detection and management to avoid long-term cardiovascular and neurodevelopmental sequelae. However, the current first line treatment, adenotonsillectomy, is not always curative, particularly in vulnerable populations such as in children with Down syndrome. Recent evidence in adults indicates that ventilatory control instability maybe involved in the

development of OSA and treatments that target ventilatory control has the potential to improve the management of this condition. Newly developed techniques have enabled the quantification of the stability of ventilatory control system non-invasively using mathematical modelling. Using these techniques, my thesis aims to gain a more comprehensive understanding of ventilatory control instability as a tool for characterising periodic breathing in preterm infants and as a contributory mechanism to OSA in children.

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## **Dr Shamil Cooray, Monash Centre for Health Research and Implementation (3:15pm – 3:30pm)**



Shamil is an Endocrinologist with clinical appointments at Monash and Alfred Health. He is also a PhD candidate at the Monash Centre for Health Research and Implementation. He is supported by an NHMRC Postgraduate Scholarship, the Australian Academy of Science and Diabetes Australia. During his PhD, he undertook a Clinical Research Fellowship in Clinical Prediction Modelling at the Barts Research Centre for Women's Health at Queen Mary University London funded by the Endeavour Leadership Program.

### **Prediction for Risk-Stratified care for women with Gestational Diabetes (PeRSONal GDM)**

Current gestational diabetes (GDM) diagnostic criteria identify pregnant women with highly diverse risks of adverse pregnancy outcomes. Understanding personal risk can enable shared decision-making and stratified care, targeting preventative and therapeutic antenatal interventions to those at highest risk of adverse pregnancy outcomes. An objective, systematic and robust approach to risk identification is an established priority, especially with resource and systems constraints during and post COVID-19.

More than one hundred clinical prediction models are published each year, but few are suitable for implementation into clinical practice. This talk will describe my PhD research program to create a novel clinical risk calculator for adverse pregnancy outcomes in women diagnosed with GDM. Major components of this research program included the design of the prediction model to meet a clinical need and informed by a systematic review and critical appraisal, which identified the methodologic limitations of existing models. We developed and validated the model using a retrospective population-based cohort consisting of routinely-collected health data from 2,702 deliveries and state-of-art statistical methods. We evaluated the clinical utility of the validated model using decision curve analysis. It demonstrated that using the model to guide clinical decision-making around the need for intensive antenatal management, would offer a net benefit compared to

the current one-size-fits-all approach. Finally, we transformed the statistical model into a web-based clinical risk calculator that can be implemented into clinical practice to enable a more personalised, risk-stratified approach to this global public health concern.

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