



TOW RESEARCH AWARDS

ABSTRACTS 2026

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RANDWICK HEALTH &
INNOVATION PRECINCT

The future of lifelong health

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About **Tow Research Awards**



The Tow Research Day and Awards were initiated due to the vision of Dr Wally Tow, a visitor from Singapore in the early 1970s, who passed away in 2019.

The Tow Research Day provides a common forum on the Randwick Health & Innovation Precinct called the Tow Research Day for junior investigators to present their basic and clinical research. This fosters collaborations between clinical investigators and research scientists who are located at the many research institutes and hospitals around the Randwick Precinct.

The Coast Medical Association Tow Research Committee was created and registered as a charitable entity in 1973 in recognition of the origin of the Tow Research Awards, which was part of the annual meeting of the Coast Medical Association.

The purpose of the Committee is to foster the conduct of research at the Randwick Health & Innovation Precinct.



Welcome Message

It's wonderful to be back! After taking a break in 2025, we are delighted to welcome you to the 2026 Tow Research Awards to celebrate research excellence, innovation and collaboration across our community.

This year, we received 64 applications, with the top four applicants from each of our four award divisions selected to deliver 16 oral presentations, alongside 15 poster presentations. Congratulations to all applicants and finalists on their achievements!

We are delighted to welcome our keynote speakers, Dr Didu (Sandi) Kariyawasam, a paediatric neurologist and UNSW researcher advancing clinical trials and genetic therapies for childhood neurological conditions, and Professor Jane Currie, UNSW's inaugural Discipline Lead for Nursing, whose work is driving healthcare reform through co-designed models of care.

We acknowledge the late Dr Wally Tow, whose vision established these awards as a forum for emerging researchers to share their work and foster collaboration across clinical and scientific disciplines.

Our sincere thanks to the judges, Committee members and everyone who has contributed to this year's Awards. We encourage you to connect with colleagues, enjoy the presentations and vote in the People's Choice Awards.

Keynote

Dr Didu (Sandi) Kariyawasam



Dr Didu (Sandi) Kariyawasam is a paediatric neurologist, and post-doctoral researcher at UNSW Sydney. She completed her Masters at the University of Cambridge, UK, subsequently graduating from University College London in 2007. She embarked on her training in Paediatric Neurology at John Radcliffe Hospital, Oxford, UK, gaining specialist expertise in the management of complex epilepsy (Great Ormond Street Hospital, London), movement disorders (Evelina Children's Hospital London) and neuroinflammation (John Radcliffe Hospital, Oxford). In 2022, Sandi successfully completed a PhD in the investigation of pathways to optimise diagnosis and care for children with Neurogenetic disease.

Sandi currently practices clinically at Sydney Children's Hospital (Randwick), and as an early career researcher, holds the title of senior lecturer at the University of New South Wales. She completed her PhD in 2022, evaluating the novel diagnostic and management pathways in paediatric neuromuscular disease (NMD).

Sandi is active in the field of clinical trials and is part of the clinical research team providing access to new genetic therapies in the field of childhood onset neurological disease. Her work has been translational in the domain of paediatric neuromuscular disease where she strives to improve health and psychosocial outcomes for affected children and their families. Her goal is to provide optimal care and informed choice for families.

Keynote

Prof Jane Currie



Dr Jane Currie is the inaugural Discipline Lead for Nursing at UNSW, leading systemic healthcare reforms for Australia's most vulnerable populations, with her co-designed models of care translating lived experience directly into practice and policy. Her program of research explores the impact of health services on access to health care for priority populations, particularly those experiencing homelessness, domestic and family violence. She uses participatory research methods, including co-design, which ensures voices of lived experience are at the centre of solutions to improve healthcare access.

Currently, she serves as Chief Investigator (CIA) on the MRFF Healthy & HomeED program optimising emergency department responses to people experiencing homelessness, alongside a Rosemary Bryant Foundation grant to empower nurse-led scope of practice in specialist homeless clinical services. Jane's extensive education and clinical leadership is decorated with an Australia Day Medallion, an Army Service Medal, and an Australian Award for University Teaching Citation, with her military service spanning 20 years, including regular and reserve Army service across the British and Australian Armies.

She is currently Chair the Service Delivery Clinical Governance committee at Micah Projects, Brisbane and is currently the nursing Editorial Advisory Committee member for the Australian Prescriber.

Awards Day

- 09:00** Welcome and Acknowledgement of Country
- 09:15** Basic Science Division
- 10:15** Morning Tea and Poster Viewing
- 10:45** Clinical Division
- 11:45** Keynote Speaker: Dr Didu (Sandi) Kariyawasam
- 12:05** Lunch, Poster Vieweing, and Poster Judging
- 13:05** Honours and Independent Learning Project (ILP) Division
- 14:15** Allied Health, Nursing, and Midwifery
- 15:15** Keynote Speaker: Prof Jane Currie
- 15:35** Afternoon Tea and Awards Ceremony
- 16:15** Event Ends

Division:
**Allied
Health
Nursing and
Midwifery**



Applicant: Jennie Cusiter
Supervisor: Professor Patricia McCabe

Efficacy of the Launch to School Emergent Literacy Intervention for Preschoolers with Communication Difficulties: A non-randomised pragmatic controlled trial.

Jennie Cusiter (1, 2, 3), Natalie Munro (6), Annabel Webb (2, 5), Patricia McCabe (2), Kate Short (2, 3, 4)

1. Sydney Children's Hospital Network, NSW, Australia;
2. The University of Sydney, NSW, Australia;
3. South Western Sydney Local Health District, NSW, Australia;
4. Ingham Institute for Applied Medical Research, Liverpool, NSW, Australia;
5. Cerebral Palsy Alliance Research Institute, NSW, Australia;
6. Southern Cross University, QLD, Australia

Background: Preschool children with communication disorders are at significant risk of literacy difficulties (1). Launch to School (L2S) is a combined language and code intervention designed to strengthen emergent literacy skills before school entry. This study had three aims: 1) to examine the immediate impact of L2S on composite language and code outcomes; 2) to explore intervention effects on specific language and code subskills post-intervention and at four-month follow-up; and 3) to examine impacts on broader receptive and expressive language outcomes at follow-up.

Methods: The L2S trial was a pragmatic non-randomised control study conducted within a health service. Children aged four to six years received either L2S ($n = 174$) or business-as-usual standard speech pathology care (BAU; $n = 75$).

Results: Post-intervention, children who received L2S showed significantly greater gains than BAU in composite language ($d = 0.21$, $p = .008$) and composite code outcomes ($d = 0.40$, $p < .001$). Significant improvements were observed in phonological awareness, letter knowledge, name writing, vocabulary, and inferencing, but not narrative outcomes. At follow-up, intervention effects were maintained for vocabulary ($d = 0.20$, $p = .036$), inferencing ($d = 0.26$, $p = .009$), and print concepts ($d = 0.33$, $p = .032$). Children who received L2S also demonstrated stronger expressive language skills ($d = 0.28$, $p < .001$) than those receiving standard care.

Conclusion: Findings suggest that, compared with standard speech pathology care, a combined multitarget language and code intervention can improve emergent literacy and expressive language outcomes for children with communication disorders.

References:

1. Catts HW, Fey ME, Tomblin JB, Zhang X. A longitudinal investigation of reading outcomes in children with language impairments. *Journal of Speech, Language and Hearing Research*. 2002;45:1142-57.

Applicant: Georgia Lloyd
Supervisor: Dr Felicity Wright

Partnered Pharmacist Medication Charting for Children and Young People: A Retrospective Cohort Study.

G. Lloyd (1, 2) B. McCarthy (1), P. Ng (1), C. Johansson (1) and F. Wright (1).

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2. School of Health Sciences, University of New South Wales, Sydney, New South Wales.

Background: Medication errors are a major source of preventable harm in hospitalised children. Partnered pharmacist medication charting (PPMC) is an admission medication reconciliation model, in which a pharmacist obtains a best possible medication history (BPMH), collaborates with a medical officer to agree a medication management plan for pre-admission medicines, and charts the agreed plan. PPMC reduces prescribing errors in adult hospitals, but paediatric evidence is limited (1). To determine whether PPMC reduces medication errors in children presenting to a paediatric emergency department and explore its association with hospital length of stay (LOS).

Methods: A retrospective cohort study at a tertiary paediatric hospital compared three sequential models of care: usual care (T1, n=126), early best possible medication history (BPMH) by an emergency department pharmacist (T2, n=122), and PPMC (T3, n=103). Eligible patients took at least one home medication and had a BPMH. The primary outcome was the proportion of patients with ≥ 1 prescribing error, with clinical significance assessed by a blinded expert panel.

Results: Patients with ≥ 1 prescribing error fell from 70.6% with usual care to 50.8% with early BPMH and 5.8% with PPMC ($p < 0.001$). One additional patient avoided a prescribing error for every two receiving PPMC (NNT=2). High or extreme-risk errors fell from 39.7% to 1.9% (NNT=3). Median LOS was shorter with PPMC than usual care (2.3 versus 3.3 days; $p = 0.012$).

Conclusion: PPMC reduced prescribing errors compared to usual care and early BPMH and was associated with a reduced LOS, supporting expansion to other areas of the hospital.

References:

1. Tong, E.Y. & Yip, G. (2024) Aust. Prescr. 47, 48–51.

Applicant: Shivam Sharma

Supervisor: Dr Daniel Treacy

Perturbation-based Balance Training Reduces Falls and Fall Injuries in Older People: Insights on Mechanisms and Training Parameters from a Systematic Review and Meta-analysis.

Shivam Sharma (1, 2), Ildiko Zsuzsa Szabo (3), Mathias Brix Danielsen (3), Stig Andersen (3), Jens Eg Nørgaard (3), Stephen R. Lord (1, 2), Yoshiro Okubo (1, 2), Martin Gronbech Jørgensen (3)

1. Falls, Balance and Injury Research Centre, Neuroscience Research Australia

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3. Aalborg University Hospital, Denmark

Background: Perturbation based balance training (PBT) specifically targets reactive balance, which is the ability to rapidly recover from slips and trips (1). However, uncertainty remains regarding its effectiveness, underlying mechanisms and optimal training dose. This review aims to clarify the efficacy of PBT in reducing falls and fall-related injuries among older adults. It further explores optimal training parameters to inform clinical practice and fall-prevention guidelines.

Methods: Randomised controlled trials involving community-dwelling adults aged ≥ 65 years were included if they evaluated PBT effects on falls, injurious falls or fall-risk factors. Random-effects metaanalyses were conducted, and certainty of evidence was assessed using the GRADE framework.

Results: Twenty-five randomised controlled trials involving 2,659 participants were included. PBT reduced fall rates by 23% compared with control interventions (rate ratio 0.77, 95% CI 0.60–0.99; lowcertainty evidence) and injurious falls by 24% (rate ratio 0.76, 95% CI 0.58–0.98). PBT significantly improved reactive balance, including performance during laboratory-induced trips and slips, but had limited effects on other fall-risk factors such as gait. Dose-response analysis indicated that programs involving ≥ 6 hours of training reduced falls by approximately 33%.

Conclusion: PBT reduces falls and related injuries, likely through enhanced reactive balance rather than physical improvements. While most PBT programs are low doses (≤ 2 hours), higher doses (6+ hours) likely offer greater fall protection. Further high-quality trials using accessible PBT methods are required to inform policy and guideline development and support scalable implementation of PBT in fallprevention strategies.

References:

1. Mansfield A, Wong JS, Bryce J et al. Does perturbation-based balance training prevent falls? Systematic review and meta-analysis of preliminary randomized controlled trials. *Phys Ther* 2015;95:700–709.
2. Gerards MHG, McCrum C, Mansfield A et al. Perturbation-based balance training for falls reduction among older adults: current evidence and implications for clinical practice. *Geriatr Gerontol Int* 2017;17:2294–2303.

Applicant: Willis Trinh
Supervisor: Ms Suzanne Sheppard-Law

SELF-ASSESSMENT FOR SKIN INTEGRITY_EMPOWERING PEOPLE LIVING WITH A SPINAL CORD INJURY TO REDUCE PRESSURE INJURY RISK – A QUALITATIVE STUDY.

Willis Trinh (1), Ruyi Yao (1), Alexandra Crawford (1), Carrie Balthazaar (1), Deborah Debono (2), Scott Brunero (1), Suzanne Sheppard-Law (1, 2)

1. Prince of Wales Hospital, Randwick, New South Wales, Australia

2. University of Technology Sydney, School of Nursing & Midwifery, New South Wales, Australia

Background: This study hypothesised that providing individuals with spinal cord injury (SCI) a long-handled mirror, embedded within person-centred care and education, would empower independent selfskin assessment, enhance early pressure-injury (PI) detection, and reduce long-term complications. By enabling routine inspection of common PI sites, the mirror was expected to improve safety, foster psychological well-being, and support sustained self-management behaviours among SCI patients at Prince of Wales Hospital from 2019 onward.

Methods: A qualitative descriptive design with in-depth, semi-structured interviews was employed between May and September 2025. Participants with tetraplegia or paraplegia provided consent, completed a brief demographic and clinical questionnaire, and attended audiorecorded interviews in a private room. Open-ended questions elicited experiences of using the mirror for self-skin assessment and early PI detection. Data collection continued until saturation. Transcripts were de-identified, coded, and analysed using Braun and Clarke's (2006) six-phase thematic analysis. Lead nurse researchers received mentorship from experienced nurse academics throughout the research process to build capacity and skill.

Results: Following ethical approval, fourteen participants completed face-to-face interviews. Preliminary analysis revealed four themes: (1) Using the mirror, (2) Empowering independence and dignity, (3) Overcoming embarrassment, and (4) Learning about pressure-injury prevention. Participants described increased confidence, autonomy, and reduced reliance on others for skin checks, while also noting initial self-consciousness that diminished with familiarity and education.

Conclusion: This study is the first to describe the experience and impact of a long-handled mirror as an intervention promoting safety, empowerment, and self-management among people with SCI. Findings support practice change and enrich nursing knowledge. Future co-designed research will refine the mirror's usability and flexibility to enhance patient-centred outcomes.

Applicant: Dr Michael Doumit

Supervisor: Andrew Gorrie

How best to detect airway bacteria in children with cystic fibrosis and bronchiectasis who don't have a cough.

Michael Doumit (1, 2), Ayesha Delaney (1), Brendan McMullan (1, 3), Bernadette Prentice (1, 3)

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3.UNSW

Background: Children with cystic fibrosis (CF) and bronchiectasis often have difficulty expectorating sputum. Less invasive methods such as oropharyngeal (OP) swabs and cough swabs (CS) are commonly used alternatives, but their diagnostic yield and feasibility relative to induced sputum (IS) remain uncertain in non-expectorating children.

Methods: Children provided paired IS, OPS and CS. Diagnostic accuracy of OPS and CS compared to IS was calculated. Feasibility was assessed using collection time and distress ratings. Associations between cough quality (wet/dry), sample appearance (sputum/saliva) and pathogen detection were examined.

Results: Seventy-four participants (mean age 12, range 4-18yrs) provided 102 complete sample sets. IS, OPS and CS were pathogen positive in 39%, 40% and 9% of samples respectively. OPS had superior diagnostic accuracy compared to CS. Sensitivity for *Pseudomonas aeruginosa* detection was 100% (95%CI 51-100) for OPS and 0% (95%CI 0-49%) for CS. For *Staphylococcus aureus*, sensitivity for OPS was 57% (95%CI 39-73) and 18% (95%CI 8-36) for CS. Samples from children with dry versus wet cough were pathogen positive in 53% and 54% of cases respectively. Samples which appeared to contain sputum and samples that were salivary in appearance were pathogen positive in 42% and 67% cases respectively. All sampling methods were acceptable with low levels of distress, however induced sputum was most time/resource consuming.

Conclusion: OPS showed the closest agreement with IS and CS showed low pathogen detection. Neither cough quality nor sample appearance predicted pathogen yield, indicating a dry cough on presentation or a sample of salivary appearance should not preclude induced sputum being collected and analysed.

Applicant: Tamarah Katz
Supervisor: Professor Keith C.Y. Ooi

Consensus-based guidance for the nutritional management of children with cystic fibrosis on Elexacaftor/Tezacaftor/Ivacaftor.

Tamarah Katz (1,2)*, Josie van Dorst (1), Bernadette Prentice (1,3), Christine L. Chan (4), Dimitri Declercq (5), Tanja Gonska (6), Jodi Grunert (7), Daina Kalnins (8), Christina N. Katsagoni (9), Amanda Leonard (10), Catherine M. McDonald (11), Paul McNally (12), Monika Mielus (13), Anne Munck (14), Lutz Naehrlich (15), Elizabeth Owen (16), Chris Smith (17), Sarah Jane Schwarzenberg (18), Vito Terlizzi (19), Michael Wilschanski (20), Chee Y. Ooi (1,21)

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15. Department of Pediatrics, Justus Liebig-University Giessen, Germany
16. Department of Nutrition, Great Ormond Street Hospital for Children, London, UK
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18. Pediatric Gastroenterology, Hepatology and Nutrition, MHealth Fairview Masonic Children's Hospital, Minneapolis, MN, USA
19. Meyer Children's Hospital IRCCS, Department of Paediatric Medicine, Cystic Fibrosis Regional Reference Center, Florence, Italy
20. Department of Gastroenterology, Hadassah, Hebrew University Hospital, Jerusalem, Israel
21. Department of Gastroenterology, Sydney Children's Hospital Network, Randwick, Australia

Background: The introduction of CFTR modulators such as elexacaftor/tezacaftor/ivacaftor (ETI) has significantly altered the nutritional trajectory of children with cystic fibrosis (cwCF). While most eligible children in high resource countries have commenced ETI, the rollout has outpaced the development of nutritional guidance. This study aimed to: (1) systematically review the literature on ETI and nutrition (2) develop expert consensus based statements and (3) highlight existing research gaps and priorities.

Methods: A systematic review and guideline development process was registered on PROSPERO (ID: CRD42024587618). An expert panel of 22 professionals, including dietitians, gastroenterologists, respirologists, endocrinologists, and a parent representative was convened with attention to global representation. Research questions were developed using the Population, Intervention, Comparison, Outcome (PICO) framework. A comprehensive literature search was conducted across Medline, Embase, CINAHL, and Cochrane (January 2010 to April 2025). Studies were independently screened, assessed for quality using Scottish Intercollegiate Guidelines Network (SIGN) criteria, and extracted into evidence tables. Draft statements were developed and refined through iterative feedback and online discussion. Final consensus was achieved using realtime Delphi, with $\geq 80\%$ agreement required for endorsement. Reporting followed Accurate Consensus Reporting Document (ACCORD) guidelines.

Results: 67 consensus-based statements were developed. The top research priorities were identified based on the greatest proportion of “strongly agree” responses.

Conclusion: ETI has altered nutritional requirements in cwCF, yet evidence remains limited. This study presents the first consensus-based guidance for the nutritional care of cwCF receiving ETI, providing interim, expert informed recommendations and highlighting research priorities, particularly the need to re-evaluate traditional BMI targets.

Applicant: Mary Mulcahy
Supervisor: Karen Tuqiri

Hospital-Wide Implementation of iPAKT: Translating Person-Centred Care Measurement into Sustainable Practice Improvement.

Mary Mulcahy, Nurse Educator – Person Centred Care Karen Tuqiri, Director of Nursing
Professor Val Wilson

Prince of Wales Hospital

Background: Person-centred care is a strategic priority for healthcare organisations; however, measuring care from the consumer perspective remains challenging. The iPAKT App was developed to measure validated Person-Centred Nursing and Midwifery Key Performance Indicators (KPIs). Aim: To evaluate the feasibility, implementation and organisational outcomes of the iPAKT program.

Methods: A mixed-methods implementation study was conducted using the iPAKT App. Data collection included patient surveys and stories, structured observations and document reviews measuring eight person-centred KPIs. Implementation expanded from two pilot units to 29 clinical units across inpatient, day centre, community and virtual care settings. Focus groups with iPAKT leads explored implementation experiences, enablers, challenges and perceived impact. Quantitative and qualitative data were analysed using the App's integrated reporting system.

Results: Over 18 months, 580 patient surveys, 87 patient and carer stories, 87 structured observations (2,610 minutes) and 290 document reviews were collected. Implementation demonstrated high feasibility and strong performance across all eight KPIs. Results showed high levels of patient safety (89.5%), respect for patient preferences (86.7%), and confidence in nurses' knowledge and skills (84.1%). Five themes emerged: amplifying the patient voice, strengthening person-centred nursing practice, driving quality improvement through meaningful data, building nursing leadership capability and creating sustainable practice change.

Conclusion: Findings informed local action plans, increased use of patient communication boards and strengthened person-centred discussions during handover and safety huddles. The iPAKT App provided a practical, scalable and sustainable nursing-sensitive measurement system that strengthened nursing leadership, embedded consumer feedback into governance and quality processes, and supported continuous person-centred improvement across the organisation.

Applicant: Rachel Spillane
Supervisor: Dr Claire Boswell-Ruys

Seated Balance and Abdominal Functional Electrical Stimulation in People with Chronic Spinal Cord Injury (SCI).

R. Spillane (1), J. Butler (2), A. Palermo (1, 2, 3) and C. Boswell-Ruys (1, 2, 4)

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3. TIRR Memorial Hermann, Houston, Texas, US.
4. Prince of Wales Hospital, Randwick, Sydney, NSW, Australia

Background: Trunk control is frequently impaired after spinal cord injury (SCI), compromising seated balance and increasing falls risk. Abdominal functional electrical stimulation (AFES) may enhance trunk stability by activating the abdominal muscles, but the proportion of people with SCI who benefit is unclear. We hypothesised trunk control scores would be greater with the application of motorthreshold AFES than sub-motor-threshold AFES.

Methods: Thirty-two participants with chronic SCI completed a randomised crossover trial comparing motor-threshold and sub-motor-threshold AFES conditions, delivered via a Chattanooga stimulator, during trunk assessments. Trunk function was assessed using the Function In Sitting Test for SCI (FIST-SCI), and seated balance using the maximum balance range test (MBRT). FIST-SCI and MBRT scores were non-normally distributed (Shapiro-Wilk, $p=0.007$); within-participant differences were analysed using Wilcoxon signed-rank tests.

Results: There was no significant difference in the FIST-SCI between conditions ($W=171.5$, $p=0.919$). Three participants (9.4%) had a score at least 4-points greater in the motorthreshold than the sub-motor-threshold condition, reaching the FIST-SCI minimal detectable change ($MDC \geq 4$); while four participants (12.5%) scored at least 4-points greater in the sub-motorthreshold than the motor-threshold condition. There was no significant difference in MBRT between the conditions for 15 participants with paired data ($W=54.0$, $p=0.762$).

Conclusion: These findings suggest considerable individual variability in trunk function response to AFES, with no difference between motor-threshold and sub-motor-threshold conditions overall. Only a small subgroup reached the FIST-SCI MDC compared to the other condition. Future work should identify characteristics predicting individual response to motor-threshold versus submotor-threshold AFES, to better target this intervention.



Applicant: Chelsea Valentin
Supervisor: Dr Christina Signorelli

Occupational Therapy, Sydney Children's Hospital Randwick; Behavioural Sciences Unit, School of Clinical Medicine, UNSW Sydney

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Increasing survival rates for children diagnosed with cancer have resulted in the need for more holistic models of care during treatment, including occupational therapy (OT) services (1). OT is already being delivered in paediatric oncology to promote children's participation in everyday tasks and minimise the adverse developmental impacts of cancer (2). However, the lack of sufficiently developed evidence-based practice guidelines means that many children miss out on essential supportive care, exacerbating poor health related and functional outcomes (3). The purpose of this study was to examine paediatric oncology OT practices across Australia and New Zealand to identify variations in practice and research priorities.

Our multidisciplinary research group developed a 25question binational e-survey audit and disseminated it online, to OT departments and via professional OT networks across Australia and New Zealand.

Results from 20 respondents indicated some differences in frequency and types of assessments and interventions utilised at various stages of treatment. Respondents described a belief that early and proactive OT referrals are warranted to appropriately provide comprehensive cancer care. Respondents identified barriers to utilising OT in paediatric oncology included lack of funding, health structures and insufficient guidelines. All respondents called for improved learning opportunities and a consistent evidence-based OT approach to guide clinical practice. This study highlights variations and key challenges within this field, and opportunities to improve clinical practice to enable holistic care during and post treatment. Further research is critical to build OT evidence-based guidelines to standardise care and optimise functional outcomes for children affected by cancer.



Applicant: Karen Tuqiri
Supervisor: Dr. Valarie Wislon

Understanding the Relationship Between Person-Centred Practice and Patient Safety in Acute Care: A Multiple Case Study

Karen Tuqiri¹, Rebekkah Middleton², Valerie Wilson^{2,5}, Tanya McCance^{2,3}, Kelly MarriottStatham^{2,4}
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Background: Patient safety remains a global healthcare priority, yet preventable harm continues despite substantial investment in quality and safety initiatives. Traditional approaches have focused predominantly on systems, measurement, and compliance, while person-centred practice has been associated with improved patient and workforce outcomes. However, the relationship between person-centred practice and patient safety remains poorly understood. Aim: To explore and explain the relationship between person-centred practice and patient safety within acute care and identify the mechanisms through which safety is enacted in practice.

Methods: An explanatory multiple case study design informed by critical realism was undertaken across three clinical units in a large metropolitan tertiary hospital in New South Wales, Australia. Data collection included interviews, focus groups, observations of practice, and analysis of organisational data, including quality and safety metrics, workforce indicators, and staff and consumer experience data. Within-case analysis and cross-case synthesis were undertaken to identify patterns and underlying mechanisms. The Person-centred Practice Framework [1] informed interpretation of the findings.

Results: Patient safety was enacted through relational and context-dependent processes rather than technical systems alone. Knowing the patient as a person enabled the development of shared understanding of individual needs, risks, and care priorities. Communication, collaboration, and collective sense-making supported timely recognition of risk and coordinated responses to care. Leadership, culture, and facilitation influenced how these processes were enacted across settings.

Conclusions: Person-centred practice functions as a key mechanism through which patient safety is achieved. Findings indicate that safety is co-produced through interactions between patients, families, staff, teams, and organisational systems. A conceptual model of person-centred patient safety was developed to advance understanding of how safe care is enacted within complex healthcare environments. Reference [1] McCormack B, McCance T. Person-Centred Practice in Nursing and Health Care: Theory and Practice. 3rd ed. Oxford: Wiley Blackwell; 2021.

Applicant: Kulvara Lapanan
Supervisor: Dr. Stephen Lord

Thinking on Their Feet: Cognitive-Motor Stepping Is Slower After Stroke

K. Lapanan, J.C. Menant and S.R. Lord. Neuroscience Research Australia.

Balance and mobility impairments are common following stroke and include reduced walking speed (Moore et al., 2022), increased gait asymmetry (Chen et al., 2005), and reduced weight-bearing on the affected side (Patterson et al., 2008). Stroke can also impair executive functions important for safe mobility, including processing speed, selective attention, and inhibitory control (PlummerD'Amato et al., 2008; Yogev-Seligmann et al., 2008). These cognitive-motor impairments may compromise the ability to navigate complex environments, particularly when rapid stepping responses are required. This study compared cognitive-motor stepping performance between people with chronic stroke and healthy older adults. Fifty stroke survivors (aged 64 ± 10 years; 27 women) and 50 healthy older adults (aged 76 ± 12 years; 35 women) completed the Choice Stepping Reaction Time test (CSRT) and the congruent and incongruent conditions of the Stroop Stepping Test (SST-con and SST-incon). Compared with healthy older adults, stroke survivors had significantly slower response times across all three stepping tasks ($P < 0.001$) and slower movement times on the CSRT ($P < 0.01$). However, stepping errors did not differ significantly between groups on the CSRT, SST-con, or SST-incon ($P = 0.39$, $P = 0.40$, and $P = 0.05$, respectively). Stroke survivors also reported more recent falls ($P = 0.0003$) and greater fear of falling ($P < 0.0001$), and had poorer functional mobility, indicated by slower Timed Up and Go performance ($P < 0.0001$). People with chronic stroke preserved stepping accuracy but demonstrated substantially slower cognitive-motor responses, alongside poorer functional mobility, greater fear of falling, and more recent falls. The contrast between slower response speed and preserved accuracy suggests that response time may capture an important aspect of post-stroke mobility not identified by accuracy alone. These findings highlight cognitive-motor stepping as a potentially important rehabilitation target and support further investigation of interventions combining cognitive challenge with rapid, adaptive stepping.

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Division:
**Basic
Science**



Applicant: Erin Coll
Supervisor: Professor Paul Ekert

A conserved tumour–vascular axis organises T-cell localisation and immune-regulatory signalling in paediatric rhabdoid tumours.

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Background: Rhabdoid tumours (RTs) are aggressive paediatric malignancies driven by SMARCB1 loss. Despite low mutation burden many are immunologically active (1), yet checkpoint blockade is largely ineffective. We hypothesised that anti-tumour immunity is constrained by tissue architecture and spatially restricted signalling rather than by immune cell abundance.

Methods: We profiled 173 samples from 34 patients, most contributing multiple samples across imaging mass cytometry, multiplex immunofluorescence and Xenium spatial transcriptomics. Xenium provided single-cell annotation and pathway level signalling analysis, with neighbourhood structure recovered independently by antibody and transcript-based platforms.

Results: Samples were cold (n=46), excluded (n=82) or inflamed (n=44). IPASS, a bulk RNA sequencing immune signature (2), correlated with T-cell abundance ($R=0.32$, $P=0.024$) but not spatial immune infiltration ($R=0.12$, $P=0.39$). Neighbourhoods formed a conserved tumour–vascular axis, from tumour core through HLA-positive tumour and fibrovascular interface niches to myeloid and vascular compartments. HLA-positive tumour cells occupied tumour–stromal interfaces, expressing antigen-presentation programmes. T-cell programmes shifted from exhaustion near tumour, through effector cytotoxicity at the interface, to chemokine-receptor and naive-memory states near vessels. In excluded tumours, T cells accumulated in myeloid inflammatory and fibrovascular interface niches (29.6%) versus 0.3% in tumour cores. Excluded fibrovascular interfaces expressed *TGFB1*, *CXCL12*, matrix genes and *PDGFRB*, and myeloid niches *CXCL9-11* and *HAVCR2* (TIM-3); fibroblasts and myeloid cells contacting T cells adopted IFN-responsive, chemokine- and IDO1-high states.

Conclusion: Immune exclusion in RTs is structural: competent T cells are held at fibroblast- and myeloid-rich interfaces, nominating LIF (3), *PDGFRB* and TIM-3 as spatially defined targets.

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Applicant: Hannah Hartley
Supervisor: Dr Emmy Dolman

Exploiting DNA damage response–epigenetic interplay: ATR–LSD1 combination targeting in high-risk neuroblastoma.

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Background: Disrupting cancer cell dependency on the replication stress (RS) response by ATR inhibition (ATRi) is a promising strategy for children with high-risk neuroblastoma, particularly aggressive MYCN-amplified disease (1, 2). However, combination therapies are needed to overcome ATRi resistance. Epigenetic regulation is essential for the DNA damage response (DDR), providing a rationale for ATRi combination treatment.

Hypothesis: ATRi combined with epigenetic targeting will exacerbate lethal DNA damage, causing cell death by mitotic catastrophe.

Methods: Whole-genome and RNA-sequencing data from patients (n=138) enrolled in the Australian ZERO Childhood Cancer program (3, 4) were analysed to define DDR and epigenetic landscapes of neuroblastoma. Gene Set Enrichment Analysis (GSEA) identified pathway regulation, unsupervised clustering defined transcriptional subgroups. ATRi ceralasertib was evaluated in combination with LSD1 inhibitor seclidemstat in classical and patient-derived neuroblastoma cell lines, then in transgenic Th-MYCN alginate-based tissue encapsulation (ALTEN) models ex vivo. Cell cycle resolved DNA damage was characterised at single cell resolution using high-content quantitative image-based cytometry (QIBC).

Results: Transcriptomic profiling identified three tumour subgroups with DDR-high/epigenetic-low, epigenetic-high/DDR-low, or intermediate pathway enrichment; the former subgroup was significantly associated with samples at relapse, MYCN amplification, and chromosome 11q loss ($p<0.05$). ATR–LSD1 inhibition induced potent cell killing in MYCN-amplified classical and patient-derived cell lines. γ H2AX expression and micronuclei formation increased across cell-cycle populations compared with either agent alone. In Th-MYCN ALTENs, the combination significantly reduced metabolic activity ex vivo across 6 days ($p<0.001$).

Conclusion: Combined ATR–LSD1 inhibition demonstrates efficacy ex vivo and induces DNA damage across the cell cycle, supporting further mechanistic investigation in neuroblastoma.

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Applicant: Sahar Mafi
Supervisor: Dr Jamie Fletcher

Targeting MYCN-associated vulnerabilities through LSM4 disruption and dual BCL2/AURKA inhibition.

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Background: Neuroblastoma is the most common extracranial solid tumour in children and causes ~15% of childhood cancer-related deaths(1). Outcomes remain poor for MYCN-amplified neuroblastoma (MNA-NB), highlighting the need to identify MYCN-associated dependencies (2). Using RNAseq data, we found Like-Sm protein 4 (LSM4) is highly expressed in MNA-NB. Preclinical PDX testing identified venetoclax–alisertib as an effective combination for MNA-NB. Here, we investigated LSM4 as an oncogenic driver and therapeutic target and determinants of response to venetoclax–alisertib.

Methods: LSM4 function was examined using siRNA knockdown and doxycycline-inducible CRISPR–Cas9 knockout. Effects on proliferation, clonogenicity, apoptosis and in vivo tumour growth were assessed. Venetoclax–alisertib efficacy was evaluated in PDX models using a clinical trial-like (n=1) design. A genome-wide CRISPR screen was performed to identify determinants of sensitivity and resistance.

Results: LSM4 expression correlated with MYCN, was higher in MYCN-amplified tumours, and was associated with poorer event-free and overall survival, independent of clinical prognostic factors. LSM4 depletion reduced N-Myc expression, cell proliferation and clonogenic capacity, with minimal effect on apoptosis. LSM4 targeting prolonged median survival from 15 to 37.5 days in SK-N-BE(2)C xenografts and from 21 to 66.5 days in Kelly xenografts. Venetoclax–alisertib produced objective responses in 22 PDXs, with greatest efficacy in MYCN-amplified models. The genome-wide CRISPR screen has been completed, with analysis underway.

Conclusion: These findings identify LSM4 as a MYCN-associated functional dependency and therapeutic target in neuroblastoma. Dual BCL2/AURKA inhibition with venetoclax–alisertib is effective in MNA-NB, and CRISPR analysis will identify response determinants, biomarkers and therapeutic targets.

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Applicant: Zahra Sheybani
Supervisor: Associate Professor Charles De Bock

Genome-wide CRISPR/Cas9 screening reveals synergy between targeting of the Fanconianaemia pathway and ACHM-025 in TCF3::HLF B-ALL.

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Background: ACHM-025 is a novel AKR1C3-activated prodrug that generates a potent DNA-crosslinking agent. We previously demonstrated profound and curative efficacy in T-cell acute lymphoblastic leukaemia patient-derived xenograft (PDX) models, directly correlated with AKR1C3 expression (1). We subsequently identified similarly high AKR1C3 expression in TCF3::HLF B-cell acute lymphoblastic leukaemia (B-ALL), a high-risk, chemoresistant subtype. We therefore aimed to determine ACHM-025 sensitivity in TCF3::HLF B-ALL PDX models and identify genes conferring ACHM-025 sensitivity or resistance in this subtype.

Methods: ACHM-025 efficacy was assessed in 14 TCF3::HLF PDX models using single-mouse trials. Genome-wide CRISPR/Cas9 screening was performed in ACHM-025-treated TCF3::HLF UoC-B1 cells. Candidate hits were individually validated, and the prioritised target was advanced to combination testing.

Results: ACHM-025 significantly prolonged event-free survival in 10 PDX models (treatment/control range: 2.68–6.30). CRISPR screening identified significant enrichment of the Fanconi anaemia/interstrand crosslink repair pathway as a major determinant of resistance, highlighting USP1 as a therapeutic vulnerability. USP1-mediated deubiquitination regulates Fanconi anaemia and translesion synthesis, supporting efficient DNA-crosslink repair (2). Combining ACHM-025 with the USP1 inhibitor KSQ-4279 produced synergistic activity in UoC-B1 cells, accompanied by increased DNA damage (gamma-H2AX) and apoptosis (cleaved PARP and cleaved caspase-3). RNA-seq profiles from 14 PDX models and two cell lines were integrated with ACHM-025 response data to identify candidate biomarkers that may support patient stratification.

Conclusion: ACHM-025 demonstrates strong preclinical activity against TCF3::HLF B-ALL, while USP1 inhibition represents a promising strategy to enhance its activity. Ongoing studies are evaluating this combination in vivo and investigating transcriptomic determinants of response heterogeneity.

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Applicant: Lara Knight
Supervisor: Professor Michelle Haber

Optimising Polyamine Depletion Therapy for Clinical Translation in the Treatment of Childhood Neuroblastoma.

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Background: High-risk neuroblastoma has survival rates around only 50%. This tumour relies on high polyamine levels for continued proliferation and immunosuppression, and combination of the polyamine synthesis inhibitor DFMO and polyamine transport inhibitor AMXT1501 limits tumour progression in neuroblastoma mouse models¹. A phase I clinical trial of DFMO/AMXT1501 in adults with advanced cancers (NCT03536728) demonstrated tolerability², but in a recent clinical trial testing higher doses of intravenously-administered DFMO (NCT05500508), several patients had cardiac-related adverse events. To further advance polyamine depletion therapy into paediatric clinical trials, we aim to understand and mitigate potential cardiotoxicity associated with DFMO/AMXT1501 treatment *in vivo*.

Methods: Mice (n=4/group) were treated for up to 6 weeks with DFMO (1.5% in drinking water plus 600mg/kg or 1000mg/kg intraperitoneally) and escalating subcutaneous doses of AMXT1501 up to 2.5mg/kg. Cardiac function was monitored by weekly echocardiograms, heart histology, and longitudinal measurement of plasma biomarkers including troponins and NT-ProBNP.

Results: Treatment with high-dose DFMO alone resulted in plasma levels comparable to patients and was well tolerated in combination with AMXT1501 up to 1.25mg/kg. However, escalation to 2.5mg/kg AMXT1501 combined with DFMO resulted in severe, acute toxicity. Contrary to expectations, neither echocardiograms nor histology revealed any observable cardiac abnormalities. However, haematological analysis revealed markedly decreased platelets and white blood cells, suggesting a potential avenue of haematological toxicity. Interestingly, plasma NT-ProBNP was elevated, consistent with cardiac stress due to reduced blood pressure.

Conclusion: Our current data suggests potential haematological toxicity of DFMO/AMXT1501 treatment in mice, warranting further investigations into bone marrow and white blood cells following treatment.

POSTER

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Applicant: Jessica Perry
Supervisor: Associate Professor Kelly Clemens

Prenatal Sodium Butyrate Minimizes Long-term Neural Dysregulation Following Prenatal Methadone Exposure.

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Background: Opioid use during pregnancy has increased 333% over the past two decades (Haight et al., 2018). This is detrimental as opioids readily cross the placenta, and disrupt molecular pathways critical for neurodevelopment (Sarah K Griffiths, 2015). Whilst maintenance therapies, including methadone, improve on birth outcomes of children prenatally exposed to illicit opioids, long-term cognitive and behavioural deficits persist (Andersen et al., 2020; Aslaksen et al., 2024; Gill et al., 2003; Gupta et al., 2012; Hamilton et al., 2010; Hutchings, 1982; Konijnenberg & Melinder, 2015; McGlone et al., 2014; Nygaard et al., 2015; Nygaard et al., 2017; Rosen & Johnson, 1985; Whitham et al., 2010). However, the molecular mechanisms underpinning these impacts are poorly understood. We aimed to identify neural dysregulation induced by prenatal methadone exposure (PME) and assess whether sodium butyrate (NaB) mitigated these changes in adult offspring.

Methods: Prefrontal cortex was collected from three male and female sub-adult rat offspring each from four treatment groups. Three groups' mothers had received methadone during pregnancy, with two methadone groups receiving pre- or postnatal NaB. mRNA sequencing was analyzed using a standard bioinformatics pipeline, with subsequent differential gene expression (DeSeq2) and Gene Ontology enrichment analyses.

Results: PME and NaB treatment induced sex-specific effects. PME males had 1359 DEGs versus control, characterized by proteostasis upregulation and widespread neuronal downregulation. Smaller signatures included immune and inflammatory upregulation and downregulation of DNA and histone methyltransferases. Pre- and postnatal NaB treatment reduced DEG numbers to 20 and 30 versus control respectively, with few associated pathways.

Conclusion: Consequently, PME induced persistent neural dysregulation in adult males, supporting a molecular basis for reported long-term cognitive and behavioural deficits and sex-biases in effects following PME. To our knowledge, this is the first evidence suggesting this may be modulated by modifications to histones. Early-life NaB demonstrated therapeutic potential by almost completely minimizing dysregulation, with flexible treatment timing aiding translation.

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POSTER

Applicant: Benjamin Wu
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Age-mismatched cumulus-oocyte complexes to restore oocyte quality and fertility.

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Background: Age-related female infertility is driven by oocyte quality decline. Oocytes are surrounded by cumulus cells (CCs), together forming the cumulus-oocyte complex (COC). CCs facilitate oocyte development by transporting nutrients via transzonal projections (TZPs) (1). Whether CC ageing influences oocyte ageing and quality is poorly understood. We aim to reaggregate young CCs with aged oocytes to form an age-mismatched COC, to test if soma-germline communication can be reestablished.

Methods: Young cumulus cells or oocytes from young (4-8 weeks old) or old (52-58 weeks) hyperstimulated/unstimulated outbred Swisstac mice were subjected to a reaggregation protocol with pre-in vitro maturation (pre-IVM) and IVM culture for 24-48 hours. TZPs were quantified via immunocytochemistry to evaluate re-establishment of CC-oocyte communication.

Results: After generating reaggregated COCs using CCs plus denuded (DOs) or naked oocytes (NOs) of different ages (young CCs/old NOs, old CCs/young NOs, young CCs/young NOs), TZP density was partly restored vs respective young or old non-reaggregated NO controls (all $p < 0.001$). The ability to prevent precocious maturation, important for oocyte development during pre-IVM culture, trended higher in young CC/old NO reaggregations versus old non-reaggregated NOs ($p = 0.0847$), while in age-matched young CC/young NO reaggregations there was no difference versus young nonreaggregated oocytes. Using an in vitro meiotic ageing model, morphology of meiotic spindles improved for age-matched young CC/DO ($p < 0.01$) and CC/NO ($p < 0.05$) reaggregations, and chromosomal alignment for young CC/DO ($p < 0.05$) but not CC/NO ($p = 0.317$) reaggregations.

Conclusion: Overall, reaggregation partly restored multiple aspects of oocyte-CC communication, providing proof of concept for investigating if reaggregation with young CCs can improve old oocyte quality.

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POSTER

Applicant: Anthony Zhou
Supervisor: Associate Professor Fatima Valdes Mora

Modelling the immunosuppressive tumour immune microenvironment of neuroblastoma in an intact ex vivo platform.

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Background: Anti-GD2 therapy has limited success in neuroblastoma. Improving efficacy requires deeper understanding of the tumour immune microenvironment (TIME) and developing better physiologically relevant models to study the underlying causes of immunotherapy resistance and explore novel immunotherapeutic agents. Aims: 1) Characterise the neuroblastoma TIME in immunocompetent mouse models and patients. 2) Determine whether ALTEN (alginate-based tissue engineering) can model neuroblastoma while preserving this TIME. 3) Test current and novel immunotherapeutics in ALTEN as an ex vivo platform.

POSTER

Methods: Published MYCN-amplified mouse (n=6) and human (n=23) single-cell RNA sequencing datasets were analysed in Seurat. Mouse and patient tumour pieces were encapsulated in alginate, Alamar blue assessed viability, QuPath to quantify immune infiltration from immunohistochemistry and tested 5-azacytidine, PROTACs, AURKA inhibitors and anti-GD2 at clinically achievable doses.

Results: Single cell transcriptomics identified a conserved, heterogeneous immunosuppressive myeloid compartment: angiogenic and immune checkpoint-enriched tumour-associated macrophages, polymorphonuclear myeloid-derived suppressor cells and tumour-associated neutrophils, with minimal T and B cell infiltration, confirming an immune-cold TIME. ALTENs preserved this context, maintained tumour viability and retained CD45+ immune cells in situ, single-cell characterisation of these myeloid populations is ongoing. ALTENs reproduced the anti-GD2 responses expected in vivo and in patients, while the novel agents AURKA PROTACs and 5-azacytidine showed the most promising therapeutic activity.

Conclusion: By maintaining viable tumour tissue with immune cells in situ, ALTEN offers an immune-competent platform for interrogating immunomodulatory agents. Future work will apply single-nucleus RNA sequencing and spatial transcriptomics to characterise immune and tumour responses in ALTENs to current and novel immunotherapies.



Applicant: Jennifer Chen
Supervisor: Dr Manu Singh

FUNCTIONAL SCREENING OF CANDIDATE ANTIGENS THAT MAY BE DRIVING THE EXPANSION OF CD8+ T-CELL CLONES WITH LYMPHOMA DRIVER MUTATIONS IN TYPE I REFRACTORY CELIAC DISEASE

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Decoding the antigen specificities of autoreactive T-cells remains a major bottleneck in understanding the drivers of autoimmune disease. Celiac disease is treated by removing its known trigger antigen, gluten, from the diet. Approximately 1% of individuals non-responsive to a glutenfree diet are diagnosed with type I refractory celiac disease (RCD-I). We recently identified expanded T-cell clones carrying somatic mutations in RCD-I duodenal biopsies such as expanded CD8+ T-cell clones with STAT3 gain-of-function mutations (1). While these findings implicate these mutated Tcell clones in disease pathogenesis, their functional relevance is unclear since the antigen specificity of their T-cell receptors (TCRs) is unknown.

We developed a modular antigen discovery platform informed by neoantigen screening to identify T-cell reactivity to candidate antigens. Our methodology leverages engineered HLA-matched antigenpresenting cells and tiled minigene libraries for systematic interrogation of candidate antigens by in vitro functional assays. Proof-of-concept experiments established the platform's ability to investigate antigens presented by HLA class I and II molecules. Overnight co-culture with gliadin minigeneexpressing EBV-immortalised human B-cell lines activated Jurkat-76 cells expressing a glutenreactive DQ2.5-restricted TCR. Compatibility with HLA class I restricted TCRs was demonstrated by the activation of CD8+ Jurkat-76 cells expressing the 1G4 TCR after co-culture with NY-ESO-1 minigene expressing EBV immortalised human B-cell lines. NY-ESO-1 is the cancer-testis antigen recognised by the 1G4 TCR. Establishing sensitive methods for investigating TCR specificity could reveal previously undescribed antigens recognised by T cells that may contribute to RCD-I pathogenesis and inform new therapeutic strategies to improve clinical outcomes.

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Applicant: Kate Murray
Supervisor: Dr Marion Mateos

Developing Combination Treatment Approaches in High-Risk Childhood Medulloblastoma

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Background: MYC-amplified Group 3 medulloblastoma is a high-risk childhood brain tumour with poor survival outcomes, below 50%, and are incurable at relapse. As recurrent oncogenic drivers are rarely directly targetable, effective treatment is likely to require rational combination strategies. The DNA damage response (DDR) and PI3K/AKT/mTOR pathways are recurrently dysregulated in medulloblastoma and have clinically developed inhibitors, however none are currently in use for medulloblastoma patients.

Aims: To evaluate clinically-developed DDR and PI3K/mTOR inhibitors and conventional cytotoxic agents in MYC-amplified Group 3 medulloblastoma and prioritise combinations for in vivo translation.

Methods: Seventy-two-hour cytotoxicity assays were performed across five MYC amplified Group 3 medulloblastoma cell lines and primary cultures. Seven agents, including paxalisib, AZD9574 and gemcitabine, were profiled as single agents within a broader combination panel. Based on published evidence and ongoing clinical trial evaluation of related combinations, the analysis prioritized paxalisib combined with gemcitabine or AZD9574 as well as triple combinations of paxalisib or AZD9574 with temozolomide and SN-38.

Results: Chemotherapy agents gemcitabine and SN-38 demonstrated nanomolar single agent potency, whereas the dual PI3K/AKT/mTOR inhibitor paxalisib, ATR inhibitors ceralasertib and ART0380 and the selective-PARP1 inhibitor AZD9574 exhibited activity in the micromolar range. Paxalisib combined with gemcitabine or AZD9574 produced greater cytotoxicity than the corresponding single agents. In pilot experiments, paxalisib/temozolomide/SN-38 and AZD9574/temozolomide/SN-38 triple combinations demonstrated greater sensitivity than the corresponding single- and double-agent treatments.

Conclusion: These findings identify paxalisib- and AZD9574-based combinations as candidates for further preclinical evaluation in MYC-amplified Group 3 medulloblastoma. CRISPR-based screening will complement these studies by identifying tumour dependencies and therapeutic vulnerabilities and refine combination selection prior to in vivo testing.

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Applicant: Jasmine Jin
Supervisor: Dr Klaartje Somers

CBL0137 reduces immunosuppression in the tumour microenvironment of the Th-MYCN model of high-risk neuroblastoma

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Tumour-induced immunosuppressive mechanisms in the tumour microenvironment limit the efficacy of immunotherapies in solid childhood cancers. We recently established the anticancer efficacy of the novel drug, CBL0137, in poor outcome childhood cancer models, findings that led to its testing in the first clinical trial in children with cancer. We also found that, in addition to directly killing cancer cells, CBL0137 induces genome-wide nucleosome disassembly, activating interferon signalling within tumour cells and the tumour microenvironment.

As suppression of interferon signalling is a well-established mechanism of tumour immune evasion and immunotherapy resistance, we hypothesised that CBL0137 can rewire the immunosuppressive tumour microenvironment and potentiate immunotherapies. This study aimed to characterise CBL0137-induced changes in the tumour microenvironment of the Th-MYCN mouse model of high-risk neuroblastoma. The effects of CBL0137 were assessed in tumour samples obtained from homozygous Th-MYCN mice by comprehensively profiling immune cell populations by OPAL, a multiplex immunohistochemistry platform. CBL0137 treatment induced a significant increase in CD45⁺ immune cells, accompanied by trends in increased levels of plasmacytoid dendritic cells, inflammatory monocytes, and M1 macrophages. Notably, reductions in neutrophil and monocytic myeloid-derived suppressor cell (M-MDSC) populations were also observed, indicating a shift towards a less immunosuppressive tumour microenvironment.

Collectively, our findings suggest that CBL0137 reshapes the tumour immune microenvironment towards a less immunosuppressive state, paving the way for its use as an immunoadjuvant to enhance the efficacy of immunotherapies for neuroblastoma.



Applicant: Abigail Marcus
Supervisor: Associate Professor Kelly Clemens

Hope in Prevention: N-acetylcysteine Protects Against Long-Term Cognitive Impairments of Perinatal Methamphetamine Exposure

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Methamphetamine (MA) is the fastest-growing illicit drug in Australia, and its use during pregnancy is a growing concern (1). However, long-term impacts are poorly defined, and there are no established treatments (2). We hypothesised that N-acetylcysteine (NAC), an inexpensive and clinically available antioxidant, would prevent MA-induced deficits. Pregnant Long-Evans rats received MA (5 mg/kg/day) or saline via subcutaneous injections from gestational day 10 through to postnatal day 21, alongside NAC (1% w/v) or regular drinking water in bottles. Infant rats perinatally exposed to either MA or NAC showed reduced early weight gain, indicating that each compound independently affects early growth. In adulthood, MA-exposed rats showed reduced lever-pressing in a sign-tracking task, consistent with impaired reward processing, while NAC had no effect. MA-exposed adult rats also showed deficits in associative interference during latent inhibition, suggesting persistent impairments in cognitive control. Critically, adult rats exposed to both MA and NAC performed normally on this task, indicating that NAC can prevent long-lasting cognitive impairments, which may be driven by oxidative stress. These findings identify NAC as a promising candidate for preventing cognitive deficits after perinatal MA exposure. With MA use in pregnancy rising, an accessible and preventative treatment may help reduce long-term developmental harm to affected children and the associated burden on families and health services.

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Applicant: Isabel Zaide
Supervisor: Caitlin Cowan

Mental health difficulties often emerge during childhood and adolescence, highlighting the importance of identifying early developmental pathways that contribute to vulnerability and resilience. Increasing evidence suggests that the gut microbiome may be one such pathway. Through the microbiota–gut–brain axis, gut microorganisms can interact with the developing brain via immune, metabolic, neuroendocrine, and neural mechanisms. However, much of the existing research has focused on associations between the microbiome and established mental health disorders, providing limited insight into whether early-life microbiome variation contributes to the emergence of transdiagnostic characteristics that precede clinically significant mental health difficulties. My PhD will investigate whether the early-life gut microbiome is associated with, and may contribute causally to, developmental pathways of mental health risk and resilience. The research will focus on two transdiagnostic behavioural characteristics, social fear and irritability, which are observed across multiple forms of psychopathology and can emerge early in development. First, longitudinal human data from a large cohort of Australian children will be used to examine whether variation in the gut microbiome during early development is associated with developmental trajectories of social-emotional functioning and later mental health outcomes. Second, faecal microbiota transplantation will be used to experimentally investigate whether microbiota from children characterised by higher versus lower levels of mental health risk can influence fear- and irritability-related behaviours in rodents. This approach addresses a key limitation of human observational research by enabling causal investigation under controlled environmental conditions.

Division:
Clinical



Applicant: Syeda Mah-E-Muneer
Supervisor: Associate Professor Nusrat Homaira

From Infancy to Adolescence: High burden of Respiratory and Mental Health Hospitalisations Among Children with Bronchopulmonary Dysplasia in a Population-Based Cohort.

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Background: Bronchopulmonary dysplasia (BPD) is associated with long-term morbidity, but its impact on severe acute lower respiratory infection (ALRI) and mental health (MH) hospitalisations across childhood and adolescence remains unclear.

Methods: A population study using linked NSW health administrative datasets for 1,045,234 children born between 2005–2015 and followed until 2023. We evaluated ALRI and MH hospitalisation among preterm BPD children, preterm without BPD and term children. ALRI and MH were identified using ICD-10-AM codes.

Results: 1,832 (0.18%) were preterm with BPD and their ALRI hospitalisation incidence was highest during the first year of life, reaching 346.2, as compared to 89.3 and 39.0 per 1,000 person-years of no-BPD preterm and term children. Adjusted risk of ALRI hospitalisation compared to term was higher in BPD children (aHR 7.77, 95%CI 7.18–8.41) than no-BPD preterm (aHR 1.94, 1.89–1.99). By age 17 years, cumulative incidence of ALRI hospitalisation was 46.8% (95%CI 44.48–49.14), 14.1% (13.79–14.32) and 7.4% (7.31–7.41) in BPD preterm, no-BPD preterm and term children respectively.

In contrast, the median age at first MH hospitalisation was 5.0, 7.5 and 9.8 years among BPD preterm, no-BPD preterm and term children. First MH hospitalisation incidence peaked during adolescence, reaching 12.3, 5.5 and 4.4 per 1,000 person-years, respectively. Compared with term children, MH hospitalisation risk was higher among BPD preterm (aHR 2.45, 1.81–3.32) than noBPD preterm adolescents (1.37, 1.27–1.47).

Conclusion: Children with BPD experience a distinct life-course pattern of morbidity, with ALRI hospitalisations concentrated in infancy and MH hospitalisations peaking during adolescence. Long-term multidisciplinary follow-up are warranted.

Applicant: Kate Maston
Supervisor: Professor Aliza Werner-Seidler

RECIPROCAL RELATIONSHIPS BETWEEN DEPRESSION, SLEEP AND FAMILY INTERACTIONS ACROSS ADOLESCENCE: A FIVE-YEAR LONGITUDINAL STUDY.

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Background: Depression and poor sleep are prevalent in adolescence, associated with significant health burden, and commonly co-occur with family tension and conflict. However, little is known about how these three factors interact within the same individual over time. We examined within-person relationships between sleep quality, depression symptoms and family interactions throughout adolescence. We hypothesised that poorer sleep quality would be associated with higher depression symptoms at the between-person level. Given limited existing evidence, examination of withinperson associations between sleep, depression and family interactions was exploratory.

Methods: Data were drawn from N=6,388 Australian adolescents assessed annually at school between Years 8-12. Random-intercept cross-lagged panel models separated stable between-person differences from within-person change over time. Exploratory multigroup models examined patterns by gender.

Results: Consistent with our hypothesis, poorer sleep quality was strongly associated with higher depression symptoms between individuals ($r=.80$, $p<.001$). Within individuals, sleep quality and depression symptoms were bidirectionally associated across adolescence. Negative family interactions also showed consistent bidirectional relationships with sleep and depression, while associations involving positive family interactions were limited. Gender-specific patterns also emerged; sleep-depression associations were evident earlier in adolescence for girls and later for boys. Positive family interactions were more strongly associated with better sleep and lower depression in girls, whereas negative family interactions were more strongly associated with higher depression in boys.

Conclusion: Findings highlight the varied ways in which sleep, depression and family interactions interrelate across adolescence. Gender-specific differences may inform the focus and timing of prevention and early intervention efforts to address adolescent mental health.

Applicant: Dalia Metwally

Supervisor: Dr Lisa Ewans

Equity in rare disease genomic diagnosis: quantifying diagnostic disparity for priority populations and co-designing an equitable clinical pathway.

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Background: Rare diseases affect two million Australians and are predominantly monogenic, making genomic testing central (1,2). National policy recognises priority populations, including Aboriginal and Torres Strait Islander, culturally and linguistically diverse, socioeconomically disadvantaged and rural communities, as under-served (3), yet their diagnostic outcomes are unquantified. We hypothesised that priority populations achieve lower diagnostic yield, recognised anecdotally but never demonstrated.

Methods: In the first Australian study to quantify this, we audited 631 consecutive referrals to a tertiary paediatric clinical genetics service (January-June 2024), comparing attendance, investigation ordering, diagnostic yield and research enrolment by priority-population status, and thematically analysed two staff focus groups against the Consolidated Framework for Implementation Research (CFIR) (4).

Results: Priority populations (n=196, 31.1%) attended less (75.0% vs 84.8%, $p=0.006$). Investigation ordering was equitable (87.4% vs 88.6%, $p=0.720$), yet molecular diagnosis was halved (24.0% vs 49.1%, $p<0.0001$), falling to 20.0% for Aboriginal and Torres Strait Islander and 10.3% for socioeconomically disadvantaged patients. Research enrolment was uniformly low (~5%). Clinician focus groups described vulnerability recognised too late to arrange supports, and low genetic literacy and fear deterring research.

Conclusion: The hypothesis was confirmed, but not through unequal testing: equal effort did not produce equal outcomes. This equity paradox locates disparity downstream of the test, in genomic database representation and research access (5). These findings underpinned Diagnosis4All, an MRFF-funded program. The doctoral work extends this from characterising the inequity to co-designing, with communities and clinicians, equitable pathways from variant characterisation to participation in our undiagnosed disease program, integrating CFIR 2.0 with the equity-centred IM4Equity framework.

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Applicant: Emily Upton
Supervisor: Professor Jill Newby

A Pilot Trial of Brief Tailored Online Treatment for Rumination and Worry in Premenstrual Dysphoric Disorder.

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Background: Premenstrual Dysphoric Disorder (PMDD) affects up to 8% of menstruating individuals and involves severe cyclical mood disturbance. Accessible psychological interventions for PMDD are urgently needed. Repetitive Negative Thinking (RNT; rumination, worry) is implicated in PMDD severity and represents a novel treatment target.

Methods: This single-group pilot trial evaluated the feasibility, acceptability, and preliminary outcomes of a brief, clinician-supported online CBT intervention we developed targeting RNT in PMDD. N=37 Australian women with elevated premenstrual distress (91.9% [n=34] with probable PMDD) and elevated RNT received the 4-module program over 4-8 weeks. Assessments were conducted at baseline, post-treatment, and 5-week follow-up (one menstrual cycle post-treatment). Primary outcomes were PMDD symptom severity and impact (PSST). Secondary outcomes included RNT, rumination, worry, depression, suicidality, anxiety, distress, wellbeing, and functioning. Satisfaction and qualitative feedback were collected post-treatment.

Results: Linear mixed models showed significant, large improvements from baseline to posttreatment and follow-up in PMDD symptom severity and impact ($ps < .001$; $g = 1.18-1.81$), as well as RNT, rumination, worry, depression, anxiety, wellbeing, and functioning ($ps < .05$; $g = 0.52-1.82$). Satisfaction was high (93% mostly-very satisfied). Participants reported improved understanding of PMDD and gaining practical skills to manage RNT and premenstrual symptoms.

Conclusion: This pilot supports the preliminary feasibility, acceptability, and efficacy of a brief RNT-focused online CBT intervention for PMDD. Findings suggest targeting RNT may offer a scalable, accessible treatment approach for this population, and warrant evaluation in a larger randomised controlled trial. Ongoing research is underway to expand the program using participant feedback to address broader PMDD symptomatology.

Applicant: Temesgen Getaneh Molla

Supervisor: Professor Kei Lui

From Birth to Discharge: A Staged Prediction Approach for Death or Neurodevelopmental Impairment in Extremely Preterm Infants.

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Background: Survival among extremely preterm infants (EPIs) has improved, but neurodevelopmental impairment (NDI) remains common. Early identification of infants at increased risk is important. However, existing prediction models are not aligned with key clinical decision points.

Methods: This study developed and internally validated staged models to predict death or NDI at 2–3 years using routinely collected data. Methods: EPIs born at <28 weeks' gestation between 2010 and 2019 were included from the Australian and New Zealand Neonatal Network. Three multivariable logistic regression models were developed at predefined clinical timepoints (birth, after early severe morbidities, and discharge) to predict the composite outcome of death or NDI at 2–3 years of age. Model performance was assessed using discrimination, calibration, and the Brier score, with internal validation using bootstrap resampling.

Results: A total of 8,445 EPIs were included. Model discrimination was good with optimism-corrected area under the receiver operating characteristic curve (AUC) values of 0.741, 0.703, and 0.696 for Model 1, 2 and 3, respectively. Calibration was satisfactory across all time points, with intercepts close to zero (−0.001, −0.024, and −0.050) and slopes close to one (0.994, 0.982, and 0.967). Prediction accuracy improved, as reflected by decreasing Brier scores (0.183, 0.137, 0.124). For NDI-only prediction, discrimination was moderate but improved progressively as additional variables and neonatal morbidities were incorporated (AUCs 0.658, 0.684 and 0.698).

Conclusion: The prediction models demonstrated good calibration and acceptable discrimination. These models may support individualized risk assessment, and parental counselling, although external validation is needed before clinical application.

Applicant: Dr Rebecca Moses

Supervisor: Dr Antonia Shand

Misoprostol Inductions and Outcomes in pregnancy loss (the MISO study): A three-hospital retrospective cohort study.

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Background: Misoprostol regimens for induction of labour following pregnancy loss vary widely and the dose required to achieve timely birth while optimizing maternal outcomes remains uncertain (1, 2, 3, 4, 5). Aim: To determine the association between misoprostol dose and vaginal birth ≤ 24 hours and maternal morbidity, in women with pregnancy loss.

Methods: A multicentre, retrospective cohort study, across three tertiary hospitals in Sydney Australia was performed. Women with stillbirth or medical termination of pregnancy ≥ 20 weeks gestation who underwent misoprostol induction between January 2019 – July 2024 were included. Multivariate logistic regression assessed associations between misoprostol dose (mcg/hr), vaginal birth ≤ 24 hours and composite measure of maternal morbidity, defined as, blood transfusion, transfer to operating theatre, uterine rupture, hysterectomy, intensive care unit admission or maternal death.

Results: Of 556 women, 475 (85%) achieved vaginal birth ≤ 24 hours. Compared with ≤ 25 mcg/hr, increasing dose was associated with greater odds of vaginal birth < 24 hours: 26100 mcg/hr, 101–200 mcg/hr and ≥ 201 mcg/hr had increasing odds of vaginal birth ≤ 24 hours (adjusted odds ratio (aOR) 2.11 (95% CI, 1.04–4.36), 10.8 (95% CI, 4.07–31.2) and 43.8 (95% CI 7.84–828), respectively). Maternal morbidity occurred in 74 (13%) women. Increasing dose was not associated with maternal morbidity: aOR 1.22 (95% CI 0.49–3.17), 1.01 (95% CI 0.37 – 2.91) and 1.23 (95% CI 0.42–3.96, respectively).

Conclusion: Following pregnancy loss ≥ 20 weeks of gestation, a higher misoprostol dose, particularly $> 100\text{mcg}$ per hour, was associated with increased likelihood of vaginal birth within 24 hours, without an observed increase in maternal morbidity.

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Applicant: Riley Nicholson
Supervisor: Dr Claire Boswell-Ruys

Optimal stimulation train duration for abdominal functional electrical stimulation to augment tidal volume in healthy adults.

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Background: Respiratory failure is a leading cause of death after spinal cord injury (SCI). Abdominal functional electrical stimulation (FES) drives expiration below functional residual capacity, assisting the subsequent inspiration via elastic recoil (1). Previous work investigated fixed 1s trains to support tidal volumes in people with SCI (2–4). We hypothesised that the volume generated by trains individualised to expiratory duration (T_e) would vary from quiet breathing, and from fixed 1s trains.

Methods: In twenty healthy adults (11 male, 22–50 years), posterolateral electrodes (5, 6) delivered biphasic stimulation (50Hz, 200 μ s) triggered at expiratory onset, at maximum tolerated intensity (7/10 discomfort). Four train durations (1s, 75%, 100% and 125% of T_e) were tested in balanced random order, on single breaths and over 30s of consecutive breaths. Data were analysed using linear mixed models.

Results: All conditions increased expired volume above quiet breathing (0.92L; 95% CI 0.70–1.14L), by 0.40–0.64L across the four train durations (single breaths) and 0.65–0.91L (consecutive; all $p < 0.001$). The 1s train generated smaller volumes than 100% and 125% T_e ($p < 0.05$), shortened expiration and raised respiratory rate. T_e -referenced trains did not differ from each other in volume. The only condition where expiratory duration and respiratory rate did not change from quiet breathing was 100% T_e . No adverse events occurred.

Conclusion: Trains matched to expiratory duration generated larger breaths than fixed 1s trains without displacing the breathing pattern, making them a viable option in future research to generate breathing patterns for patients with SCI.

POSTER

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Applicant: Xian Zou
Supervisor: Dr Marion Mateos

Understanding oncologists' therapeutic decision-making for children with high-risk cancer receiving a precision-guided recommendation.

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Background: Understanding paediatric oncologists' decisions to pursue molecular tumour board (MTB)-recommended precision-guided treatment (PGT) is important for supporting clinical decision-making and equitable access to targeted therapies. To date, no study has systematically examined this process or the factors influencing integration of precision medicine into practice. This study aimed to (1) identify factors influencing paediatric oncologists' adoption of PGT recommendations and (2) elucidate their support and training needs.

Methods: We invited 57 paediatric oncologists treating patients enrolled in the PRISM trial, a national paediatric precision medicine trial for poor-prognosis cancers, to participate in semistructured interviews. Interviews explored experiences and decision-making related to PGT use and clinician training needs. A hybrid analysis approach, supported by NVivo 14, used an initial coding framework while allowing new categories to emerge. Three predefined scenarios ("PGT implemented", "PGT not implemented", and "PGT deferred") were used to explore variation across clinical contexts.

Results: Thirty paediatric oncologists participated. Eight factors influencing decision-making were identified across three domains: decision-maker-related criteria (clinician attitudes, patient and family preferences); decision-specific criteria (drug formulation and toxicity, strength of evidence); and contextual factors (treatment accessibility). Five categories of clinician training and support needs were identified, including genetic concepts, psychosocial support, and understanding MTB recommendations.

Conclusion: PGT decision-making was described as complex and context dependent, influenced by clinical, psychosocial, and system-level factors beyond genomic actionability alone. Improving implementation will require clinician training, multidisciplinary support streamlined treatment access, and clearer guidance on integrating PGT with standard therapies. Future research should quantify key decision-making trade-offs and incorporate patient and parent perspectives.

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Applicant: Claire Lawley
Supervisor: Dr Hiroko Asakai

Profile and outcome of children reaching intensive care following out of hospital cardiac arrest

Abstract Background The causes and outcomes of out of hospital cardiac arrest (OHCA) in children are much less researched than in adults. **Objective** To report the incidence, aetiology, presenting rhythm and survival of children with return of spontaneous circulation (ROSC) after an OHCA.

Methods A retrospective cohort study including all infants and children (age 0-16 years) following OHCA who were admitted to a Paediatric Intensive Care Unit (PICU) in New South Wales, Australia (approximate population 8 million), from January 2009 to December 2019. Subgroup analysis of arrests due to ventricular tachycardia (VT) and ventricular fibrillation (VF).

Results 296 children (female n=109, 36%), median age 2.5 years, were admitted following OHCA. Bystander cardiopulmonary resuscitation (CPR) was documented as performed in 216 (76%), which was associated with a lower odds ratio of death when compared to no CPR documented (OR 0.417 95% CI 0.236-0.726, p=0.002). Of the 283 (96%) children with known presenting rhythm, 240 (85%) presented in asystole or pulseless electrical activity (PEA), 41 (15%) in VT/VF, together termed 'shockable rhythm' and 2 (<1%) in complete heart block. Of children with VT/VF, 23 (56%) had a potentially heritable cardiac condition including catecholaminergic polymorphic ventricular tachycardia (CPVT), 9/41 (22%), hypertrophic cardiomyopathy, 6/41 (15%). 160/296 (54%) children survived to hospital discharge, with highest survival rate in those presenting with VT/VF, 34/41 (83%).

Conclusion Improved survival to hospital discharge was associated with documented bystander CPR and those children with a documented shockable rhythm. When a heritable cause was found as the cause of VT/VF, the commonest in this era was CPVT.



Applicant: Neevika Manoharan
Supervisor: Professor David Ziegler

autologous third generation GD2-CAR-T cell therapy in children with diffuse midline glioma: anti-tumour activity with minimal toxicity

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Chimeric antigen receptor T (CAR-T) cells are a promising therapeutic strategy for the treatment of diffuse midline glioma (DMG), the most aggressive paediatric brain cancer. We present interim results of the first Australian phase 1 clinical trial of autologous GD2-specific CART therapy with a third-generation (14g2a.OX40.CD28.zeta) signalling CAR-T construct. In contrast to previous studies, our GD2-CAR-T is administered intravenously in combination with anti-VEGF therapy (bevacizumab) to mitigate potential oedema from on-target, on-tumour CAR-T effects after lymphodepleting chemotherapy (fludarabine/cyclophosphamide).

Among 8 treated patients with 18 infusions on study to date, there were no dose limiting toxicities (DLTs) at dose level 1 and 1a (DL1 and DL1a) with a single DLT (Grade 4 cytokine release syndrome) at dose level 2. Three patients demonstrated tumour volume reductions exceeding 50% without the severe hyperinflammation seen with other CAR-T therapies, with one patient achieving a 97% volume reduction. Sustained radiological responses correlated with objective neurological improvements in these patients (two thalamic and one pontine DMG). A further four patients achieved radiological stable disease with only one patient having no evidence of tumour response. Patients who exhibited tumour responses showed distinct proteomic signatures associated with T-cell activation and recruitment, including elevated plasma and cerebrospinal fluid (CSF) granzyme B. Despite the administration of lymphodepleting chemotherapy, anti-GD2-CAR antibodies emerged with sequential infusions and were associated with loss of GD2-CAR-T persistence.

Our results indicate anti-tumour activity of third-generation GD2-CAR-T cells administered with anti-VEGF therapy. The trial will further investigate regimen safety, efficacy and determine the optimal therapeutic dose.



Applicant: Elijah Tyedmers
Supervisor: Professor Natalie Taylor

Supporting access to targeted therapies recommended through the ZERO paediatric precision oncology program: A national type 3 hybrid effectiveness-implementation trial of a novel digital medicines access tool (ProCure)

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Background: Precision oncology can identify targeted therapies for children, but recommendations may be difficult to translate into treatment when therapies require off-label access.

Aim: To evaluate implementation and effectiveness of ProCure, a digital tool supporting access to therapies recommended through the ZERO Childhood Cancer Program.

Methods: Guided by the Consolidated Framework for Implementation Research 2.0, in a pre-trial phase we beta-tested ProCure and co-refined an implementation support package (ISP). Then we conducted a type 3 hybrid effectiveness-implementation trial across 8 hospitals.

Results: At trial baseline, 18 consultants, 7 fellows and 13 oncology pharmacists responded, and 30/38 (79%) managed compassionate access applications in the past 6 months. Among 17 oncologists, 14 (82%) spent ≥3 hours per application, including 7 (41%) spending ≥6 hours. Of 11 pharmacists, all spent ≥2 hours assisting applications. Confidence was low for identifying pathways among 22/38 (58%) and completing applications among 16/38 (42%). Additionally, 25/38 (66%) reported high need for ProCure (≥7/10). Among 12 beta-testers in the pre-trial phase, ProCure's acceptability and appropriateness averaged 4.7/5 and 4.5/5. ProCure's implementation feasibility averaged 4.75/5 after ISP co-refinement.

Preliminary trial findings from Drug Access Navigator self-reported activity logs indicated that ProCure contained all information required for clinical advice in 86% of uses and estimated 100 hours saved since April 2026. Conclusion: ProCure demonstrates early promise as a scalable implementation strategy to reduce clinician burden and improve access to targeted therapies within paediatric oncology. Evaluations in April 2027 will assess implementation, application time and clinician confidence in pursuing targeted therapies.



Applicant: Dr. Jenny Sohn
Supervisor: Professor Karen Zwi

Listening to Young Patients: A Qualitative Study of Hospital Experiences of Children and Young People with Disabilities

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Children and young people (CYP) with disabilities experience significant health inequities and high healthcare utilisation compared to their non-disabled peers (1,2). Despite frequent hospital contact, little is known about how CYP with disabilities experience paediatric hospital care. Existing evidence is largely quantitative or based on proxy perspectives, with limited research directly capturing CYP voices (3,4).

Our study explored how CYP with disabilities and their caregivers experience hospital care and identify factors influencing their care and generate recommendations to inform hospital service improvements.

We conducted a qualitative study using semi-structured interviews with CYP with disabilities and their caregivers who had accessed care at Sydney Children's Hospital Network. Participants were purposively sampled through hospital recruitment and clinician referral. Interviews were conducted in person or via videoconferencing between July 2022 and January 2024. Transcripts were analysed using reflexive thematic analysis following Braun and Clarke's approach.

Sixteen participants (eight CYP and eight caregivers) participated in individual or dyadic interviews. Six interrelated themes were identified: negotiation of agency and voice; cumulative emotional toll of healthcare engagement; identity and development shaped and contested within healthcare; relationships as the foundation of care experience; ruptured supports during transition to adult healthcare; material and environmental conditions impacting care.

Hospital experiences for CYP with disabilities were shaped by relational dynamics, agency, and environmental conditions, with relational factors central to perceived care quality. Our findings support inclusive communication, proactive psychosocial support, strengthened care coordination, and earlier transition planning. Hospital care should recognise healthcare as context for socioemotional development, identity formation, and preparation for adulthood.

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Applicant: Cameron Hicks
Supervisor: Professor Stephen Lord

Simple Changes, Better Stratification: Optimising the World Falls Guidelines Fall Risk Algorithm

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The World Falls Guidelines (WFG) fall risk algorithm was developed to stratify older adults into low-, intermediate- and high-risk groups [1]. However, several cohort studies have found the algorithm does not identify a sizeable intermediate-risk group, limiting its ability to support a threetiered intervention model. This research outlines the development and validation of two modifications to improve fall risk stratification by rebalancing the low- and intermediate-risk groups.

A cohort study [2] and two individual participant-data meta-analyses (IPDMA) [3,4] identified, refined and validated modifications to the WFG algorithm across six international cohorts of older adults.

Two modifications were identified: (1) incorporating mobility assessment among individuals reporting no fall-related concerns and (2) adopting more conservative mobility cut-points for gait speed and the Timed Up and Go test. An IPDMA demonstrated that a gait-speed threshold of <1.0 m/s identified substantially more fallers than the current <0.8 m/s threshold while maintaining comparable sensitivity and specificity for predicting falls. Across six international cohorts, application of the modified algorithm increased the median (IQR) proportion classified as intermediate risk from 1.8% (0.5-8.4%) to 14.7% (7.1-30.5%), while preserving risk discrimination, with fall rates remaining substantially higher in the high-risk group than in the low- (IRR=3.40, 95%CI:2.67-4.33) and intermediate-risk groups (IRR=3.12, 95%CI:2.16-4.51).

Simple modifications to the WFG algorithm produced a more balanced and clinically meaningful three-tiered risk classification without compromising risk discrimination. The revised algorithm identifies substantially more older adults with mobility limitations at intermediate risk, creating greater opportunity for targeted exercise and early fall-prevention intervention.

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Applicant: Vinuri Peiris
Supervisor: Dr Matthew Brodie

VALIDATING THE REALISM OF THE PADDLETRIP SYSTEM: COMPARISONS WITH A TRIP WALKWAY AND SURFACE PERTURBATION TREADMILL

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One in three older Australians fall each year (1), and related injuries cost the health system \$3.2 billion (2). Reactive balance training involves external perturbations (3) and can reduce falls (4,5). The cost-effective PaddleTrip treadmill uses rotating paddles to induce trips. This study aimed to determine realism of these obstacle-induced trips.

Twenty adults (38.3 ± 16.7 years; range: 21–72) completed walking-perturbation conditions: (A) PaddleTrip treadmill, (B) 8-m walkway with two trip boards, and (C) surface-perturbation treadmill (12 m/s²; M-Gait). PaddleTrip and walkway conditions included four left foot trips (two elevating and two lowering recovery steps). In the surface-perturbation treadmill condition, four belt accelerations were delivered during right stance to ensure the left foot initiated the recovery step. Participants rated realism relative to an overground obstacle trip, balance effort, anxiety, pain, and confidence in avoiding a fall using 21-point scales.

PaddleTrip realism (median 14.5 [IQR 10–18]) was lower than walkway realism (18 [17–20], $P = .007$), but higher than surface-perturbation treadmill realism (5.5 [4–10.5], $P = .004$), which rated lower than the walkway ($P < .001$). Other ratings did not differ ($P > .05$). Pain ratings were <2 across conditions and one knee-pain event occurred after the surface-perturbation treadmill. Five PaddleTrip (4.3%) and five walkway trials (4.8%) resulted in falls into the harness; no surface-perturbation treadmill falls occurred. Kinematic analyses are ongoing.

PaddleTrip trips were perceived as less realistic than walkway trips, but more realistic than treadmill belt accelerations. Future work should examine whether PaddleTrip perturbation training reduces fall risk.

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Applicant: Shivam Sharma
Supervisor: Dr Yoshiro Okubo

Effects of the ReacStep training program on balance recovery and fall risk factors in older people: an assessor-blinded randomised controlled trial

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Background: Reactive balance training may improve recovery from trips and slips, but existing approaches often require costly or specialised equipment (1-3). This study evaluated the effects of ReacStep, a simple and low-cost reactive balance training program for older people.

Methods: In this assessor-blinded randomised controlled trial, 88 community-dwelling adults aged ≥ 65 years were allocated to ReacStep training ($n=43$) or control ($n=45$). Both groups completed homebased strength training for 8 weeks. The intervention group additionally completed weekly tetherrelease reactive stepping and intentional-slip training for 6 weeks. Reactive balance, physical function and falls were assessed at baseline and post-intervention. Falls in daily life were monitored for 12 months using weekly SMS surveys.

Results: Mean participant age was 72 years (SD 5.6). Adherence to ReacStep sessions was 90%. There were no significant between-group differences in laboratory-assessed reactive balance falls or falls during daily life over 12 months ($P=.19$). However, ReacStep significantly improved maximum step length and choice stepping reaction time compared with control ($P<.05$).

Conclusion: ReacStep was well tolerated and demonstrated excellent adherence. Although it improved important stepping measures, these gains did not translate into fewer laboratory-induced or daily-life falls. Further optimisation using more ecologically representative perturbations is warranted.

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Applicant: Yixuan He
Supervisor: Dr Yoshiro Okubo

Measuring balance without a motion-capture laboratory: deep-learning calibration of low-cost wearable trackers for virtual reality fall-prevention training

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Trips and slips cause most falls in older people (1), and people with Parkinson's disease (PD) fall even more often (2). Our virtual reality (VR) obstacle training reduces hazard contacts (3,4), and margin of stability (MoS) shows which contacts threaten balance (5), but both require a motioncapture laboratory. Deep learning has estimated MoS from inertial sensors (6), but not, to our knowledge, from the trackers that already animate the feet in our VR training. We hypothesised that deep-learning calibration would make these trackers accurate for gait and stability, even a single sacral one.

Ten healthy adults walked on a treadmill at 0.5–2.0 m/s wearing three HTC VIVE Ultimate Trackers (sacrum, both feet) alongside Vicon (7). A convolutional neural network–Transformer model (leave-one-participant-out cross-validation) corrected tracker coordinates and estimated whole-body centre of mass from the sacral tracker alone (8).

Raw tracker positions agreed closely with Vicon (concordance >0.98) (7), and calibration reduced coordinate error by 28–55% (gait-parameter errors ≤4.6 mm). From the sacral tracker alone, calibration reduced MoS bias from –75 to –3.5 mm and raised agreement (intraclass correlation) from 0.09–0.79 to >0.99, although limits of agreement remained –46 to 39 mm (8).

Under controlled conditions, one low-cost tracker on the lower back matched laboratory MoS on average. Because our VR training already uses these trackers, balance could be monitored in every session, in clinics and the community. Next, we will test this in people with PD within the StepUP treadmill-training trial (9).

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Applicant: Dr Helen Nguyen
Supervisor: Associate Professor Susan Adams

Beyond clinical evidence: health system barriers to implementation of a statewide paediatric splenic injury management guideline

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Background: Variation in management of paediatric splenic injury exists across the trauma network. Clinical guidelines can reduce unwarranted variation, but only when they can address context-specific, system-level barriers. However, barriers to paediatric splenic injury management remain poorly explored in New South Wales (NSW). This study aims to identify barriers to statewide implementation and adoption of paediatric splenic injury management guidelines in NSW.

Methods: Online focus group discussions were conducted with 97 clinicians across rural, regional and metropolitan NSW. Clinicians were asked to discuss existing and anticipated barriers to implementation and long-term adoption of paediatric splenic injury management guideline within their clinical setting. Transcripts were transcribed verbatim and inductive-deductively coded using the Consolidated Framework for Implementation Research, with themes organised across constructs in the Inner/Outer Setting, the Innovation and Implementation, and Individual domains.

Results: Five themes emerged from the focus groups; two aligning with constructs from the Inner/Outer Setting, three with Innovation and Implementation, and two with Individual domains. Clinicians identified variations in splenic injury management to be driven by resource constraints, staffing limitations, and a "transfer by default" culture across settings. For successful guideline implementation, clinicians emphasised strong governance, leadership support and multidisciplinary champions as key enablers. They also recognised the critical role of education and simulation-based training in supporting ongoing guideline adherence.

Conclusion: Statewide implementation of paediatric injury management guidelines may reduce unwarranted variation in care, but successful implementation and long-term adoption will require addressing resource constraints and an entrenched transfer culture, alongside strong governance, leadership, and multidisciplinary engagement.

Applicant: Dr Jing Du

Supervisor: Associate Professor Aswin Ratheesh

Developmental Reconfiguration of the Allostatic-Interoceptive Network during Adolescence

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Background: Adolescence is a critical period when mood disorders emerge. Although developmental changes in some canonical brain networks are well established, the development of allostatic-interoceptive network (AIN) (1), which supports interoception of bodily signals and emotion regulation, remains unclear. Guided by predictive-coding theory (2), we tested whether healthy maturation of AIN shows pathway-specific reconfiguration.

Methods: Resting-state fMRI from 2,289 psychiatrically healthy participants in the ABCD Study (3) were analysed (baseline age: 9.93 ± 0.62 years), comprising 6,680 scans collected at baseline and 2-, 4-, and 6-year follow-ups. Among them, 536 completed all four assessment waves. Fisher z-transformed functional connectivity was estimated for five pathway-level classes: agranular visceromotor, granular viscerosensory, limbic, thalamic and brainstem. Longitudinal mixed-effects models tested developmental changes, adjusting for age, sex, scanner, and head motion.

Results: Comparing with baseline, viscerosensory-thalamic connectivity progressively decreased (adjusted change: -0.008 , -0.020 and -0.020 at Years 2, 4 and 6), whereas viscerosensory-limbic connectivity increased ($+0.006$, $+0.009$ and $+0.013$). Thalamic-thalamic connectivity showed the strongest cumulative increase ($+0.010$, $+0.027$ and $+0.044$). Principal later-wave patterns were replicated in the complete-case sensitivity analysis. All reported changes were statistically significant after FDR correction ($p < 0.05$).

Conclusion: Healthy adolescence is characterised by progressive rebalancing within the AIN. Strengthened thalamic integration and viscerosensory-limbic coupling, alongside reduced viscerosensory-thalamic and limbic-brainstem connectivity, is consistent with increasing influence of centrally generated predictions relative to ascending bodily sensory signals. These trajectories may provide a normative benchmark for identifying atypical AIN development and circuit-level vulnerability to mood disorders.

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Applicant: Dr Kayla Steele
Supervisor: Profesor Jill Newby

Understanding the mental health support needs of women and their partners undergoing in-vitro fertilisation (IVF) treatment

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Background: Infertility affects one in six people worldwide, and in vitro fertilisation (IVF) is associated with elevated anxiety, stress and depression. Psychological burden is a leading reason for discontinuing treatment, yet mental health support in fertility care is inconsistent and scalable options are lacking. To our knowledge, this is the first Australian study of the mental health support needs of women undergoing IVF and their partners/support people.

Aims: To examine anxiety, stress and worry during IVF, mental health support needs, gaps in fertility care pathways, and attitudes towards a digital intervention.

Methods: A developmental mixed-methods design, co-developed with lived experience advisors. Australians undergoing IVF (current or past 12 months) and their partners/support people complete an online survey (DASS-21, RTQ-10, FertiQoL and openended questions) and semi-structured interviews. Focus groups with patients, partners and fertility care stakeholders (e.g., clinicians, counsellors) explore intervention adaptation. Analyses use descriptive statistics, logistic regression and qualitative descriptive analysis, with findings integrated. Anticipated

Results: Recruitment is ongoing (n=200 surveys completed); data collection concludes January 2027. Findings will report levels of depression, anxiety and stress symptoms; fertility-related quality of life; pregnancy, fertility and fertility treatment experiences; experiences of accessing mental health support; and attitudes towards a brief digital tool to support stress, worry and anxiety. Conclusions: This study will identify who is most at risk and what support is needed, informing co-design of an accessible, scalable digital intervention adapted from an evidence-based cognitive bias modification program (RELAX) to reduce stress, worry and anxiety during fertility treatment.



Applicant: Yunjin Fang
Supervisor: Dr Antonia Shand

Seatbelt use among pregnant women in Australia and New Zealand: a survey of healthcare providers

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Introduction: Motor vehicle crashes (MVCs) are a major cause of blunt trauma during pregnancy. Correct seatbelt use reduces the risk of injury to both the pregnant woman and fetus; however, previous Australian research found that most pregnant women had not received information from a clinician about correct seatbelt use.

Hypothesis: Clinicians are not routinely providing pregnant women with information about correct seatbelt use.

Objective: To assess maternity clinicians' knowledge, behaviours and attitudes towards providing advice about correct seatbelt use during pregnancy.

Methods: An anonymous REDCap survey was distributed through RANZCOG and the Australian College of Midwives between March and August 2026. Clinician knowledge of correct seatbelt use in pregnancy, counselling practices, confidence, attitudes and previous education, as well as demographic characteristics.

Results: Of 333 respondents, 75% were midwives and 93% were women. Although 78% agreed that clinicians should provide advice about seatbelt use during pregnancy, only 48% had ever done so. Most correctly identified correct shoulder-belt (79.3%) and lap-belt (89%) positioning, while 35% knew the function of the locator mechanism. Only 45% felt confident providing advice, 88% had received no education on seatbelt use in pregnancy, and 86% had not read relevant guidelines or recommendations.

Conclusion: Despite recognising the importance of providing advice about seatbelt use during pregnancy, many maternity clinicians do not provide such advice and lack confidence in doing so. Knowledge gaps were also identified regarding correct seatbelt use. These findings highlight an important opportunity to improve clinician education and guidance on seatbelt use during pregnancy.

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Applicant: Dr Sharman Tan Tanny
Supervisor: Professor Susan Adams

QUALITY ASSESSMENT OF CLINICAL PRACTICE GUIDELINES FOR SPLENIC INJURY IN CHILDREN USING THE AGREE II INSTRUMENT

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Background: Evidence-based clinical practice guidelines (CPG) are utilised to guide assessment and management of splenic injury in children. There are differences in how different countries develop CPGs, but these have yet to have their quality assessed.

Aim: We aimed to undertake an appraisal of internationally published splenic injury management guidelines, alongside those developed in the Australasian context, using Appraisal of Guidelines for Research and Evaluation (AGREE II) methodology (1).

Methods: Four databases (Pubmed, MEDLINE, EMBASE and Cochrane) and websites of Australasian Children's Hospitals were systematically searched by two authors, for guidelines on management of paediatric splenic injury, published from January 2015 to November 2025. Inclusion criteria were CPGs published in English, that provided recommendations for paediatric splenic injury. Twelve clinicians (various specialties experienced in trauma) independently evaluated the CPGs (four appraisers per CPG) using the AGREE II instrument. Scores were interpreted according to published scoring systems.

Results: Among 300 records initially identified, six (three USA, two Australasia, one Europe) met inclusion criteria: four published and two local. Only published guidelines were strongly recommended. Across all guidelines, scope and purpose, and presentation were generally strong (median score > 50%), while stakeholder involvement, rigour of development, applicability, and editorial independence, scored lower (median score < 50%).

Conclusion: There is need for improved quality processes in paediatric splenic injury guideline development, with increased focus on broader stakeholder involvement, developmental rigour and attention to contextual considerations, implementation, and evaluation. This will enable better care for patients across the range of settings they present in.

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Applicant: Joesphine Flohr
Supervisor: Dr Ana Rita Barreiros

Within-participant comparison of psychological insight following ketamine and Ketamine with Integrated Psychotherapy for treatment-resistant depression

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Ketamine is an established treatment for treatment-resistant depression (TRD), but the psychological processes associated with treatment response remain unclear. Ketamine with Integrated Psychotherapy (KWIP) combines ketamine with structured psychotherapy around the ketamine experience and the elicited neuroplastic window (1). Psychological insight, broadly defined as increased understanding of one's thoughts, feelings and behaviours, is associated with psychotherapy outcomes (2) and has been implicated in psychological change following psychedelic experiences (3). Its role following ketamine treatment has not been established.

This observational mixed-methods study will examine psychological insight in adults previously treated with ketamine and/or KWIP for TRD. Participants will retrospectively complete the Psychological Insight Scale (PIS) for each treatment type received. Within-participant differences in PIS scores between ketamine and KWIP will be examined using a linear mixedeffects model, adjusting for recall interval, concurrent depression severity and cumulative ketamine exposure. A subset of participants who have experienced both treatments will complete semistructured interviews exploring how they experienced each treatment and made sense of perceived psychological change. Interviews will be analysed using Interpretative Phenomenological Analysis.

This will be the first study to compare psychological insight following ketamine and KWIP and the first to apply the PIS in a clinical ketamine-treated population. As ketamine treatment for TRD expands, understanding the psychological factors associated with different treatment approaches may help optimise how ketamine treatment is delivered, with the longer-term aim of improving outcomes sooner and for more patients.

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Applicant: Dr Kiera Roberts
Supervisor: Professor Susan Adams

CONTEMPORARY OUTCOMES OF CONGENITAL DIAPHRAGMATIC HERNIA

K. Roberts¹, J. Young², H. Ravindranathan², S.Adams¹ 1. Department of Paediatric Surgery, Sydney Children's Hospital 2. Children's Intensive Care Unit, Sydney Children's Hospital

Current outcome data for congenital diaphragmatic hernia (CDH) is predominantly based on international cohorts or historic time periods. This study aims to provide contemporary, local data on outcomes for infants with CDH, to allow benchmarking against international cohorts. A retrospective review of all patients with CDH managed at the Sydney Children's Hospital from January 2000 – December 2024 was performed, excluding patients who presented outside the neonatal period. The primary outcome was survival, with secondary outcomes including length of stay (LOS), surgical management and use of extracorporeal membrane oxygenation (ECMO). Data were analysed in five-year time periods. Ethics approval was obtained from the local research governance body.

159 patients with CDH were born during the time period (left-sided n = 133 / right-sided n = 26). Prenatal diagnosis rates increased over time (50-61% from 2000-2014, compared with 72-79% from 2015-2024), with a similar increase in number of inborn compared with outborn. Overall survival was 77.4% (123/159) and did not vary between time periods. Median LOS (days) decreased from 21 (2000-2004) to 13 (2019-2024). 136/159 (86%) underwent surgical repair (median age 3 days). ECMO was used in 7 cases (4.4%) with a mortality of 57% (4/7) and median LOS of 99 days for the surviving patients. Four patients commenced on ECMO pre-operatively, two post-operatively and one did not have an attempt at repair.

Our reported mortality is comparable to internationally published data, despite significantly lower use of ECMO. Although survival did not change, there was a trend towards shorter LOS over time.



Division:

Honours and Independent Learning Projects

Applicant: Katia Bjorkmann
Supervisor: Dr Christina Signorelli

Let's get moving: Co-designing physical activity resources for paediatric cancer patients.

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2. Minderoo Children's Comprehensive Cancer Centre, Sydney Children's Hospital, Randwick, Australia
3. Little Big Steps Organisation
4. Move Well Lab, The University of the Fraser Valley, British Columbia, Canada

Background: Movement during cancer treatment is critical for physical functioning and psychosocial wellbeing, yet children with cancer report lower physical activity levels compared to their peers (1). Opportunities for physical activity remain limited by a lack of oncology-specific, age-appropriate resources (2).

Methods: This mixed-methods study aimed to co-design resources for children on treatment by exploring their physical activity information needs, barriers, motivators, and resource preferences. We combined i) cross-sectional surveys in young people with cancer (aged 8-25) and parents, and ii) online co-design workshops with physiotherapists, to develop resource recommendations across three developmental age groups (0-5, 6-12 & 13-17 years). We conducted hybrid inductive/deductive content analysis, and mapped the findings to the Capability, Opportunity, Motivation Behaviour (COM-B) model to identify behavioural determinants and guide resource design (3).

Results: Fifteen young people (mean age=14.6, SD=4.7) and 16 parents (75% female) completed surveys. 13% of young people met movement guidelines during treatment, with capability barriers including fatigue (81% of respondents), and lack of oncology-specific physical activity information hindering participation. Despite this, motivation appeared high across respondents (90% reported young person movement goals), driven by social connection, achievement, and a desire to return to pre-diagnosis fitness. Physiotherapists (n=4, n=8 workshops), recommended resources that accommodate children's fluctuating capacity, offer impairment-specific modifications (e.g., for chemotherapy-induced peripheral neuropathy) and support parent and child-facing delivery.

Conclusion: These insights support the design of tailored, age-appropriate resources to encourage safe and confident physical activity engagement during treatment. To ground resources in lived experience, we will conduct co-design workshops with children and families.

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Applicant: Manal Khan
Supervisor: Dr Bernadette Prentice

Growing Older, Growing Data: Internationally Benchmarking the Australian Cystic Fibrosis Data Registry in an Era of Improved Survival and Therapeutics.

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Background: Improvements in cystic fibrosis (CF) treatment and survival have shifted CF towards a chronic, predominantly adult disease (1). Longer survival introduces new complications and care needs, requiring data collection to evolve alongside clinical practice and international standards. The Australian Cystic Fibrosis Data Registry (ACFDR) has been continuously refined since commencing in 1998 (2), however, its alignment with the changing disease course and international registry standards has not been systematically assessed. This cross-registry comparative analysis aims to benchmark current ACFDR data elements against international CF registries and identify priority areas for data collection refinement and harmonisation.

Methods: ACFDR data elements were mapped against eight international CF registries, using available data dictionaries. Recommendations were prioritised using a tiered Core/Enhanced/Granular framework and reviewed with the ACFDR Steering Committee.

Results: Important gaps were identified across multiple domains. ACFDR does not record quantitative glucose measurements or distinguish CF-related diabetes from Type 1 or 2 diabetes. Lung function data lack Lung Clearance Index. Cancer classification does not include blood and gynecological categories. Mental health fields capture screening but not diagnosis. Hypertension and renal complications were consistently captured by comparator registries but not by ACFDR. Additional gaps were identified in pregnancy and sociocultural fields, although ACFDR provided greater detail than several comparator registries in cancer and allied health domains.

Conclusion: ACFDR requires specific updates to remain clinically relevant and internationally comparable as the CF population ages and treatment evolves. Tiered recommendations balance data burden against the value of harmonised, comprehensive data collection to support future research and quality improvement.

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Applicant: Hannah Ku
Supervisor: Professor Kei Lui

EVALUATION OF MINIMALLY INVASIVE SURFACTANT TREATMENT IN PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME – AN AUSTRALIAN AND NEW ZEALAND NEONATAL NETWORK STUDY 2017–2022.

Hannah Ku

University of New South Wales, Royal Hospital for Women

Background: Minimally invasive surfactant therapy (MIST) has been introduced to reduce the need for mechanical ventilation (MV) and its associated complications in preterm infants with respiratory distress syndrome. This study evaluated the of real-world uptake of MIST and its association with respiratory outcomes in surfactant-treated infants.

Methods: A retrospective cohort study was conducted among surfactant-treated preterm infants admitted to neonatal intensive care units participating in the Australian and New Zealand Neonatal Network data collection between 2017 and 2022. MIST success was defined as avoiding mechanical ventilation within the first 72 hours after birth.

Results: Among 12,703 surfactant-treated preterm infants, the use of MIST increased over the study period, with the greatest uptake observed among infants born at 28–31 weeks' gestation, increased from 6.2% in 2017 to 30.4% in 2022. Among infants <28 weeks who received MIST, 58% were treated within 2 hours of life. MIST success increased with advancing gestational age, with success rates of 65.2% among infants <28 weeks, 81.5% among 28–31 weeks, and 80.6% among 32–36 weeks. The estimated probability of MIST success exceeded 50% at 24+6 weeks and 75% at 27+4 weeks. Higher gestational age and birth weight z-score were associated with successful MIST, whereas intubation at delivery and additional surfactant doses were associated with MIST failure. Compared with successful MIST, MIST failure had significantly longer durations of MV and a higher risk of chronic lung disease.

Conclusion: MIST uptake increased in contemporary practice and achieved higher success rates with advancing gestational age, particularly beyond 25 weeks.

Applicant: Uen Tsun Eugenia Yau

Supervisor: Dr Didu Kariyawasam

“A double-edged sword”: perspectives of parents and healthcare professionals involved in newborn screening scoping study for Duchenne muscular dystrophy.

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Background: Although Duchenne muscular dystrophy (DMD) is included in several newborn screening (NBS) programs worldwide, evidence on families' experiences, needs and perspectives on acceptability of DMD NBS remains limited, underscoring the need for family-centred research to inform future policy and practice.

Methods: An Australian prospective, population-based NBS pilot study for DMD ran from April 2025 to March 2026, using a three-tiered, biochemical-genomic algorithm. Parents' and healthcare professionals' (HCPs) experiences and psychological impacts of a DMD diagnosis through NBS were assessed via questionnaires, with quantitative and qualitative data analyzed using a convergent mixed-methods design.

Results: 78,721 infants were screened for DMD, the perceptions of 29 parents and HCPs following a positive result in six newborns were ascertained. Parents (n = 9) described a complex interplay of emotional and practical factors. Whilst a DMD diagnosis generated grief and distress (median Kessler Psychological Distress Scale [K10] score = 16; interquartile range, 15–22), positive adaptation was evident, including coping, resilience and strengthened family bonds. Knowledge also enabled early action in a changing therapeutic landscape, including early intervention and informed family planning. All parents (9/9, 100%) supported the continuation of DMD NBS, while 12/20 HCPs (60%) endorsed DMD NBS through either an opt-in or mandated model.

Conclusion: An integrated model of care comprising timely diagnosis, specialist and multidisciplinary care, psychological support and genetic counselling, and clear, sensitive communication is essential to maximize benefits and minimize harms of DMD NBS. These are critical to maintaining public acceptability and supporting sustainable implementation of DMD NBS.

Applicant: Hafsah Atif
Supervisor: Dr Omid Faridani

To Enrich or Not to Enrich? Direct Sequencing of CTC-Derived Nucleic Acids from Blood in Childhood Cancer.

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Background: Liquid biopsy offers a minimally invasive approach to tumour detection and disease monitoring. Circulating tumour cells (CTCs) provide clinically informative material for genomic characterisation; however, their rarity in blood has limited widespread clinical application. Current CTC-based approaches typically rely on specialised enrichment or isolation workflows that are technically complex, difficult to standardise, and may result in loss of an already rare cell population. We hypothesised that clinically relevant tumour-derived molecular information could be recovered directly from blood without prior CTC enrichment or isolation.

Methods: Nucleic acids were extracted from peripheral blood samples from patients with neuroblastoma and analysed using low-pass whole genome sequencing (lpWGS) and targeted hybridisation capture workflows. Sequencing libraries were successfully generated from unenriched blood samples without dedicated CTC isolation.

Results: lpWGS identified tumour-associated genomic signals, demonstrating that biologically meaningful molecular information can be recovered directly from unenriched blood. Targeted hybridisation captures further detected tumour-associated molecular features, providing additional evidence that clinically relevant tumour-derived information remains accessible without enrichment.

Conclusion: These findings support the feasibility of a simplified CTC-informed liquid biopsy strategy based on direct molecular analysis of unenriched blood. By reducing reliance on specialised CTC isolation technologies, this approach may improve scalability, standardisation, and translational feasibility while retaining clinically relevant tumour-derived information. Further evaluation across additional molecular modalities may help define the sensitivity and broader clinical utility of this approach.

Applicant: Matthew Henry Koh

Supervisor: Dr Sarah Ellis

Feasibility and acceptability of a nurse-led patient-reported outcome measure model of care in paediatric oncology: the KidsVoice Stage 2 pilot.

Matthew Koh, Joanna Fardell, Sarah Ellis

University of New South Wales, Behavioural Sciences Unit

Background: Patient-reported outcome measures (PROMs) are age-appropriate surveys capturing children's own symptom experiences, complementing clinician and caregiver-reports. Despite improving outcomes in adult-settings, paediatric implementation remains inconsistent. KidsVoice is a co-designed, nurse-led PROM model of care addressing this gap in paediatric oncology.

Methods: In this single-centre, mixed methods, pre-post implementation feasibility pilot, families, recruited from the Kids Cancer Centre, Sydney Children's Hospital, completed baseline and six-month follow-up surveys. Measures assessed healthcare satisfaction and supportive care utilisation (YHC-SUN/CHC-SUN), health-related quality of life (CHU9D, EQ-5D-5L), distress (Emotion Thermometer), barriers to psychosocial support, and carer-rated feasibility and acceptability of the PROM process.

Results: Twenty-seven carers and six patients completed baseline surveys; three carers completed follow-up. Most patients were under four years (48.1%), and the most common diagnosis was leukaemia (55.6%). Carer-rated child quality of life was lower than children's own rating (CHU9D index 0.426 vs 0.561). Most carers (70.4%) reported psychological distress despite strong overall satisfaction with care. Psychological counselling was the greatest unmet need (60.0%), and "not knowing where to look or who to ask" was the most common barrier to psychosocial support (81.5%). The PROM process was rated feasible and acceptable at follow-up (n=3).

Conclusion: This nurse-led PROM model of care proved feasible and acceptable, capturing actionable data on family-reported quality of life, distress and psychosocial need. The link between carer distress and unmet psychological support needs reflects both a resource shortage and difficulty navigating existing services, warranting evaluation at scale, with potential to identify unmet needs more broadly across paediatric oncology.

Applicant: Janelle Lee
Supervisor: Dr Jennifer Hudson

Toxigenic *Clostridioides difficile* in children with Cystic Fibrosis.

Janelle Lee (1) , Jennifer Hudson (1), Josie van Dorst (1), Michael Coffey (1, 2) and Chee Y. Ooi (1, 2)

1. School of Clinical Medicine, Discipline of Pediatrics and Child Health, UNSW Medicine and Health, The University of New South Wales, Sydney, Australia.
2. Department of Gastroenterology, Sydney Children's Hospital, Randwick, Australia.

Background: *Clostridioides difficile* (*C. difficile*) infection is a globally significant healthcare-associated gastrointestinal infection, strongly linked to antibiotic and healthcare exposure. Cystic Fibrosis (CF) is a disease characterised by higher *C. difficile* carriage rates in adults¹, however, colonisation patterns in children with CF (cwCF) remain incompletely understood. This study investigated the prevalence and abundance of *C. difficile* in 50 cwCF and 50 healthy controls (HC). *C. difficile* and toxin gene carriage were assessed by targeted PCR, with microbial diversity and composition assessed using 16s rRNA amplicon sequencing.

Methods: *C. difficile* detection did not differ between CF (32%) and HC (42%; $p=0.42$), despite higher relative abundance in CF. Among carriers, 37.5% of CF and 47.6% of HC harboured toxigenic *C. difficile* ($p=0.74$). Majority of toxin-positive participants encoded for the *tcdA* gene (less potent variant) (CF: 66.7%; HC: 100%), however, two cwCF additionally carried the *tcdB* gene (more potent variant). Moreover, *C. difficile* presence was associated with reduced intestinal alpha-diversity (CF: $p<0.05$; HC: $p<0.002$) and altered microbial community composition (CF: $p=0.04$; HC: $p=0.009$).

Results: Despite higher *C. difficile* abundance, carriage and toxigenicity were not higher in CF. However, dual *tcdA/B* gene carriage in CF could indicate higher infection risk, warranting further investigation. Diversity analyses suggest that reduced intestinal microbial diversity may support *C. difficile* colonisation in both CF and HC cohorts, with *C. difficile*-associated microbiome interactions more pronounced in HC.

Conclusion: Together, these results demonstrate that *C. difficile* is associated with gut microbiome profiles, facilitating future risk stratification and microbiome-targeted prevention strategies in children.

References:

1. Bauer, M. P., Farid, A., Bakker, M., Hoek, R. A., Kuijper, E. J., & van Dissel, J. T. (2014). Patients with cystic fibrosis have a high carriage rate of non-toxigenic *Clostridium difficile*. *Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases*, 20(7), 0446–0449. <https://doi.org/10.1111/1469-0691.12439>

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Supervisor: Dr Jennifer Hudson

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POSTER

Results: A total of 104 eligible responses were received from practitioners working across 16 countries in the region. Most responders (83%) were paediatric gastroenterologists and 70% of respondents completed 100% of the survey. Significant variation was found in PAP management across the region, particularly regarding fluid resuscitation and nutritional protocol, demonstrating notable divergence from non-Asia Pacific guideline recommendations. There were also substantial practice disparities between high- and middle-income respondents, concerning time to obtain diagnostic tests and imaging, time to transfer patients, frequency of lab repeats, and extent of diagnostic and aetiological investigation. The most common constraints affecting PAP care included cost and financial burden of treatment, access to genetic testing and therapeutic interventions, and logistical challenges accessing adult services.

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Applicant: Mia Rutherford
Supervisor: Dr Michael Coffey

Management of paediatric acute pancreatitis in the Asia Pacific region: An international survey.

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Background: Paediatric acute pancreatitis (PAP) has a rising global incidence and significant morbidity (1,2). There are currently published North American, British, and European PAP guidelines as well as adult acute pancreatitis (AP) guidelines; however, it is unknown if clinical practice in the Asia Pacific region follows or diverges from this guidance.

Methods: This was a cross-sectional survey study, assessing self-reported clinical practice approaches to PAP of practitioners managing the condition in the Asia Pacific region, including Australia. The survey was distributed electronically, and responses were recorded between March and April 2026. Respondents were grouped into high- and middle-income cohorts based on the FY27 World Bank Group country classification by income level. Statistics were performed using R 4.5.3.

Applicant: Chiara Speranza
Supervisor: Dr Jennifer Hudson

Toxigenic *Clostridioides difficile* in children with Cystic Fibrosis.

Janelle Lee (1) , Jennifer Hudson (1), Josie van Dorst (1), Michael Coffey (1, 2) and Chee Y. Ooi (1, 2)

1. School of Clinical Medicine, Discipline of Pediatrics and Child Health, UNSW Medicine and Health, The University of New South Wales, Sydney, Australia.
2. Department of Gastroenterology, Sydney Children's Hospital, Randwick, Australia.

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Methods: *C. difficile* detection did not differ between CF (32%) and HC (42%; $p=0.42$), despite higher relative abundance in CF. Among carriers, 37.5% of CF and 47.6% of HC harboured toxigenic *C. difficile* ($p=0.74$). Majority of toxin-positive participants encoded for the *tcdA* gene (less potent variant) (CF: 66.7%; HC: 100%), however, two cwCF additionally carried the *tcdB* gene (more potent variant). Moreover, *C. difficile* presence was associated with reduced intestinal alpha-diversity (CF: $p<0.05$; HC: $p<0.002$) and altered microbial community composition (CF: $p=0.04$; HC: $p=0.009$).

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Conclusion: Together, these results demonstrate that *C. difficile* is associated with gut microbiome profiles, facilitating future risk stratification and microbiome-targeted prevention strategies in children.

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Applicant: Sarah Choo
Supervisor: Dr Yoshiro Okubo

Investigating Factors Associated with Impaired Reactive Balance in Parkinson's Disease

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Outdoor trips and slips are a major source of injury for people with Parkinson's Disease (PD), contributing to substantial burdens on individuals, caregivers and healthcare systems¹⁻⁴. Although reactive balance is critical for preventing falls after sudden perturbations, its mechanisms underlying impairment in PD remain poorly understood. We hypothesised associations between reactive balanced impairments and deficits in complex stepping tasks requiring motor-cognitive integration. In this laboratory-based cross-sectional study, 49 people with PD completed assessments to identify factors associated with impaired reactive balance following an obstacle-induced perturbation. Candidate predictors encompassed demographics, disease characteristics, physical activity, fall history, psychological and cognitive measures, mobility, physiological profiling and combined cognitive-motor abilities (visual-motor processing, inhibitory stepping and volitional stepping). Reactive balance was evaluated using a trip-and-slip paradigm designed for ecological validity, with falls defined as >30% of body weight loaded onto a safety harness. Poisson regression models were fitted for each predictor and subsequently adjusted for age and sex. 45% of participants experienced no falls, 39% had one fall, and 16% had two falls. Inhibitory choice stepping mistakes were significantly associated with reactive balance impairment (RR:1.16, 95% CI: 1.01-1.33, $p = 0.040$), independent of age and sex (RR 1.22, 95% CI 1.03-1.43, $p = 0.018$). No other candidate predictors demonstrated significant associations. These findings indicate that increased errors in inhibitory choice-stepping are independently associated with higher rates of perturbation-induced falls. This provides new insight into cognitive-motor contributors to reactive balance impairment, suggesting go/no-go trials as a measure of reactive balance.

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Applicant: Qawiem Hamid
Supervisor: Dr Mei Ling Lim

Concerns About Falling Among Older Adults Participating In Intergenerational Activities

Concerns about falling (CaF) are common among older adults and may contribute to activity restriction in daily activities. Intergenerational programs provide opportunities for physical and social engagement, but little is known about how older adults with CaF navigate these settings. This study explored how older adults with CaF experienced and managed participation in an intergenerational program.

A qualitative study was conducted among older adults who had participated in a 20-week intergenerational program delivered in Sydney preschools. Potential participants completed a telephone screening, and those with CaF during the program were invited to participate in a semi-structured interview. Interviews were audio-recorded, transcribed and analysed using inductive reflexive thematic analysis. Eleven participants with CaF or balance-related concerns were recruited. Four themes were identified: (1) balancing participation with awareness of fall risk; (2) navigating a dynamic intergenerational environment; (3) supportive environment enabled safe participation; and (4) benefits extended beyond the program.

Participants described an awareness of fall risk rather than CaF preventing participation. They adapted their movement in response to the children's unpredictable movements, environment and activity specific demands. Educator, peer and child support, together with increasing familiarity, helped participants manage these challenges. Participants also described enjoyment, social connection, greater confidence and awareness of their physical capabilities. Intergenerational programs may enable older adults with CaF to remain physically and socially engaged despite existing CaF. Future programs may benefit from screening older adults for CaF, equipping educators to provide tailored support, and linking participants with targeted falls-prevention or exercise services where needed.



Applicant: Avigayil Erlich
Supervisor: Dr Steve Kassem

Machine vs Human: Capacity of Automatic Segmentation on In Vivo MR Images of Human Subcortex

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Automatic segmentation pipelines are increasingly used in place of manual subcortical segmentation. Many integrate deep-learning modules, suggesting their potential for individually adapted, bespoke outputs rather than fixed, template-based segmentation (1). It was hypothesised that segmentation volumes would vary significantly between pipelines and from manual reference volumes, and that resolution would disproportionately affect smaller structures.

T1-weighted MRI was acquired from eleven young healthy adults: ten from the Human Connectome Project (5M/5F, 1.0 mm isotropic), and one male scanned in-house at ultra-high resolution (0.25 mm isotropic). All scans underwent segmentation via FreeSurfer Recon-all Clinical, NextBrain, and FSL FIRST, and compared with published manual reference volumes. Additionally, the ten HCP scans were segmented via FSL MIST, trained separately on male-only, female-only, and mixed-sex cohorts to explore whether training-sex composition altered the output. Repeatability was evaluated by duplicating one scan tenfold across the first three pipelines.

All four pipelines showed significant volumetric divergence across nearly all structures. NextBrain's brainstem and substantia nigra were about half their expected size. Resolution significantly impacted smaller structures more than larger ones. Automatic output diverged from manual volumes in 14 of 15 comparisons. FSL MIST's results varied with training-sex composition, a pattern also observed in NextBrain, highlighting sex-based thalamic differences (2). Recon-all Clinical, NextBrain, and FIRST produced identical outputs in ten repeat trials.

These findings indicate that automated pipelines produce deterministic yet substantially divergent outputs, questioning their readiness for clinical use, particularly when training data may not represent sex-based anatomical variation.

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Applicant: Kelly Chen
Supervisor: Professor Angela Chiew

ABSTRACT: Is More NAC Better? High-Dose Acetylcysteine in High-Risk Paracetamol Overdose

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Background: High-risk paracetamol overdose, defined by large ingested doses (≥ 30 g) or paracetamol concentrations ≥ 2 times the treatment nomogram, is associated with increased risk of hepatotoxicity despite acetylcysteine treatment. Australian and international guidelines recommend increased acetylcysteine dosing in these patients; however, evidence supporting improved outcomes remains limited and conflicting.

Methods: Retrospective observational study using two prospectively maintained clinical toxicology data sources: the New South Wales Poisons Information Centre (NSW PIC) and South Eastern Area Toxicology Service (SEATS). Patients with acute immediate-release paracetamol ingestion meeting either high-risk criterion were included. The primary outcome was hepatotoxicity (ALT >1000 U/L). Associations between standard- and high-dose acetylcysteine and hepatotoxicity were examined separately for patients with ingested dose ≥ 30 g and paracetamol ratio ≥ 2 using Firth logistic regression.

Results: Among 238 patients, 22 (9.2%) developed hepatotoxicity. Acetylcysteine was commenced in 228 (95.8%), at a median 6.5 h post-ingestion. High-dose acetylcysteine was not associated with reduced hepatotoxicity in patients ingesting ≥ 30 g (OR 1.80, 95% CI: 0.57–6.00) or with paracetamol ratio ≥ 2 (OR 0.46, 95% CI: 0.16–1.50). Delayed acetylcysteine and elevated ALT at presentation were strongly associated with hepatotoxicity. Among patients with ratio ≥ 2 , receipt of acetylcysteine dosed according to paracetamol ratio was associated with lower hepatotoxicity, although event numbers were small.

Conclusion: High-dose acetylcysteine was not associated with reduced hepatotoxicity. Early treatment remained important, while the potential benefit of ratio-directed acetylcysteine dosing warrants evaluation in larger cohorts.



Applicant: Brielle Wenham
Supervisor: Associate Professor Betty Chan

Opioid Toxicity with Nyxoid use and distribution in the South-Eastern Area Toxicology Service: A retrospective cohort study

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Objective: Nyxoid is an intranasal formulation of naloxone that is distributed by various healthcare services alongside education to those at risk of opioid overdose. This study aimed to observe the pattern and clinical presentation of opioid poisoning alongside Nyxoid distribution in this cohort of patients.

Methods: A total of 719 opioid overdose presentations from the South-Eastern Area Toxicology Service REDCap database from February 2020 to April 2026 was analysed. Further supporting data was extracted from the Electronic Medical Records. A Fisher's test was used to determine if an association existed between the five most frequently implicated opioids and naloxone treatment.

Results: Self-harm presentations were the most common (42.3%) with the majority occurring in women (58.9%) using oxycodone. Recreational presentations closely followed this (39.2%) with the majority occurring in men (76.2%) who used heroin. Heroin was the most reported opioid (30.3%) and contributed to 8 of the 10 opioid related deaths. Community administered Nyxoid use occurred in 36 patients who all survived with 34 cases involving heroin. Nyxoid was only distributed to 143 patients (19.9%) on discharge.

Conclusions: Of the patients who received Nyxoid in the community, none died from their opioid overdose despite 34 cases involving heroin. In contrast, 80% of the patients who died were exposed to heroin. There is an urgent need to improve Nyxoid access to the community to prevent opioid related deaths.



Applicant: Ethan Heng
Supervisor: Associate Professor Betty Chan

Recreational Drug-Induced Hyperthermia: A Retrospective Observational Study

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Objectives: Recreational drug-induced hyperthermia (RDIH) is a severe complication of stimulant toxicity, but evidence is largely confined to case reports and prognostic temperature thresholds remain undefined. This study characterised RDIH presentations to New South Wales EDs and examined the relationship between temperature and major complications.

Methods: Retrospective multi-centre cohort study of patients presenting to 15 NSW hospitals between January 2020 and June 2026 with a temperature of $\geq 38.0^{\circ}\text{C}$ following recreational stimulant exposure. Primary outcomes were the associations of peak temperature and hyperthermia duration with major complications.

Results: Of 115 presentations identified, 110 were included. Major complications occurred in 49 (45%) and five patients (4.5%) died. Two distinct populations emerged. Forty presentations (36%) were festival-associated, where on-site medical services are typically present; these patients were younger (median 23 vs. 31 years), almost exclusively involved MDMA (90% vs. 26%), and were less often at peak temperature on arrival (20% vs. 72%). Among non-festival presentations, the odds of a major complication rose 5.5-fold per 1°C increase in peak temperature in peak temperature (OR 5.48, 95% CI 2.61-15.34), and peak temperature identified major complications well (AUC 0.86), with a discriminating threshold of 39.2°C . In festival presentations it performed no better than chance (AUC 0.55; difference between settings $p = 0.006$).

Conclusion: RDIH was associated with substantial morbidity and mortality. Peak temperature predicted major complications in non-festival but not festival-associated presentations. Complications occurred below the 39°C threshold used to define severe hyperthermia, supporting early cooling and repeated temperature measurement.



Applicant: Alma Liu
Supervisor: Professor Angela Chiew

Novel Biomarkers of Liver Injury Following Paracetamol Overdose (ATOM-15)

Alma Liu, Professor Angela Chiew, Professor Nicholas Buckley Department of Clinical Toxicology, Prince of Wales Hospital, Randwick, NSW, Australia Faculty of Medicine, The University of New South Wales, Sydney, New South Wales, Australia New South Wales Poisons Information Centre, Sydney Children's Hospital, Sydney, New South Wales, Australia Pharmacology, Faculty of Medicine and Health, University of Sydney, Sydney, Australia

Introduction: Paracetamol overdose is a leading cause of acute liver failure. Alanine aminotransferase (ALT), the conventional biomarker of hepatocellular injury, typically rises after significant liver injury and lacks specificity to paracetamol toxicity. Novel biomarkers may allow earlier identification of patients at risk of liver injury following paracetamol overdose.

Methods: This was a biomarker sub-study of the Australian Toxicology Monitoring (ATOM) multicentre prospective observational study of paracetamol overdose. Stored serum was available from a subset of participants, including those with modified-release overdose, acute liver injury, or large ingestions. Up to three samples collected within 24 hours of presentation were analysed for glutamate dehydrogenase (GLDH), caspase-cleaved cytokeratin-18 (CCK-18), full-length cytokeratin-18 (FLK-18), microRNA-122 (miR-122), and high-mobility group box 1 (HMGB1). The primary outcome was hepatotoxicity, defined as peak ALT ≥ 1000 U/L. Initial and peak biomarker concentrations were evaluated against hepatotoxicity and peak INR.

Results: Seventy-nine patients provided 463 serum samples; 18 (23%) developed hepatotoxicity. Initial concentrations of all five biomarkers were significantly higher in patients with hepatotoxicity (all $p < 0.0001$), with miR-122 showing the greatest discrimination for hepatotoxicity (AUROC 0.956), followed by HMGB1 (0.947), FLK-18 (0.933), CCK-18 (0.922), and GLDH (0.921). Initial HMGB1, miR-122, FLK-18 and CCK-18 concentrations were also significantly higher in patients who subsequently developed hepatotoxicity. Peak biomarker concentrations were associated with peak INR.

Conclusion: Novel biomarkers of hepatocyte injury, particularly miR-122 and HMGB1, were strongly associated with hepatotoxicity following paracetamol overdose. Further studies are required to determine whether these biomarkers have a role in clinical practice.



Applicant: Beattie Sexton
Supervisor: Associate Professor Linda Martin

Resolving clinical complexity with high-dimensional imaging: distinct immune endotypes underlie diverse cutaneous toxicities of immune checkpoint blockade in melanoma

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Cutaneous toxicities (CUTOX) are the most common toxicity of immune checkpoint blockade (ICB) in melanoma. (1) Despite their clinical diversity, guidelines recommend systemic corticosteroids regardless of specific features, which may impair treatment outcomes (2,3). As a structured, immunologically rich, and accessible organ, skin is well suited to spatial approaches that characterise cell states and interactions within microenvironments.

We hypothesised distinct endotypes underlie diverse CUTOX phenotypes and mapped the immune landscape of 10 common CUTOX using a 5,000-gene Xenium spatial transcriptomics panel and multiplexed protein detection by Imaging Mass Cytometry (IMC).

We profiled lesional and control skin from 84 patients in a single-centre prospective cohort. Two dermatologists defined phenotypes by consensus using distribution, morphology and clinicopathological correlation. Pathologist-selected regions were incorporated into tissue microarrays, and Xenium and IMC were performed on the same tissue section. Cellular phenotypes, densities, and potential functions were determined. Analysis was performed in Python using standard univariate and multivariate statistics.

Profiling of 78 cell clusters revealed distinct immune profiles associated with CUTOX ($R^2=0.32$, $p=0.0002$), comprising multicellular endotypes with varying combinations and densities of innate and adaptive immune cells. A novel Th1/Th2 bias score segregated CUTOX phenotypes; Th2-skewing correlated with pruritus ($p=0.0002$). ICB treatment type had minimal impact on the immune repertoire ($R^2 = 0.08$, $p = 0.22$). IMC validation and analyses of spatial niches, cell states and cell-cell interactions are ongoing.

The clinicopathological diversity of CUTOX appears to reflect distinct endotypes, with T helper differentiation a major determinant of phenotype, irrespective of ICB treatment class. Our Th1/Th2 bias score appears to correlate with symptom burden, suggesting steroid-sparing therapies targeting Th2 pathways may improve management of pruritic CUTOX.

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