Abstract Book

Alfred Health Research Week Scientific Abstract Competition

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Table of Contents

ALLERGY, ASTHMA & CLINICAL IMMUNITY

1.

ANTIBODY RESPONSES AND B-CELL MEMORY FORMATION AFTER COVID-19 VACCINATION IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY

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Background: Primary immunodeficient (PID) patients may have poor vaccination responses and susceptibility to infections including COVID-19. We evaluated the SARS-COV-2-specific IgG and memory B-cell (Bmem) responses following COVID-19 vaccination.

Methods: 25 PID patients and 29 healthy controls were sampled one-month after doses two and three of the COVID-19 vaccination. Live virus neutralization was performed for neutralising antibody (Nab) titers. Using recombinant spike receptor-binding domains (RBD), we analysed plasma IgG by ELISA and Bmem by flowcytometry directed against ancestral and Omicron variants.

Results: Regardless of mRNA or adenoviral vector vaccine priming, ancestral RBD-specific IgG levels and Nab titers were significantly lower in PID patients than controls after both doses, with minimal boosting at dose 3. Cross-recognition of omicron variants by ancestral RBD-specific IgG and Nab titers to Omicron BA.5 were lower in patients than in controls after both doses. However, responses were boosted at dose 3 in both cohorts.

Furthermore, despite normal total Bmem numbers, numbers of ancestral RBD-specific Bmem were lower in patients than in controls at both time points, with reduced cross-recognition of both Omicron BA.2 and BA.5.

Lower numbers of ancestral RBD-specific IgG- and IgA-expressing Bmem were observed in patients compared to controls, which could explain the lower Nab titers measured in patients.

Conclusions: Together, these findings highlight impaired SARS-CoV-2-specific humoral responses in PID patients and support that Bmem numbers may represent a better marker of immune competence. Work is ongoing to assess functional competency of the T-cell compartment to accurately assess whether each individual patient has elicited a response to vaccination.

2.

SIGNIFICANCE OF INDUCIBLE LARYNGEAL OBSTRUCTION PHENOTYPES IDENTIFIED BY LATENT CLASS ANALYSIS

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Background: Inducible laryngeal obstruction (ILO) is characterised by symptomatic inappropriate adduction of the vocal cords during respiration. There is a spectrum of clinical ILO presentations, and it is unknown whether this heterogeneity reflects pathogenesis or natural history. We aimed to objectively identify clinically relevant ILO phenotypes.

Methods: We included consecutive patients assessed between March 2016 and September 2023 with laryngoscopy evidence of ILO. Patients were analysed using latent class analysis (LCA) by; age, self-reported symptom triggers, and comorbidities. LCA models were assessed by statistical criteria and for clinical plausibility. ILO phenotypes from the selected model were compared by clinical course, laryngoscopy findings, and patient-reported outcomes.

Results: LCA of 192 ILO patients identified four phenotypes labelled by predominant clinical characteristics. Isolated ILO (32.8%,n=63), characterised by inhaled and airborne triggers without comorbidities; hyperventilation-associated ILO (41.7%,n=80) characterised by hyperventilation, anxiety, sinonasal disease and triggered by inhaled and airborne exposures; polymorbid ILO (18.2%,n=35) characterised by anxiety, sinonasal disease, lower airway obstruction, obesity and gastroesophageal reflux; and pseudo allergic ILO (7.3%,n=14) characterised by patient-presumed exposure to an allergen in the absence of specific IgE sensitization. Polymorbid ILO was associated with higher Vocal Cord Dysfunction Questionnaire, higher Chemical Sensory Hyperreactivity and lower Laryngeal Hypersensitivity Questionnaire scores, and expiratory phase-limited ILO (all $p<0.01$). Pseudo allergic ILO had the shortest duration of illness ($p=0.05$) and was least likely to respond to laryngeal retraining ($p=0.02$).

Conclusions: Four identified ILO phenotypes with heterogenous and distinct clinical characteristics are further differentiated by clinical course and laryngoscopy providing support for distinct pathogenic pathways in ILO.

3.

REDUCED IMMUNE COMPETENCE TO SARS-COV-2 VACCINATION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE RECEIVING ANTI-TNF TREATMENT

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Background: Booster vaccinations are recommended to improve protection against SARS-CoV-2 (COVID-19) infection, particularly in people with a compromised immune system. These people may generate poor antibody responses to vaccination, however the memory B cell response is not well defined. Here, we assessed immune competence to SARS-CoV-2 booster vaccination, evaluating the capacity and durability of the antibody and memory B cell response in patients receiving anti-TNF treatment.

Methodology: Peripheral blood was sampled before, 1 month and 6 months post booster vaccination in healthy controls and 23 patients with inflammatory bowel disease (IBD) receiving intravenous Infliximab. SARS-CoV-2 recombinant spike receptor binding domain (RBD) proteins from ancestral, Omicron BA.1, BA.5, XBB.1.5 and JN.1 variants were produced for ELISA-based serology to determine RBD-specific IgG antibody levels and tetramerised for immunophenotyping of memory B cells (MBCs) using flow cytometry

Results: Ancestral-RBD specific IgG levels in patients were significantly increased from pre to 1-month post but declined after 6 months to be similar to pre-vaccination levels and significantly lower than controls. Variant specific IgG as a proportion of total ancestral-RBD specific IgG significantly increased from pre to 1-month post booster vaccination in patients but was significantly lower than controls. The proportion of variant specific IgG declined after 6 months in patients and was significantly lower than controls. Absolute numbers of MBCs in patients increased from pre to 1-month post vaccination but were still significantly lower than controls.

Conclusion: Infliximab treated IBD patients have reduced capacity to generate antibodies and memory B cells in response to SARS-CoV-2 booster vaccination compared to healthy controls. Antibody responses in patients have limited durability and are diminished against recent variants. This preliminary data suggests that overall immune competence is reduced in patients, however further Immunophenotyping of RBD-specific memory B cells is ongoing to assess durability at 6 months post vaccination.

4.

ACCURATE DIFFERENTIAL DIAGNOSIS OF ALLERGEN SENSITIZATION IN PATIENTS WITH ASTHMA AND ALLERGIC RHINITIS WITH A SINGLE MULTIPLEX CYTOBAS ASSAY INCLUDING 8 MAJOR COMPONENTS

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BACKGROUND: Allergic rhinitis and asthma can be triggered by a variety of aeroallergens, including from house dust mites (HDM), grass pollen, and household pets (cat and dog). Correctly identifying the relevant allergen is critical for lifestyle changes and treatments including allergen immunotherapy. We here assessed the diagnostic performance and clinical utility of basophil staining to major aeroallergen components in a single flow cytometry assay (AeroDiff CytoBas).

METHODS: In 156 atopic patients with allergic rhinitis/asthma and 21 non-atopic individuals, allergen-specific IgE levels were determined by ImmunoCAP™, and component-specific IgE by ELISA to Der f 1, Der p 1, Der p 2, Lol p 1, Lol p 5, Phl p 1, Fel d 1 and Can f 1. PBMCs were analyzed by flow cytometry with basophils markers and the eight fluorochrome-conjugated allergen component tetramers.

RESULTS: Patients were stratified by ImmunoCAP™ for sensitization to each of the four allergens. Allergen-component staining in a single multiplex CytoBas assay and component-specific IgE serology performed similarly for Der p 2, Lol p 1, Fel d 1, and Can f 1 (ROC AUC: 0.76-0.97 vs. 0.73-0.93). CytoBas had greater diagnostic accuracy than component-specific IgE serology ($p<0.001$) for HDM sensitization using Der f 1 or Der p 1, and grass pollen using Lol p 5 or Phl p 1. Furthermore, the combined evaluation of Der p 1 and Der p 2 with CytoBas was 96.3% sensitive and 90.7% specific for HDM sensitization. Combined evaluation of Lol p 1 and Lol p 5 achieved 95.4% sensitivity and 96.4% specificity for ryegrass pollen sensitization.
CONCLUSION: AeroDiff CytoBas has similar to superior diagnostic accuracy than singleplex IgE serology, with the additional advantage of a single assay to evaluate multiple allergens. This enables precise and efficient component-resolved diagnosis of aeroallergen sensitization to guide personalized treatment for patients with allergic rhinitis and/or asthma.

5.

EARLY-LIFE BACTERIAL DYSBIOSIS DRIVES SYSTEMIC IMMUNE ALTERATIONS IN CHILDREN WHO HAVE WHEEZED IN EARLY-LIFE

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The first year of life is a critical period during which the infant's airways are colonised by a dynamic microbial community made of bacteria, fungi, and viruses. How this early colonisation shapes the developing immune system and its potential consequences for respiratory diseases remains largely unknown.

AIM: We aimed to investigate the role of multiple microbial kingdoms (bacteria, fungi, and viruses) in shaping both local (nasal) and systemic (blood) immune responses in infants, comparing those who wheezed in their first year of life to healthy controls.

METHODS: We conducted a longitudinal analysis of 256 infants from the *Breathing Together* birth cohort, with samples collected from birth to 1 year of age. Using a multi-omics integrative approach, we combined bacterial and fungal nasal amplicon sequencing, viral profiling via qPCR, and immune gene expression profiling from both nasal (local) and blood (systemic) samples. This comprehensive integration allowed us to investigate the relationships between microbial communities and immune responses across multiple microbial kingdoms.

RESULTS: Infants with a history of wheezing exhibited significant nasal bacterial dysbiosis, predominantly driven by *Haemophilus influenzae* and *Moraxella*, with no notable changes in fungal or viral communities. Remarkably,

this dysbiosis was evident even in the absence of respiratory symptoms. This bacterial imbalance was strongly associated with both local and systemic immune alterations, characterised by an upregulation of monocyte-related genes in both nasal and blood samples.

CONCLUSION: This study sheds new light on how airway bacterial dysbiosis, rather than fungal or viral shifts, can shape both local and systemic immune responses in wheezing infants, even in the absence of symptoms. These insights could pave the way for targeted early interventions aimed at modulating the airway microbiota to prevent respiratory diseases.

ALLIED HEALTH

6.

ESTABLISHING THE SAFETY, EFFICACY AND VALUE ADD OF A PHYSIOTHERAPY LED TRAUMA TERTIARY SURVEY

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INTRODUCTION: The Trauma Tertiary survey (TTS) is an essential part of trauma patient care and aims to identify injuries not diagnosed on primary or secondary survey. This ensures appropriate and timely management before hospital discharge and has been found to reduce rates of missed injuries, which in turn may improve patient outcomes.

METHODS: Most TTS are completed by junior medical staff and/or specialist trauma nurses. This project aimed to provide additional training and supervision for experienced senior trauma physiotherapists to complete TTS within a shared model of care. Delayed diagnoses (found >48 hours after patient admission), missed injuries (found after TTS) and outcomes of any injuries found were compared between baseline (six months), and the Physiotherapy led TTS service (12 months).

RESULTS: The number of reportable delayed diagnoses were 38 at baseline and 57 during the project, of which 13 were found on Physiotherapy led TTS (since most TTS were completed within 48 hours). There were 120 injuries found on Physiotherapy led TTS, with the majority undergoing a specialist team review (n=86) and eight requiring surgery. Some of these injuries have not been well recognised in previous TTS literature (such as acromioclavicular joint injuries, post traumatic vertigo and rotator cuff injuries). Other benefits and learnings from the role will be discussed.

CONCLUSIONS: This project used an innovative model of care to train experienced trauma physiotherapists in TTS completion. It was found to be safe, effective and well supported by the trauma medical and nursing teams.

7.

IS THE HOME SUPPORT NEEDS ASSESSMENT USEFUL FOR CARE PLANNING WITH COMMUNITY-LIVING OLDER ADULTS RECEIVING HOME CARE PACKAGES?

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Introduction: Government funded Home Care Packages (HCP) support older adults to live at home. The Home Support Needs Assessment (HSNA) was recently introduced for routine use by case managers from varied health professions to inform development of HCP care plans by identifying older adults' support needs for community living.

Objectives: To (1) describe how the HSNA data aligned to HCP care plans documented in the medical records and (2) explore the usefulness of the HSNA to case managers in assessing the support needs of older adults with HCPs.

Method: A parallel mixed methods research design was used. Quantitative data were collected and analysed descriptively from completed HSNAs and HCP client care plans. Qualitative data were gathered through semi-structured interviews with case managers. Interview transcripts were analysed using Braun and Clarke's reflexive thematic analysis.

Results: HSNA data (N=32) from initial HCP assessments were collected. HSNA scores were higher for older adults whose current supports were perceived as inadequate ($p<0.001$) and not sustainable ($p=0.006$). There was >80% consistency between HSNA item scores and care plan intervention for 18 of the 27 items. Three themes were developed from qualitative data: Introducing the HSNA has benefits; It's great in theory but... and; It's most helpful for complex cases.

Conclusion: The HSNA can be used to determine support needs for older adults living in the community and is particularly beneficial for those with complex needs. This assessment tool can be useful as a learning and teaching tool for case managers.

8.

CURRENT EVIDENCE-BASED PRACTICES AND CLINICAL DECISION-MAKING FOR UPPER LIMB REHABILITATION AFTR TRAUMATIC BRAIN INJURY

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Introduction
Upper limb (UL) motor impairment is common after traumatic brain injury (TBI). Due to recovery-related factors and the complexity of impairment, the provision of rehabilitation after TBI can be challenging, and an Australian guideline is lacking. UL rehabilitation practices nationally remain largely unknown.

Objective
To understand UL rehabilitation practice parameters, factors influencing clinicians' decision-making and implementation of best-practice guidelines when working with adults with TBI across the recovery continuum.

Methods
A within-participant case-cross-over, online survey was conducted. Three case studies were included, and a mixed-effect regression statistical analysis was performed. Snowball recruitment occurred via social media and professional contacts. Australian allied health clinicians (occupational therapists, physiotherapists, assistants) working with people with TBI were invited to participate in the survey.

Results
110 consented and commenced the survey; of these 71% were Occupational Therapists. On average, clinicians (n=71) reported commencing UL rehabilitation in the acute hospital setting within 7 days post-injury. Clinicians (n=93) described providing an average of 39 minutes of UL rehabilitation per day, and 8 sessions per week. Compared to current international best-practice guidelines, inconsistencies were identified with interventions. Clinician and assistant availability were the most common factors influencing decision-making.

Conclusions
Our survey showed that current UL rehabilitation practice following TBI in Australia varies and does not consistently adhere to guidelines. Clinicians report resourcing as a major barrier to delivery. Future research should consider multi-component strategies to manage common recovery-related factors that influence therapy provision. Developing Australian TBI guidelines may assist in providing recommendations about UL rehabilitation.

9.
GIVING VOICE TO THE VENTILATED: ALFRED ICU GETS IN-LINE

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Introduction: Communication in mechanically ventilated patients is very restrictive. Depression, amotivation and poor adherence to recommendations have been reported in patients unable to verbally communicate. In tracheostomised patients, the introduction of a one-way valve (OWV) to the ventilator circuit with the cuff deflated, redirects the expiratory flow via the upper airway allowing restoration of voice. In-line OWVs are associated with improvements in quality of life, however, were not in use at The Alfred prior to February 2023.

Objectives: To establish in-line OWVs for patients ventilated via a tracheostomy to facilitate earlier verbal communication in The Alfred ICU.

Methods: Two Plan-Do-Study-Act (PDSA) cycles were completed to support the establishment of in-line OWVs as standard practice. In PDSA cycle one, a multidisciplinary team was formed to determine safety of new practice. Progression to OWV trials on four ICU patients was completed. Results were used to refine guidelines for practice. PDSA cycle two was then conducted to establish OWVs as standard ICU practice with the revised guidelines. Outcome measures were collected via review of medical records and included: (1) number of in-line OWV sessions per patient, (2) time to verbal communication post tracheostomy insertion, and (3) number of adverse events.

Results: In PDSA cycle one, four patients completed 15 sessions with no adverse events.
In PDSA cycle two, 20 patients completed 111 sessions; median of 3.5 sessions (IQR: 2-8) per patient. Median time to verbal communication was six days (IQR 4-15); an eight day decrease from baseline practice. Four patients died prior to liberation from ventilation. Five minor adverse outcomes were recorded.

Conclusion: Introduction of in-line OWVs has provided patients with access to verbal communication significantly earlier than previous practice. It has also afforded communication opportunities to patients who are not liberated from ventilation. A third PDSA cycle will support training of nursing staff.

10.

OUTCOMES FOLLOWING INTENSIVE ALLIED HEALTH THERAPY IN THE ACUTE HOSPITAL FOR TRAUMA PATIENTS

Lara Kimmel

The majority of patients hospitalised for trauma survive their injuries, with the quality of the survival potentially influenced by early acute hospital rehabilitation. The aim of this study was to review the outcomes of patients managed under an intensive Allied Health Model of Care (AHMOC) compared to a baseline cohort.

Methods: The AHMOC was established in February 2020 on the Trauma ward at Alfred Health for 12 months. The baseline group included patients admitted to the trauma ward in 2019. All patients who were registered by either the Victorian Orthopaedic Trauma Outcomes Registry (VOTOR) or the Victorian State Trauma Registry (VSTR)The association between care group and outcomes were assessed using logistic (discharge destination, 12-month return to work) and linear (length of stay (LOS)) regression.

Results: There were 1644 in the baseline group and 1732 in the AHMOC group. After accounting for confounders, the adjusted odds of discharge home and RTW at 12 months were 53% (AOR 1.53 95% CI 1.29, 1.82) and 65% (AOR 1.65 95% CI 1.24) higher for the AHMOC group compared to baseline, respectively. There was also a 6% reduction in the LOS in the AHMOC group compared to baseline (Adjusted mean difference 6%; 95% CI (0.881, 0.999) p value = 0.050).

Conclusion: The availability of early and intensive allied health should be considered in the development of future trauma models of care and guidelines given these positive hospital based and 12 month outcomes.

11.

THE EFFECTIVENESS AND FEASIBILITY OF THE IMPLEMENTATION OF A NON-WEIGHT BEARING (NWB) COORDINATOR WITHIN ALFRED HEALTH – A SCOPING REVIEW

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Background: Emerging evidence suggests that early weight bearing is safe and effective in elderly patients, although in practice non-weight bearing (NWB) orders are often made. The aim of this project was to determine effectiveness and feasibility of introducing a NWB coordinator within Alfred Health.

Methods: Patients admitted under General Medicine between June and December 2023 with a fracture were reviewed retrospectively. Following this, a four-week prospective audit was undertaken by a senior orthopaedic physiotherapist of all patients with a fracture managed under a non-orthopaedic/trauma bed-card. Patients considered appropriate for an alteration of WB status were discussed with a consultant surgeon. The number of changes to WB status and the patient's short-term outcomes was reviewed.

Results: 140 patients in a 6-month period were admitted under General Medicine with a fracture, with a median (IQR) LOS of 6 (3-10) days and only half were discharged home, including those with isolated upper limb fractures (21/43 discharged home). 88 patients were admitted with fractures under non-orthopaedic/trauma units in a Feb/March 2024 (4-week period). A senior orthopaedic physiotherapist facilitated a progression of orthopaedic care for 13 patients. Potential savings per patient ranged from 18 to 56 subacute/transitional care bed-days, with a conservatively estimated accumulative total of 261 bed-days

Conclusion: Introducing a NWB coordinator may increase bed capacity by modifying the orders of some NWB patients. This role may improve access to best care throughout the hospital journey for all patients admitted with a fracture regardless of bed-card.

12.

IMPROVING THE ACCURACY OF TRIAGE IN A TERTIARY OUTPATIENT NEUROSURGERY SERVICE: USE OF A STANDARDISED TOOL TO TRIAGE PATIENTS WITH SPINE PAIN

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Traditional triage of neurosurgery spine referrals has resulted in inconsistent priority allocations. The Modified Spine Severity Scale (MCSSS) is a standardized screening tool based on clinical, pathological and radiological features of referred surgical outpatients.

AIM: To describe characteristics of referred patients and compare traditional triage processes to results from the MCSSS used by Advanced Musculoskeletal Physiotherapists (AMPs).

METHODS: Demographic data for referrals received between June to August 2023 were collected. Referrals were triaged by 3 blinded assessors (Priority (P)1 high risk of deteriorating, P2 likely operative, P3 likely non-operative); 2 surgeons used traditional triage (50% of referrals each) and 2 AMPs each scored all referrals using the MCSSS (scale 0-15 classified as 0-5 P3, 6-8 P2, 9-15 P1). Patient characteristics were described descriptively, agreement between surgeons and AMPs was assessed using weighted kappa (K_W 0.41-0.60 moderate agreement) and interrater reliability between AMP1 and AMP2 using intraclass correlation coefficients (ICC, 0.75-1.00 excellent agreement).

RESULTS: 271 referrals were received. Most participants were female (57%), aged 50-64 (34%), living in metropolitan regions (70%) and referred for spine and limb pain (86%); primary degenerative spine pathology (94.5%). According to MCSSS triage processes, referrals were classified as n=150 P3, n=100 P2 and n=21 P1. There was moderate agreement between traditional and MCSSS classifications (surgeon 1 K_W 0.57 95%CI 0.48 to 0.68, surgeon 2 K_W 0.56 95%CI 0.47 to 0.65). The agreement between traditional and MCSSS classifications were 90-95% for P1, 74-75% for P2 and 61-67% for P3. Excellent interrater reliability using MCSSS was demonstrated (AMP 1 and 2 ICC 0.99 95%CI 0.98 to 0.99).

CONCLUSION: Use of the MCSSS to triage spine referrals by AMPs was excellent for P1 patients who are at highest risk of deterioration. With moderate agreement for P2 and P3 patients, further refinement is required to optimise clinical application.

13.

EFFECTIVENESS OF COGNITIVE REHABILITATION INTERVENTIONS FOR HOSPITALISED ADULTS WITH TRAUMATIC BRAIN INJURIES

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Current cognitive rehabilitation international clinical practice guidelines for adults with Traumatic Brain Injury (TBI) are mostly limited to rehabilitation and community settings. Hence, there is a gap in our knowledge of the most effective cognitive rehabilitation strategies delivered by Occupational Therapists for patients with a TBI during acute hospitalisation.

Aim: To determine the effectiveness of cognitive rehabilitation interventions within the scope of occupational therapy practice for hospitalised adults with TBI.

Method: Systematic review of randomised, quasi-randomised controlled trials with a meta-analysis. Six databases were searched up to July 2023 for studies published in English that evaluated an intervention (within the scope of occupational therapy practice) to address cognition in hospitalised adults with TBI. Primary outcomes included measures of specific cognitive impairment (e.g. Glasgow Coma Scale) and secondary outcomes of participation (e.g. Functional Independence Measure).

Results: After screening 11826 results, 15 papers describing 14 studies met the inclusion criteria. Interventions were designed to target sensory stimulation (n=5), concussion symptoms (n=4), specific cognitive skills (n=3), or post-traumatic amnesia (n=2). Intervention was delivered by an occupational therapist in four (29%) studies. Outcomes included cognitive impairment (n=14) and participation (n=4). Cognitive impairment data from six studies was included in a meta-analysis. Cognitive rehabilitation interventions delivered in the hospitalised setting were found to improve cognitive impairment (SMD=1.48, 95% CI 1.18 to 1.79) immediately post-treatment.

Conclusion: Interventions were found to effectively improve cognitive impairment; however, few studies measured the impact on participation. This highlights a gap for occupational therapy research with a hospitalised TBI population.

14.

FALLS AND INJURY REDUCTION VIA HOSPITAL WORKFORCE REDESIGN

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Falls and fall-related injuries are a persistent and debilitating problem in Australian hospitals. Patient education is known to be effective, yet health professional workloads are high, and it can be challenging to deliver patient education within 48 hours of admission, when most falls occur.

AIM: We conducted a hybrid implementation trial to evaluate the effects of using trained allied health assistants (AHAs) to deliver patient falls education on day 1.

METHODS: 541 patients were randomised to usual care and intervention groups.12 AHAs delivered scripted falls education in addition to usual care to the intervention group for 20 weeks. The primary outcome was feasibility assessed by time from admission to falls education, estimated cost of delivery per patient and number of adverse events per group. We also measured fall rate (falls per 1000 bed days).

RESULTS: 97% of the intervention group received education within 24 hours and 100% within 48 hours. The cost beyond usual hospital care was $200 per patient. The difference in fall rates was not significant (IRR = 0.66 (95% CI 0.32, 1.36; P = 0.26)), intervention group rate 5.69 (22 falls) and control group rate 8.07 (32 falls).

Injurious falls were 2.02 per 1000 bed days in the control group and 1.03 for the intervention group. There were no adverse events associated with the intervention.

CONCLUSION: Supplementing usual care with targeted hospital falls prevention education is feasible and beneficial when delivered by trained and supervised health assistants.

15.

THE FEASIBILITY AND ACCEPTABILITY OF MEASURING ENERGY EXPENDITURE USING INDIRECT CALORIMETRY IN SELF-VENTILATING PATIENTS FOLLOWING TRAUMATIC INJURY

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BACKGROUND: Indirect calorimetry (IC) is the gold standard method for measuring energy expenditure (EE). Despite clinical guidelines recommending nutrition be delivered based on measured EE, quick predictive equations are most commonly used in practice, with potential for over-and under-estimation of energy needs. We aimed to assess the feasibility and acceptability of measuring EE using IC and compare measured to estimated EE in patients following traumatic injury.

METHODS: In a single-centre prospective observational study, EE was measured using IC via a canopy hood in patients admitted to a trauma ward with ≥7day hospital stay. Feasibility was set at >50% of IC measurements being valid (≥5 minutes with ≤10% variation in VO2 and VCO2). Following the measurement, patients and staff completed an acceptability survey. Measured EE(kcal) was compared to estimated EE(kcal) using predictive equations (25kcal/kg, Schofield, 30kcal/kg), with ±10% difference considered clinically significant.

RESULTS: Of 30 IC measurements, 25(83%) were valid with all participants reporting the test was comfortable. Measurements were not completed or valid in 5(17%) participants due to discomfort, pain, and difficult bedspace (each n=1) and high CO2 variability(n=2). All staff agreed IC was acceptable to incorporate into usual care. Estimated EE was within ±10% of measured EE in 28%, 44%, and 60% of patients for 25kcal/kg, Schofield equation, and 30kcal/kg, respectively.

CONCLUSION: Measured EE using IC is feasible and acceptable following traumatic injury. A clinically significant difference in energy was observed between measured and estimated EE. Further research is warranted to evaluate whether IC-guided energy delivery improves patient outcomes.

16.

CO-DESIGN OF A NOVEL TELEHEALTH EXERCISE MODEL OF CARE FOR ADULTS WITH CYSTIC FIBROSIS

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INTRODUCTION/AIM: Physical activity and exercise are key components in the management of Cystic Fibrosis (CF). Co-designing interventions in partnership with patients may increase uptake, patient engagement and adherence. In our previous qualitative research, we determined that telehealth exercise programs should be tailored to the individual, include an opportunity to maintain connections with peers and the CF multidisciplinary team, and provide a method to monitor progress over time. This study aimed to progress this research, and create a telehealth exercise program for adults with CF in collaboration with patients.

METHODS: Two possible telehealth exercise programs were designed based on our previous research. Adults with CF were recruited in a purposive sample and participated in focus groups online to provide feedback on the proposed programs and finalise the design of a telehealth exercise program. Focus groups were recorded, transcribed, and analyzed by two researchers using an iterative process.

RESULTS: Three focus groups (4-5 participants each) were conducted in 14 adults with CF (8 females) aged from 22 to 59 years. The following telehealth exercise model of care was developed: After completing an in-person physiotherapy baseline assessment, participants will have the choice to complete either an independent exercise program with weekly check-in sessions online with a physiotherapist; or a live online group exercise program run by a physiotherapist. Each program will be 12 weeks in duration and participants will have access to a peer support messaging group throughout. At the end of the program the participants will complete a final physiotherapy assessment.

CONCLUSION: A novel telehealth exercise model of care for adults with CF has been developed in collaboration with people with CF. The next phase of this work is to test the acceptability and safety of the model of care in a randomised controlled feasibility trial of adults with CF.

17.

SELF-AWARENESS REHABILITATION FOR ADULTS WITH BRAIN INJURY: THE ROLE OF ENVIRONMENTAL, OCCUPATIONAL AND SOCIAL FEEDBACK MECHANISMS

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Introduction: After brain injury, a person's self-awareness of abilities and limitations in the context of meaningful activities is an important factor in rehabilitation. The hospital setting can present challenges to providing the necessary occupational and environmental opportunities for training development of self-awareness.

Objectives: The aim of this study was to explore the role of feedback mechanisms in the development of self-awareness for adults with brain injury and make recommendations for clinical practice.

Materials & methods: Data were gathered through an audit of clinical records of semi-structured interviews using the Self-awareness of Deficits Interview (SADI) with thematic analysis applied. Practice setting was a public brain injury rehabilitation unit in Australia. Participants included a convenience sample of adults with traumatic brain injury, stroke and hypoxic brain injury (*n*=173) admitted to inpatient rehabilitation who received self-awareness assessment.

Results: Data described occupational, environmental and social factors that contributed to self-awareness. Occupational factors included lack of exposure to activities in the hospital setting which was described as a barrier to learning about abilities by some participants, while for others this reinforced poor awareness of occupational limitations. Environmental factors related to being in the hospital environment the associated uncertainty of participants about their function in the home environment without exposure to this setting. Many believed they would experience no functional difficulties upon return home. Social factors included feedback from family/friends which was described as reinforcing the presence of impairments or conversely, the absence of functional changes.

Conclusion: A clinical interview using the SADI provides an opportunity to understand an individual's perspective of their abilities. Comprehensive inpatient rehabilitation to support development of self-awareness should include targeted opportunities for experiences and feedback across a range of occupations and environments taking into consideration the individual's social context.

18.

ADAPTING AND OPERATIONALISING ADULT TRAUMATIC BRAIN INJURY GUIDELINES TO AN OCCUPATIONAL THERAPY SERVICE

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There are a number of clinical practice guidelines (CPGs) relevant to working with adults with traumatic brain Injury (TBI). Having multiple CPGs presents the unique challenge to occupational therapists in knowing which recommendations to implement within their own practice. Guideline adaptation considers local resources and modifies the national or international guidelines according to local needs.

Aim: This project aimed to adapt nationally or internationally accepted occupational therapy guideline recommendations for adults experiencing traumatic brain injury into a localised protocol.

Method: The ADAPTE process and CAN-IMPLEMENT tool guided the process within an occupational therapy service in a metropolitan hospital network. First, the research steering group (n=8) identified and evaluated relevant CPGs and then screened and selected recommendations relevant to the occupational therapy service. Second, the stakeholder group (n=13) met for four 90-minute sessions to adapt and identify unmet needs for each recommendation. Third, the development and implementation of the localised protocol within the service occurred through resource development, education and training.

Results: Ninety-one recommendations from three CPGs were identified as relevant. The stakeholder group aligned guideline content to local context, identifying unmet resources. Clinical resource gaps in assessment (disorders of consciousness, spasticity, pain), intervention (cognition, self-awareness, memory, vision and perception) and family education (family support in acute) were identified. Training packages continue to be developed to support the implementation monitoring and evaluation of the localised guideline.

Conclusion: The localised guideline will provide a locally agreed standard for assessment, management and discharge planning with adults following traumatic brain injury.

19.

EVALUATION OF FAMILY VIOLENCE EDUCATION: EXPERIENCES FROM A TERTIARY HEALTH SERVICE

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INTRODUCTION/BACKGROUND
Alfred Health's Strengthening Hospital's response to Family Violence (FV) Project (SHRFV) commenced staff family violence education in 2018. Informal feedback during organisational accreditation in 2023 suggested this education required review. The aim of this evaluation was to identify gaps in design, measure effectiveness, and to describe recommendations for improvements to FV education.

METHODS
Face to face (F2F) sessions were observed, session materials collected, and all in-scope FV modules on Alfred Health's Learning Management System (LEX) were identified. Design indicators were used to examine online modules and F2F sessions. Available data aligned to Kirkpatricks Model[1] was collected and analysed.

RESULTS/EVALUATION
More than 8000 (F2F and online) FV education interactions were recorded. There is evidence linking these interactions to positive consumer impact (e.g. Case Studies) including compliments (e.g. Riskman data), and known benefits and positive outcomes amongst victim-survivors disclosing FV at Alfred Health (e.g. file audits where documentation clearly demonstrated that staff recognised the signs of FV and responded using Sensitive Practice). Areas for improvement were also identified including: enrolment and reporting gaps, inconsistent use of the LMS; design issues in particular the lack of constructive alignment throughout the majority of online modules. Effects of education on staff uptake of required FV electronic note-type appeared limited.

DISCUSSION
Findings from this review highlight examples of some positive results and impacts of FV practice on key stakeholders likely, in at least part, due to FV education completed by thousands of staff. These positive impacts could be strengthened through redesign of these important teaching and learning resources. Key recommendations include: redesign in accordance with constructive alignment[2] and Adult Learning principles; increased summative knowledge assessment; and, optimization of online module length.

20.
EFFECT OF A 28-DAY LOW FODMAP DIET ON GASTROINTESTINAL SYMPTOMS ASSOCIATED WITH ENDOMETRIOSIS (ENDOFOD) – A RANDOMISED, CONTROLLED CROSS-OVER FEEDING STUDY

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Background
Endometriosis is a common, debilitating disorder that affects around 1 in 7 Australian women. Gastrointestinal symptoms affect the majority of sufferers, but are poorly targeted by existing surgical and pharmacological treatments. While dietary approaches are frequently used to manage symptoms, data supporting the effectiveness of these strategies are lacking. We measured the effect of a low fermentable oligo-, di- and mono-saccharides and polyols (FODMAP) diet in individuals with endometriosis and poorly controlled gastrointestinal symptoms.

Methods
This single-blind randomised, controlled, cross-over, feeding trial was conducted at Monash University, Melbourne, Australia. Females aged ≥18 years with endometriosis and poorly controlled gastrointestinal symptoms at baseline were randomised to one of two diets differing only in FODMAP content – 'low FODMAP diet (LFD)' <5g/day or 'control diet' 20g/day - for 28 days, before a ≥28-day washout and cross-over to the alternate diet. The primary outcome was the proportion of responders (defined as a decrease >20-mm in visual analogue scale (VAS) from baseline and/or VAS <30-mm on the last day of each diet) in randomised participants who followed the diets for ≥7 days. Participants were monitored for gastrointestinal symptoms, health-related quality-of-life (QOL) and psychological status.

Results
Between December 2020 and February 2023, 233 participants were screened, 193 were excluded and 35 were randomised and followed diets for ≥7 days. Adherence was adequate. Twenty-one (64%) responded to the LFD which was greater (p=0.01) than 9 (31%) that responded to the control diet (RR 0.23, 95% CI: 0.08, 0.64; p=0.007). Improvement with the LFD was greater than control for abdominal pain, bloating, stool form and QOL, but not for perceived stress, anxiety or depression.

Conclusions
The LFD ameliorates gastrointestinal symptoms related to endometriosis and improves QOL. Confirmation of these findings in a real-world setting is required.

21.

MEAL SET UP PROVIDED BY HOSPITAL PATIENT SERVICES ASSISTANTS (PSA) LEAD TO POSITIVE OUTCOMES IN SUBACUTE HOSPITAL MEAL SERVICE AND DELIVERY.

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Meal assistance play a simple yet crucial role in enhancing patient centred care. 80% of patients in the rehabilitation ward require some form of meal assistance, whether it is opening packages (set up) or plate to mouth feeding (full assistance).

AIM: To improve the provision of meal set up and assistance.

METHODS: This interventional study was conducted in a subacute hospital setting. Dietitians audited lunch service across 5 days during baseline and intervention. All patients admitted to the ward were included. Collected data included assistance received, time from tray delivery to meal set up and assistance, amount of meal consumed at 45 minutes post-delivery, who provided set up or assistance, and patients' satisfaction of meal service. For the intervention, PSAs were educated on the process and rationale for meal set up in hospital. Patients were excluded from meal set up from PSAs if they had dysphagia, required full assistance, or not seated appropriately for meals.

RESULTS: Audits were conducted at baseline (n=101) and post-intervention (n=108). After intervention, the percentage of patients who received meal set up increased from 89% to 100%. The time it took from tray delivery to set up and to assistance both reduced from 4.95 to 1.36 minutes (p=1.81) and from 11.29 to 3.82 minutes (p=0.014), respectively. Average time for total meal delivery reduced from 19.25 to 17.75 minutes (p=0.69). There were no significant changes in meal consumption. The percentage of patients who received meal set up from nurses reduced from 68.63% to 22.43%, while set up received from PSAs increased from 5.88% to 63.55%. Patients had positive feedback regarding the assistance received.

CONCLUSION: PSAs providing meal set up is a feasible and efficient way to improve meal experience for patients. The reduced burden on nursing staff allows more focused time on patients requiring more care.

22.

PHYSIOTHERAPY DELIVERED TRAUMA TERTIARY SURVEY: CAN A SHARED MODEL OF CARE IMPROVE TIMELY AND QUALITY SERVICE PROVISION FOR PATIENTS FOLLOWING TRAUMA?

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INTRODUCTION: The Trauma Tertiary survey (TTS) is a clinical examination performed on all trauma admissions. Delays in its completion can potentially increase morbidity, delay discharge and hamper recovery. Trauma physiotherapists are highly skilled at assessing injured patients and may provide an avenue for increasing resources dedicated to providing quality and timely TTS assessments.

AIM: To reduce time to TTS completion and percentage of TTS completed on day of discharge through the addition of Physiotherapy delivered TTS assessment in the trauma ward of an adult level 1 trauma centre.

METHODS: Following an education package and the development of a credentialing and governance framework, senior trauma physiotherapists undertook TTS assessments alongside the medical team in a shared model of care. KPIs (including time and quality metrics) were analysed and compared to a baseline period.

RESULTS: Baseline data was collected over a six-month period (October 2022 - March 2023) and compared to 12 months (May 23 – October 2024) following the commencement of the Physiotherapy led TTS service. Median time to TTS completion improved from 48.5 hours to 40 hours ($p < 0.001$), with 12% more TTS completed within 48 hours for the target group (61% compared to 73% $p < 0.001$). Reduction in day of discharge TTS was also noted on the target ward (13% compared to 7% $p < 0.001$) compared to baseline. Other process and performance quality improvements were also noted.

CONCLUSION: The addition of senior trauma physiotherapists to the pool of practitioners credentialed to perform TTS assessments has improved TTS KPIs without safety concerns.

BASIC LABORATORY

23.
EXPLORING THE HIDDEN POTENTIAL OF NEUROIMMUNE INTERACTIONS IN LUNG FIBROSIS

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Pulmonary fibrosis (PF) is a chronic disease involving progressive scarring of lung tissue afflicting 13-20 out of every 100,000 people worldwide. Disease development is proposed to involve epithelial damage, activation of immune cells and myofibroblasts leading to inflammation, collagen deposition, a consequent decline in lung function. Currently there no cure for PF and end-stage patients depend upon lung transplantation. There is a clear unmet clinical need to discover effective strategies to prevent and/or halt disease progression.

We propose that interactions between the nervous system and immune cells are fundamental for future therapeutic interventions in PF. Indeed, interactions between the nervous system and the immune system have been shown to influence diseases ranging from inflammatory bowel disease to atopic dermatitis. However, there are substantial gaps in the knowledge surrounding neuroimmune interactions in the lung, particularly their role in chronic diseases. Activation of the lung autonomic nervous system has been implicated in PF but therapies targeting this system provide only symptomatic relief. Comparatively, disruption of lung extrinsic sensory innervation via the vagus nerve, has been shown to ameliorate PF, suggesting that the sensory nervous system represents an attractive therapeutic target.

In our forerunning studies we found: enhanced production of the sensory neuropeptide calcitonin gene related peptide (CGRP), increased numbers of CGRP-producing pulmonary neuroendocrine cells, and exaggerated branching of nerve fibres throughout fibrotic lungs with lightsheet microscopy; using single cell sequencing we found that alveolar macrophages simultaneously express the CGRP receptor and secrete factors implicated in neuronal growth and fibrosis; through microdissection of the vagal and dorsal root ganglia we have discovered that they become predisposed to enhanced nerve sprouting during PF. Uncovering the form and function of the nervous system in PF would represent a substantial advance for the field and potentially deliver new therapeutical targets to combat this devastating disease.

24.
FUNCTIONAL ASSESSMENT OF THE NOD2 SIGNALLING PATHWAY IN PATIENTS WITH INBORN ERRORS OF IMMUNITY

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BACKGROUND: Inborn errors of immunity (IEIs) are rare, inherited immunological disorders characterised by susceptibility to infection and immune dysregulation. Despite advances in genomics, the majority of IEI patients do not have a causal variant identified, limiting access to targeted therapeutics that could prevent severe organ damage and early death We developed functional screening assays in 5 commonly affected, critical immune signalling pathways.

AIM: We aimed to functionally evaluate rare, novel variants of unknown significance (VUS) affecting the NOD2 signalling pathway.

METHODS: Peripheral monocytes were evaluated by flowcytometry for L18-MDP-induced (NOD2-dependent) TNF-α production, and phosphorylation of p38 (p-p38) and p65 (p-p65). LPS-stimulated (NOD2-independent control) and unstimulated samples were run concurrently.

Results: In healthy donors (n=11), L18-MDP induced TNF-α production in 57.23% (range 22.0-90.02%) of monocytes, and a fold-change of 4.71 (range 2.97-7.62) and 3.18 (range 2.67-10.29) for median fluorescent intensity (MFI) of p-p38 and p-p65 when compared to unstimulated cells. A patient with a hemizygous XIAP variant had complete absence of NOD2-dependent TNF-α, p-p38 and p-p65, whereas a patient with a heterozygous XIAP variant had low TNF-α production (7.32%), but p-p38 and p-p65 increase within, or near, range (4.27 and 2.5, respectively).

CONCLUSION: Here we show assessment of NOD2-dependent TNF-α, p-p38 and p-p65 can identify patients with complete loss-of-function phenotypes, with potential to identify more other pathway defects. In future, we will assess more patients with a VUS within the pathway to guide interpretation of variant impact, and screen patients without a candidate causal variant for defective signalling. This ex vivo functional evaluation of immune pathways, such as NOD2, could provide rapid insights into the pathogenicity of VUS and into mechanisms of disease, thereby expediting genetic diagnosis and treatment in PAD patients.

25.

A NOVEL MOUSE MODEL OF HEART FAILURE AND CARDIAC HEPATOPATHY DRIVEN BY THE MITOCHONDRIAL INTEGRATED STRESS RESPONSE

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Mitochondrial DNA (mtDNA) is replicated by DNA polymerase gamma (PolG), which has three enzymatic actions: polymerase activity, proofreading and base excision repair. As the sole polymerase of mtDNA, PolG is essential for the replication and maintenance of mtDNA. Mutations to the PolG gene can lead to impaired mtDNA replication and/or sequential accumulation of mtDNA mutations/deletions, which can ultimately result in mitochondrial dysfunction. The existing mouse model used for the study of PolG driven mitochondrial dysfunction, the PolG "mutator" mouse, is a global transgenic with developmental and systemic symptoms that can confound experimental findings. Consequently, this provides multiple challenges for investigating PolG mediated defects in a specific tissue.

Here, we describe a floxed-PolG mutator mouse, generated by inserting LoxP sites flanking the proofreading/repair exonuclease domain of the PolG1 gene, which we have subsequently crossed with inducible MHCa-Cre mice to generate mature mice with cardiomyocyte specific exonuclease deficient PolG (Cardiac-PolG^{mut}).

Approximately 24-weeks post-tamoxifen, Cardiac-PolG^{mut} mice acutely lost weight, with progressive heart failure, cardiac hypertrophy, and eventually death at approximately 30-weeks post-tamoxifen. Heart failure signatures included reduced *Serca2, Myh6* accompanied by increased *Myh7, Nppa, Nppb,* and fibrosis markers *Col1a1* & *Col3a1*. Severe liver failure was also observed post-mortem, with Cardiac-PolG^{mut} mice presenting with cardiac hepatopathy, including significant fibrosis observed in both liver and heart. Elevated *Fgf21*, *Gdf15*, *Atf4* and *Mthfd2* transcripts were elevated at 20-weeks post-tamoxifen, indicating initiation of the mitochondrial integrated stress response (mtISR) at least 4-weeks prior to weight loss and heart failure/remodelling.

Thus, the Cardiac-PolG^{mut} model recapitulates aspects of cardiometabolic diseases where dysfunctional mitochondria and activation of the mtISR drive cardiac hypertrophy, heart failure and cardiac hepatopathy. This highlights the potential of the Cardiac-PolG^{mut} mouse as a novel model of heart failure with cardiac hepatopathy, and the advantages of investigating mtDNA mutation-driven pathology in a temporal and tissue specific manner.

26.
SELECTIVELY TARGETING GASDERMIN-D ATTENUATES CARDIAC INFLAMMATION AND FIBROSIS AFTER ISCHEMIA REPERFUSION INJURY

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Inflammation is involved in the pathophysiology of cardiac injury, playing a critical role in clearance of cellular debris to promote tissue repair. However, inadequately-controlled inflammation contributes to adverse cardiac remodelling after acute-myocardial-infarction (AMI). This is driven by persistent activation of the NLRP3-inflammasome/Gasdermin-D (GSDMD) pathway and secretion of inflammatory IL-1β.

Aim: We investigated whether FDA-approved Disulfiram, used to treat alcoholism but recently shown to inhibit GSDMD pore-formation, could reduce inflammation and improve ischemia/reperfusion (I/R)-mediated cardiac injury.

Method: Left coronary artery ligation was performed in C57BL6 mice, followed by reperfusion at 60min in the presence and absence of 25 or 50mg Disulfiram, and administered daily until termination. Cardiac function was measured by echocardiography. Fibrosis and inflammation were assessed by histology, RT-PCR and western blot at day-7 and 28 post-AMI. Flow cytometry assessed leukocyte populations in blood, spleen, bone marrow and heart. Control and Disulfiram-treated mouse BMDMs and human THP-1 cells were investigated for secreted cytokines, inflammatory gene expression and cell viability.

Result: Ejection fraction and end-diastolic volume was significantly improved by 50mg/kg Disulfiram, 7 days post-I/R injury ($p<0.01$). Cardiac fibrosis was significantly attenuated by Disulfiram at 7 and 28-days post-I/R injury ($p<0.001$). Cardiac inflammatory (IL-1ß, IL-6, IL-18, Caspase-3, GSDMD) and fibrosis (CTGF, TGF-ß) gene expression and protein levels (Caspase-3, GSDMD, NLRP3) were significantly attenuated 28-days post-I/R injury. This was associated with reduced inflammatory cell abundance at day-7 in blood, spleen, bone marrow and heart. Importantly, phenotypic switching from inflammatory Ly6C^{hi} to anti-inflammatory Ly6C^{lo} monocytes was noted in the bone marrow ($p<0.001$). In LPS/Nigericin-treated BMDMs and THP-1 cells, Disulfiram significantly attenuated IL-1ß and IL-6 secretion, and improved cell viability in a dose-dependent manner (0.1µM–50µM, $p<0.001$).

Conclusion: Inhibiting GSDMD with Disulfiram improves cardiac function post-AMI by reducing cardiac inflammation and fibrosis. Ttargeting GSDMD may represent a novel way to provide cardio-protection post-AMI.

27.
LOSS-OF-FUNCTION MUTATION OF KI67 CAUSES LYMPHOPHENIA AND IMPAIRED IMMUNE RESPONSES

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Ki67 is a nuclear protein used extensively as a marker for cell proliferation. Despite this, only recently has the function of Ki67 started to be revealed. Our recent study using a full germline knockout mouse of *Mki67* discovered that Ki67 is required for maintaining chromatin accessibility and V(D)J rearrangement during lymphocyte development. However, whether Ki67 deficiency affects immune responses is still unknown.

Here, we report a patient with bi-allelic, loss-of-function mutations in MKI67 resulting the absence of Ki67 expression. In line with the phenotypes previously observed in our *Mki67*$^{-/-}$ mice, the patient exhibited specifically reduced frequencies of B cells in the peripheral blood despite normal lymphocyte proliferation after in vitro stimulation. Both the patient and *Mki67*$^{-/-}$ mice had largely normal levels of total serum immunoglobulin titres. However, when immunised with a model antigen (NP-KLH precipitated in alum), *Mki67*$^{-/-}$ mice had significantly reduced antigen-specific germinal centre B cells and IgG1^{+} antibody-secreting cells compared to the wild-type controls. As both B and T cells are reduced in the *Mki67*$^{-/-}$ mice, to determine which cell type contributes to the defects in the primary immune response, we adoptively transferred 1) SW_{HEL} B cells + OT-II T cells, 2) Mki67$^{-/-}$.SW_{HEL} B cells + OT-II T cells, or 3) SW_{HEL} B cells + Mki67$^{-/-}$.OT-II T cells into congenically labelled recipients and immunised all groups with OVA-HEL in alhydrogel. We found that compared to mice transferred with Ki67-sufficient SW_{HEL} B cells and OT-II T cells, the IgG1^{+} germinal centre B cell responses among donor cells were impaired only when the donor B cells were deficient for Ki67, demonstrating a B cell-intrinsic defect.

Together, our results emphasise a role for Ki67 in lymphocyte development in both human and mice, and identify a B-cell intrinsic function of Ki67 in primary immune responses.

28.
CONVERSION OF VACCINES FROM LOW TO HIGH IMMUNOGENICITY BY ANTIBODIES WITH EPITOPE COMPLEMENTARITY

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Antibodies (Abs) are the key effector molecules of B cells and central to most vaccine success. The generation of protective Ab-mediated immunity is facilitated by B cells establishing germinal centres (GCs), transient structures in which Ab affinity maturation takes place. Here, building on the long-standing knowledge that Abs modulate immune responses, we precisely control Ab dose, affinity, and specificity in vivo to reveal novel insights into their role in regulating B cell response initiation and progression. Our results show that Ab-mediated GC inhibition is the consequence of both competition for antigen binding and modulation of B cell fate. Specifically, high amounts of non-competitive Abs (recognising a complementary epitope, distinct from the B cell receptor (BCR) binding site) diverted the fate of both high- and low-affinity B cells towards Ab-secreting cells (ASC), at the expense of GCs. Furthermore, our results show that small amounts of non-competitive Abs can selectively promote low-affinity B cell recruitment into GCs, allowing potent responses to otherwise poorly immunogenic antigens. Mechanistically, this response enhancement was independent of complement or Fc receptors, as is typically attributed to Ab-mediated enhancement, and rather stimulated antigen-mediated BCR engagement, promoting B cell activation and proliferation. We revealed that secondary encounter of BCR-bound antigen by Abs significantly increased antigen presentation to cognate CD4 T cells, providing mechanistic explanation for the enhanced responses observed in vivo. Importantly, Ab-mediated response promotion extended the duration of GC responses and enabled prolonged affinity maturation, crucial for protective immunity. These results applied to model antigens as well as SARS-CoV-2 mRNA-LNP vaccination, reflecting the broad applicability of our findings. Collectively, our

results provide novel insights into Ab-mediated regulation of B cell responses in a dose, specificity, and affinity-dependent manner and highlight the utility of Abs as tools to promote vaccine immunogenicity.

29.

RESPONSE AND RESISTANCE TO COMBINATION IMMUNE CHECKPOINT BLOCKADE ASSOCIATE WITH DISTINCT BASELINE AND ON-TREATMENT BLOOD T-CELL PROFILES IN MELANOMA PATIENTS.

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Introduction

Despite the success of immune checkpoint blockade (ICB), a majority of melanoma patients fail to respond or experience severe treatment-related toxicity. Currently, there are no reliable biomarkers available to predict these events and guide treatment choices. We evaluated the peripheral T-cell compartment to identify immune features associated with ICB outcome.

Methods

Blood samples were collected from 41 advanced melanoma patients at baseline and after one cycle of combination PD-1 + CTLA-4 ICB. Patients were classified as responders or non-responders based on radiographic best overall response to treatment. Absolute immune cell counts were obtained and PBMCs cryopreserved prior to spectral flow-cytometric T-cell immunophenotyping.

Results

19 patients (46%) failed to respond to treatment. At baseline, these patients had fewer T cells than age-matched healthy controls (median 780 vs. 1297 cells/μL, p=0.00012), mostly due to reduced naive CD4$^+$ (p=0.00203) and CD8$^+$ (p=0.00149) T cells, and showed an increased prevalence of a highly immunosuppressive T regulatory (Treg) cell phenotype and higher expression of the proliferation marker Ki67$^+$ across major T cell subsets compared to responders. One cycle of ICB expanded T memory, helper, and regulatory, but not naive, subsets, and responders showed greater Ki67 upregulation in CD4$^+$ central memory (Tcm) (p=0.0086), stem cell-like memory (p=0.045), and regulatory (p=0.0257) T cells compared to non-responders. Compared to Ki67$^-$ cells, these Ki67$^+$ cells expressed a higher proportion of PD-1 at baseline, expanded to a greater degree on-treatment, and generally co-expressed higher amounts of TIGIT, TIM-3, CD39, and ICOS. The fold change of Ki67 expression in CD4$^+$ Tcm cells after one cycle of treatment differentiated responders and non-responders (AUC=0.7545, p=0.0094).

Discussion

Response to ICB was associated with distinct T-cell profiles before and after one cycle of treatment, and significantly differentiated responders and non-responders. Further work using combinations of immune features promises to improve predictive capacity.

30.

P-CRESOL SULFATE ACTS ON EPITHELIAL CELLS TO REDUCE ALLERGIC AIRWAY INFLAMMATION

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P-cresol sulfate (PCS) is a microbial metabolite derived from L-tyrosine and was recently discovered to have immunoregulatory influences on allergic airway inflammation. Administering PCS to mice reduced house dust mite-induced CCL20 production, a chemokine that recruits lymphocytes and dendritic cells (Wypych et al. Nature Immunology 2021). We are using PCS as a molecular template to develop novel therapeutics against allergic asthma. Our aim is to determine the molecular mechanism of action of PCS and its molecular derivatives in alleviating allergic airway inflammation. We isolated and stimulated primary mouse lung cells with lipopolysaccharide, a strong inducer of CCL20, identifying airway epithelial cells as the main cell type affected by PCS. RNA sequencing of ex vivo mouse lung epithelial cells revealed that PCS influenced heat shock protein 90 (HSP90) gene expression, and indeed, blockade of HSP90 reduced CCL20 production, suggesting it may be involved in the mechanism of action. In silico molecular modelling indicated a shared putative binding site for PCS and two molecular derivatives in the epidermal growth factor receptor (EGFR). Additionally, RNA-sequencing of the A549 human alveolar epithelial cell line identified an increase in genes regulated by the aryl hydrocarbon receptor (AHR) in PCS and molecular derivative treated cells. These results implicate EGFR and AHR in mediating the effects of PCS and its molecular derivatives. Overall, PCS acts on lung epithelial cells to reduce CCL20 production and consequently allergic airway inflammation. Elucidation of the molecule's mechanism of action could lead to development of novel therapeutics against allergic asthma and other atopic diseases.

31.

SINGLE-CELL TRANSCRIPTOME REVEALS SEX SPECIFIC ALTERATIONS TO HEPATIC RECOVERY PATHWAYS IN METABOLIC ASSOCIATED STEATOHEPATITIS (MASH)

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Metabolic associated liver disease (MASLD) involves excessive hepatic lipid accumulation, affecting an estimated 40% of Australian adults and contributes to the development of obesity, type-2 diabetes, and increased cardiovascular risk. When left untreated, MASLD can progress to metabolic associated steatohepatitis (MASH), characterized by inflammation and fibrosis, resulting in the permanent remodelling of the hepatic microenvironment. Critically, MASH predisposes the onset of cirrhosis and liver cancer. Despite this, there are limited effective treatments for MASLD and MASH which can be attributed to a lack of thorough understanding regarding the causative agents responsible for its initial onset and subsequent advancement.

AIM: To understand the cell and disease heterogeneity driving MASH etiology

METHODS: We conducted single-cell transcriptomics on livers from mice fed an AMLN diet, an intervention known to induce MASH as observed in humans. This was performed across 3 time points (2, 8 & 24 weeks) in both male and female C57BL/6J mice (n = 4/treatment).

RESULTS: Overall, we analysed 88,000 cells at a depth of >20K genes across all conditions. This led to the identification of more than 30 cell populations, each exhibiting distinct transcriptomes across the various stage of disease pathogenesis. Importantly, we note the onset of an immune response and expansion of biliary epithelial cells (cholangiocytes) in male mice, which persists up to 24 weeks. In addition, chronic exposure to AMLN diet stimulated a regenerative response potentially acting through a hybrid hepatic progenitor cell-type.

CONCLUSION: This dataset reveals sex-specific morphological changes in chronic fatty liver disease, offering insights crucial for developing new diagnostics and therapies. Furthermore, the identification of possible regulatory bodies responsible for hepatic regeneration may recontextualize the permanent remodelling induced by MASH.

32.

TEMPORAL MINERALOCORTICOID RECEPTOR ACTIVATION REGULATES THE MOLECULAR CLOCK AND TRANSCRIPTION OF CARDIOVASCULAR DISEASE MODULATORS IN MYELOID CELLS

Seamus Heanue

The mineralocorticoid receptor (MR) is an established target in the treatment of heart failure, as a mediator of cardiac inflammation and fibrosis. We have shown that the MR in macrophages/monocytes plays a critical role in the progression of cardiac inflammation and fibrosis. Recently, we identified a bidirectional regulatory role for the MR and the peripheral molecular clock in cardiac cells. Given that immune cells can mediate cardiac pathology, we investigated whether the MR also modulates temporal transcription of the molecular circadian clock and inflammatory mediators in spleens from myeloid MR null mice (MyMRKO), and in immortalised bone marrow derived cells (BMDCs). Whole transcriptome analysis of spleens from wild type (WT) or MyMRKO revealed differential expression of clock genes Per2, Cry1, REV-ERBα, and DBP at ZT0 versus ZT12. 10nM aldosterone or corticosterone modulated the 24hr expression pattern of Per2, REV-ERBα and other clock components in cultured BMDCs, supporting a direct role of MR in timekeeping. MR modulation of genes involved in inflammatory responses in macrophages such as iNOS, IL-1β, Arg-1, IL-10, CCL2 and Spp1 was evident at the start of the 'lights on' phase in mice. Genes related to PPARγ signalling, a key pathway in the development of cardiovascular disease, also demonstrated MR-dependent regulation in a temporal manner. Temporal MR modulation of gene targets differed between males and females. Our findings underscore the dynamic influence of the MR on circadian rhythms and inflammatory pathways in myeloid cells, highlighting sex-based differences and offering insights into its pivotal role in cardiovascular disease pathogenesis.

33.

MULTI-OMICS PROFILING OF LUNG TRANSPLANT RECIPIENTS IDENTIFIES PREDICTIVE BIOMARKERS OF CHRONIC LUNG ALLOGRAFT DYSFUNCTION

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Long-term survival of lung transplant recipients remains limited by chronic lung allograft dysfunction (CLAD). In the majority of patients CLAD manifests as obliterative fibrosis of the small airways. This results in the irreversible deterioration of the patient's lung function and terminates in the failure of the allograft. The immunological drivers of CLAD are unclear, hence there are no biomarkers able to predict its onset prior to its clinical manifestation.

AIM: To discover metabolites, lipids and genes that predict the onset of CLAD prior to the irreversible decline in lung function.

METHODS: We performed metabolomics, lipidomics and transcriptomics on longitudinal broncho-alveolar lavages (BAL) from 56 lung transplant recipients who remained CLAD-free over 30 months post-transplant, and 13 who developed CLAD.

RESULTS: In CLAD-free patients, the first 6 months post-transplant were hallmarked by diminished microbial diversity and increased abundance of Staphylococcus and Candida, coupled with upregulated macrophage anti-microbial responses, and elevated nitric oxide metabolism (FDR < 0.05). This was superseded by homeostatic tissue repair after 3 months, indicating the return to stability in CLAD-free allografts. In contrast, incipient CLAD patients had significantly elevated expression of genes and molecules linked to the endothelial glycocalyx and the sphingolipid metabolism (FDR < 0.05), suggestive of increased vascular permeability and immune cell graft

infiltration prior to CLAD onset. Application of a machine learning model trained on all significant features predicted CLAD onset as early as the first 2-6 months post-transplant (ROC = 0.93), with molecules showing higher predictive potential compared to genes.

CONCLUSION: We have identified important immunological processes underlying CLAD development, and metabolites, lipids and genes able to predict CLAD prior to its onset. After validation in future transplant cohorts, candidate biomarkers can be used to better stratify patients into select CLAD-risk trajectories, enabling timely intervention prior to the irreversible decline in lung function.

34.

SURFACEOME MAPPING OF THE VASCULAR ENDOTHELIUM TO IDENTIFY THERAPEUTIC TARGETS FOLLOWING MYOCARDIAL INFARCTION

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Myocardial infarction (MI) is a major cause of death globally, with 30% of survivors developing heart failure due to ischemia-reperfusion injury. Selective therapeutic delivery to the heart after a heart attack remains a clinical challenge. The surfaceome of heart cells serves as a molecular platform for therapeutics to modulate cellular function and enhance delivery.

AIM: To map the coronary vascular surfaceome in healthy mouse and human endothelial cells under ischemia-reperfusion (I/R) injury, identifying potential therapeutic targets for I/R-related treatments.

METHODS: We used chemical labelling and MS-based proteomics to map the mouse coronary vasculature surfaceome and examine protein shifts in an I/R injury model. Surface proteins were labelled with biotin-saline and enriched via neutravidin. Human endothelial cells (HUVECs, HAECs) were exposed to hypoxia/reoxygenation to simulate I/R injury.

RESULTS: 353 proteins from mouse coronary vascular surfaceome, with known localised factors associated with vascular surface identified to support cell migration, angiogenesis, and vessel stability (i.e., TEK, VASP and ANXA2). Overall, 2091 and 1600 surface proteins were identified in HUVEC and HAEC, respectively. From those surfaceome populations, 537 and 1140 surface proteins were significantly dysregulated (student's t-test, FDR<0.05) in HUVEC and HAEC following I/R injury. Further, 206 surface proteins were commonly dysregulated in these two cell lines. Functional enrichment analysis reveals significantly enriched terms including "cell adhesion" (GO:0050839, p-adjusted value: 3.19E-27), "angiogenesis" (GO:0001525, p-adjusted value: 1.32E-07) and "integrin cell surface interactions" (REAC: R-HSA-216083, p-adjusted value: 4.56135E-05). More importantly, we have identified key proteins relating to inflammatory processes (i.e., MARCKS, IL6ST, TEK, WDFY1) which are hallmarks of I/R injury.

CONCLUSION: We describe a chemical labelling technique using membrane-impermeable biotin and quantitative MS-based proteomics to map heart surface proteins accessible from circulation in a mouse model. Surfaceome mapping aids in identifying heart vasculature-specific targets for treating I/R-related injuries.

35.

SEX-SPECIFIC TRAUMATIC BRAIN INJURY AND POST-TRAUMATIC EPILEPSY OUTCOMES IN SPRAGUE-DAWLEY RATS

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Purpose: Despite Traumatic brain injury (TBI) being one of the main leading causes of death and disability, the sex disparities in short-term and long-term outcomes, including posttraumatic epilepsy (PTE), are unclear. There is an urgent need to bridge the gap of knowledge of gender differences in the field of translational TBI and epilepsy research. The aim of this study was to investigate the differential response of male and female rodents to TBI and the development of PTE utilising the lateral fluid percussion injury (LFPI) model.

Method: TBI was induced in 11-week-old male (n = 107) and female (n =123) Sprague-Dawley (SD) rats. After LFPI, mortality rate, apnoea, pain response, and righting reflex were recorded. Weight was recorded throughout the study. Six months post-TBI, epidural video-EEG was recorded continuously for 4 weeks to identify the development of post-traumatic epilepsy (PTE). MRI scanning on day 9 and 5-month post LFPI and behavioural tests for neuromotor function, cognitive deficits and depression-like and anxiety-like behaviour were performed.

Results: We did not see any significant difference in short-term outcomes ($p > 0.05$), including mortality rate, apnoea time, pain response, and righting reflex recovery time in male rats compared to females. However, male rats had a higher incidence rate (40.7%) of PTE compared to female animals (24.3%). Interestingly, female SD rats did not develop PTE after LFPI showed faster injury recovery compared to male rats with or without PTE. The analysis of MRI and behavioural tests are ongoing.

Conclusion: This study identified similarities in multiple acute and chronic TBI outcomes between male and female rats. However, we identified a higher PTE rate in male rats compared to females. Additionally, our results suggested that there might be a subset of female animals that could recover faster and be less susceptible to PTE.

36.

A LIPID ATLAS OF HUMAN AND MOUSE IMMUNE CELLS PROVIDES INSIGHTS INTO FERROPTOSIS SUSCEPTIBILITY: APPLICATION IN ADOPTIVE CELL THERAPY

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The cellular lipidome is comprised of thousands of unique lipid species. Using mass spectrometry-based targeted lipidomics we have recently characterized the lipid landscape of human and mouse immune cells (www.cellularlipidatlas.com). Using this resource, we show that immune cells have unique lipidomic signatures and that processes such as activation, maturation and development impact immune cell lipid composition. To demonstrate the potential of this resource to provide insights into immune cell biology, we determined how a cell-specific lipid trait, differences in the abundance of poly-unsaturated fatty acid-containing glycerophospholipids (PUFA-PLs), influenced immune cell biology. Given the importance of these distinct phospholipids in ferroptosis and our lipidomic data, we therefore explored the susceptibility of immune cells to ferroptosis. We firstly show that differences in PUFA-PL content underpins the differential susceptibility of immune cells to ferroptosis, and secondly, that manipulating the intracellular PUFA-PL content promotes ferroptosis resistance in ferroptosis sensitive immune cells (i.e. T and B cells). Therapeutically, we employed our lipid manipulation strategy in adoptive

cell therapy where our preliminary data demonstrates equipping these cells with a 'lipid-shield' *ex vivo* prior to transplantation protects them against ferroptosis. Collectively, we show that the lipid landscape is a defining feature of immune cell identity and cell-specific lipid phenotypes underpin aspects of immune cell physiology. Moreover, our work identifies the basis for previously described differences in immune cell susceptibility to ferroptosis and raises exciting novel therapeutic opportunities in adoptive cell therapy.

37.

DORNASE ALPHA POTENTIATES CLOT LYSIS WITH TENECTEPLASE: INSIGHTS FROM EX-VIVO LYSIS OF THROMBECTOMY CLOTS

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Background and Aims

Dornase alpha, a recombinant human deoxyribonuclease I, can potentiate alteplase-mediated clot lysis via breakdown of neutrophil extracellular traps. We aimed to determine if dornase potentiates clot lysis in combination with tenecteplase (TNK) using endovascularly retrieved clots and to determine how clot components interact with lytic agents in the presence of dornase.

Methods

We modified tenecteplase with a histidine tag at its C-terminal (TNK-His) to allow visualisation of TNK-His complex formation. 21 retrieved clots were divided and suspended either in buffer or pooled plasma and incubated with 15nM TNK-His alone or combination with either 10U/ml or 100U/ml of dornase. Clot weight was measured over 120-minutes. Clot lysate supernatants were then assessed for fibrinolytic activity by fibrin zymography and western blotted to detect TNK-His complex formation, changes in plasminogen, antiplasmin, fibrin degradation products (FDPs).

Results

Addition of TNK-His to retrieved clots suspended in buffer resulted in reduction to 42.9+/-29.6% (mean ± std dev) of the initial clot weight after 120-minutes. This was further reduced to 20.6+/-13.4% in the presence of 100U/ml of dornase ($p<0.01$ compared to TNK-His alone). Addition of 10U/ml of dornase reduced clot weight to 32.7±18.5% but this was not statistically significant compared to TNK-His alone. Further, incubation in plasma resulted in a clot weight reduction to 64.3+/-25.4% in the presence of TNK-His. However, there was no statistically significant reduction with further addition of Dornase to TNK-His in plasma. Western blotting revealed presence of TNK-His complexes, increase in FDPs and consumption of plasminogen and antiplasmin in the presence of dornase.

Conclusion

This study demonstrates that 100U/ml dornase potentiates TNK-His mediated clot lysis in buffer, however, this effect is reduced in plasma. TNK complex formation and increased consumption of fibrinolytic components occurs following lysis in combination with dornase compared to with TNK alone

38.

NEXT-GEN CLOT DETECTION: THROMBUS-TARGETING PLATELET MEMBRANES MICROBUBBLES FOR ENHANCED ULTRASOUND IMAGING

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Thrombosis-related cardiovascular diseases remain the leading global cause of mortality and morbidity. Detection and treatment of these diseases necessitate the use of advanced materials with thrombus-specific targeting capabilities. This study introduces platelet membrane-derived bubbles (PMBs), a novel biointerfaced material that enhances early diagnosis and treatment of thrombotic disorders, offering distinct advantages over conventional nanoparticles in both diagnostics and theranostics.

PMBs were fabricated via our patented rapid sonication technique. PMBs had an average diameter of 700 nm and a surface charge mirroring the attributes of parent platelet membranes. Utilising diagnostic ultrasound imaging, we demonstrated the visualisation PMBs as hyperechogenic entities in agarose phantoms (100–400-fold intensity increase vs control). We also visualised and quantified an increase in signal intensity *in vivo*, in the vessel of mice after intravenous injection (2–3-fold intensity increase vs control). Furthermore, through confocal laser microscopy, we verified the retention of crucial transmembrane proteins, such as CD41 (GPIIb) and CD42 (GPIb), pivotal in conferring platelet-specific targeting functions. Importantly, our platelet aggregation studies confirmed that PMBs do not induce platelet aggregation, as compared to the platelet agonist thrombin receptor-activating peptide. Interestingly, we demonstrated the binding ability of PMBs and their adherence to preformed platelet-rich *in vitro* thrombi. Furthermore, PMBs are highly compatible with blood and showed no toxicity to cells *in vitro*, hence these fabricated materials are prospective candidates for further development and application *in vivo*. Overall, our work showcases the safe and precise utilisation of PMBs to directly target acute thrombosis induced by laser injury in murine mesenteric veins *in vivo*, as visualised through intravital microscopy.

In conclusion, we have successfully developed a PMBs with unique ultrasound-directed and thrombus-targeting properties. These exceptional attributes of PMBs hold significant promise for advancing the field of ultrasound diagnostic thrombus imaging and clot-targeted therapy in the clinical context.

39.

POTENTIAL NEUROIMMUNE INTERACTIONS

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Neuroimmune interactions in the gut are crucial for tissue homeostasis and physiological functions such as intestinal peristalsis and nutrient absorption. Most intestinal neurons are located within the myenteric plexus of the enteric nervous system, situated in the muscularis layer. While the interactions between muscularis macrophages and neurons are well established, the characterisation of muscularis immune cell profile remains unresolved. We mapped the immune cell landscape of the muscularis, identifying a diverse array of cell types in distinct regions of the GI tract, which are further validated by their close location to neuronal cell bodies and axons. We further identified regional imprinting of specific immune cells populations found within distinct areas of the gut, highlighting potential niche-specific neuroimmune regulations. Using computational analysis of single cell RNA sequencing of neurons and immune cells, we propose novel ligand-receptor interactions that are likely to be

neuro- and immune-protective. These findings provide a reference framework on neuroimmune crosstalk and their implications on GI homeostasis and disease.

40.

TRANSFORMING A CLINICALLY RELEVANT DIETARY INTERVENTION TO TREAT INFLAMMATORY BOWEL DISEASE: A REVERSE TRANSLATIONAL 'BEDSIDE-TO-BENCH' APPROACH

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Exclusive enteral nutrition (EEN) is the only non-pharmacological therapy currently used in clinical practice to induce remission in inflammatory bowel disease (IBD), with superior efficacy in mucosal healing compared to steroids. However, the use of EEN is limited due to a solely liquid diet form. Efforts to innovate EEN for long-term therapeutic diets are currently hindered by a poor understanding of its effects in a healthy state, and mechanism of actions underpinning mucosal healing.

AIM: To assess the effects of EEN in a healthy gut and identify mechanism of actions of EEN-driven mucosal healing following inflammation.

METHODS: Using a reverse translational 'bedside-to-bench' approach, we adapted a clinical EEN formula into laboratory chow and assessed how EEN affects the gut under healthy conditions. Using a clinically relevant preclinical model of colitis, we established the clinical efficacy of EEN and explored the underlying mechanisms of mucosal healing.

RESULTS: Under healthy conditions, EEN influenced tissue physiological functions by increasing intestinal permeability and motility. These effects correlated with shorter colon, smaller crypts, goblet cell hypoplasia, and reduced gut microbiota diversity. In a model mimicking EEN's clinical use during chemically induced colitis, our preliminary studies revealed that mucosal healing relied on optimal levels of caloric energy derived from highly digestible simple carbohydrates. These carbohydrates in turn facilitated colonocyte repair, resolved ulceration, and promoted the regeneration of crypt structures.

CONLUSION: Given its impacts on intestinal architecture and microbial landscape under healthy conditions, EEN may not be ideal as a prophylactic intervention to prevent IBD relapses. The therapeutic effects and mucosal healing induced by EEN are governed by simple dietary carbohydrates that directly promotes tissue repair. This mechanistic proof-of-principle evidence is key for formulating EEN's composition and transforming its clinical use for long-term therapeutic use.

CANCER

41.
ONCOLOGICAL OUTCOMES POST FOCAL LOW-DOSE-RATE BRACHYTHERAPY IN MEN WITH LOW-INTERMEDIATE RISK PROSTATE CANCER – RESULTS FROM LIBERATE REGISTRY

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Introduction:
Focal therapy for prostate cancer has emerged as a novel approach to minimise adverse events without compromising oncological outcomes in selected patients. This study reports oncological outcomes following focal low-dose-rate (LDR) brachytherapy for low-intermediate risk prostate cancer.

Methods:
Patients were recruited from an ongoing, prospective, multi-centre clinical registry of focal LDR brachytherapy cases for the treatment of low-intermediate risk prostate cancer from September 2019 (LIBERATE Registry, ACTRN:12619001669189). Rigorous follow-up was conducted with surveillance MRI and repeat transperineal prostate biopsy completed at 18-36 months post-treatment to assess for pathological control or progression. Control was achieved on repeat biopsy if there was no cancer or ISUP GG1 in <10mm of core or GG2-3 grade cancer with treatment effect. Progression occurred if there were no pathological changes from baseline or tumour upgrading occurred compared to baseline.

Results:
Of 120 men enrolled in LIBERATE Registry, 54 (45.0%) have completed their follow-up imaging and biopsy assessment with a median follow-up of 32 months. Oncological control was reported in 42 (77.8%) patients, including 25 negative biopsies, 12 ISUP GG1, and 5 in-field lesions with treatment effect. Ten men (18.5%) had out-of-field pathological progression, of whom 7 were managed with ongoing active surveillance (5-10% pattern 4), 1 underwent salvage robotic-assisted radical prostatectomy (RARP), 1 had contralateral lobe LDR brachytherapy, and 1 proceeded to external beam radiotherapy. Two men (3.7%) had concurrent out-of-field pathological progression and in-field lesions with treatment effect; of these, 1 had salvage RARP, and 1 was managed with watchful waiting.

Conclusion:
These results suggest that focal LDR brachytherapy for low-intermediate risk, single lesion, imaging-visible prostate cancer demonstrates satisfactory oncological control at 18-36 months given the trade-off of minimised side effects and allows for early recognition of treatment failure and decision-making on further intervention. However, further follow-up is needed to assess long-term oncological outcomes.

42.
EFFECT OF COVID-19 ON PROSTATE CANCER TREATMENT: RESULTS FROM THE VICTORIAN PROSTATE CANCER OUTCOMES REGISTRY (PCOR-VIC)

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Aim: COVID-19 has been reported by others to have affected the treatment of prostate cancer. We examined this in a registry of prostate cancer in Victoria. The Australian Prostate Cancer Optimal Care Pathway guideline recommends treatment within 90 days of diagnosis, therefore we examined whether COVID affected patients were treated within ≤90 days, treatment in the public or private system, surgery type, or radiation therapy fractionation strategy.
Method: Patients in PCOR-Vic diagnosed with intermediate, or high (or very-high) risk disease were divided based on diagnosis date: pre-COVID (1st January 2019 to 29th March 2020), and peri-COVID (30th March 2020 to 31st December 2021). 30th March 2020 was the first day of lockdown in Victoria. Multivariable logistic regressions were used to evaluate the impact of COVID on timeliness of management (≤90 days from-diagnosis-to-treatment), and the use of conventional, hypofractionated, or ultra-hypofractionated external beam radiation therapy (EBRT), adjusting for age-at-diagnosis, NCCN risk-category, treatment institution type (public vs private), socioeconomic status, and remoteness-of-residency. A two-sided P-value of <0.05 indicated statistical significance.
Results: 5,967 patients received either radiation therapy or radical prostatectomy during the analysis period. Compared to patients treated in the pre-COVID period, patients in the peri-COVID period were more likely to receive surgery in the private care setting, have robotic assisted surgery, and received their treatment slightly more promptly. Patients receiving radiation therapy had little change in treatment promptness and a change towards hypofractionation.
Conclusion: The increase in robot-assisted and private care for surgical patients, and the small change in fractionation in patients treated with radiation therapy was consistent with ongoing secular changes in management present prior to COVID. Timeliness of care was essentially unaffected. Victoria's healthcare system displayed resilience in continuing to deliver prompt prostate cancer care despite the challenges posed by COVID.

43.

A 12-WEEK EXERCISE PROGRAM IMPROVES EXERCISE CAPACITY IN ACUTE LEUKEMIA PATIENTS POST INTENSIVE CHEMOTHERAPY

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Introduction – Survivors of acute lymphoblastic leukemia (ALL) and myeloid leukemia (AML) are treated with intensive chemotherapy, which can leave patients physically deconditioned. Exercise improves survivorship outcomes in other patient groups but has not been tested in early survivorship for ALL and AML patients. Accordingly, we sought to test the feasibility and efficacy of an exercise program in early survivorship.

Methods – Eighteen patients (52 ± 16y, 62% male) with AML or ALL were recruited within 3 months of completion of intensive and consolidation chemotherapy to participate in a 12-week exercise intervention. The intervention consisted of individualised aerobic training: two moderate intensity continuous (50-70% heart rate reserve (HRR); 20-30mins) and one high intensity interval (>70%HRR; 4x2-4mins) sessions per week, and two resistance training sessions per week (6-10 upper and lower body exercises). To evaluate efficacy, changes in peak oxygen uptake (VO2peak) and peak watts were assessed by cardiopulmonary exercise testing, functional capacity by change in 6-minute walk distance (6MW), and body mass index (BMI). To assess the feasibility the %sessions completed are reported (100% of completed session =36).

Results – Three participants did not complete follow up CPET due to disease relapse. Eleven participants completed >75% of the prescribed exercise, and adherence ranged from 63-97%. Training increased both absolute and relative VO2peak 14.1% (1.95±0.42 to 2.23±0.48L.min^{-1}, p<0.001) and 10.4% (23.1±5.2 to 25.5±5.2mL.kg^{-1}.min^{-1}, p<0.001) respectively; and peak watts by 16.5% (168±36 vs 195±43W, p<0.001). BMI increased by 2.8%

(29.5±6.1 vs 30.3±6.5kg/m^2, p=0.003). In a subset of patients who completed 6MW at follow-up (n=9) distance increased by 4.7% (559±39 vs 585±43metres, p = 0.02).

Conclusions – Exercise training that is individualised is feasible to complete during early AML and ALL survivorship and leads to improved cardiorespiratory fitness and functional capacity. Further research is required to determine the impact on long-term survivorship outcomes.

44.

A STUDY COMPARING THE COST-EFFECTIVENESS OF CONVENTIONAL AND DRUG-ELUTING TRANSARTERIAL CHEMOEMBOLISATION (CTACE AND DEBTACE) FOR THE TREATMENT OF HEPATOCELLULAR CARCINOMA IN AN AUSTRALIAN PUBLIC HOSPITAL

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Hepatocellular carcinoma (HCC) is a leading cause of cancer related mortality and transarterial chemoembolisation (TACE) is an established technique to treat patients with intermediate-stage HCC.

AIM: The aim of this study was to generate accurate costing data on cTACE and DEB-TACE in an Australian setting and assess whether one of the procedures offers favourable cost-effectiveness.

METHODS: Costing study using data from all TACE procedures performed at asingle centre between January 2018 and December 2022. Data were included from all direct and indirect costs including operative costs, wages, overheads, ward costs, transfusion, pathology, pharmacy and ward support. Cost-effectiveness was assessed by dividing local costs by existing high-quality data on quality-adjusted life years (QALYs).

RESULTS: 64 TACE treatments were performed on 44 patients. Mean age was 66.5 years and 91% were male. Overall median total cost per patient for the entire TACE treatment regime was AUD$7380 (range AUD$3719–$20,258). However, 39% of patients received more than one treatment, and the median cost per individual treatment was AUD$5270 (range AUD$3533–$15,818). The difference in median cost between cTACE (AUD$4978) and DEB-TACE (AUD$9202) was significant, P < 0.001. In calculating cost-effectiveness, each cTACE treatment cost AUD$2489 per QALY gained, while each DEB-TACE cost AUD$3834 per QALY gained. The incremental cost-effectiveness ratio (ICER) for DEB-TACE over cTACE was AUD$10,560 per QALY gained.

CONCLUSION: Both cTACE and DEB-TACE are low-cost treatments in Australia. However, DEB-TACE offers a solution with an ICER of AUD$10,560 per QALY gained which is below the Australian government willingness to pay threshold and thus is a more cost-effective treatment.

45.

CLINICAL UTILITY OF A COMPUTERISED COGNITIVE TEST IN IDENTIFYING IMMUNE EFFECTOR CELL ASSOCIATED NEUROTOXICITY SYNDROME FOLLOWING CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY

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Change in cognition is characteristic of immune effector cell-associated neurotoxicity syndrome (ICANS), which is a potentially life-threatening complication of chimeric antigen receptor T-cell therapy (CAR-T).

AIM: This study investigated the clinical utility of a computerised test of processing speed, visual attention, and working memory (CARTcog) in identifying ICANS.

METHODS: Thirty-one patients underwent CAR-T at the Alfred Hospital in Melbourne between 28 August 2023 and 23 April 2024. 28 patients consented to the study. Participants completed serial CARTcog assessments and immune effector cell-associated encephalopathy (ICE) scores at baseline, daily during inpatient admission, and 1-, 3-, and 6-month time points. Trajectory plots of ICE scores and CARTcog scores across time were fitted with loess smoothing functions. Linear mixed-effect modelling was constructed to investigate the association between ICANS status (predictor) and CARTcog response measures (outcome). Receiver operator characteristic curves were constructed to investigate the discriminative ability of CARTcog measures in predicting ICE scores.

RESULTS: Twenty-eight participants (78% male, 64.07±12.49 years old at infusion) completed 345 CARTcog assessments. Eight (29%) patients developed ICANS. Trajectory plots illustrated a temporal relationship between ICE scores and CARTcog scores; reaction times and accuracy scores worsen with decreases in ICE scores and recover after ICE scores improve. Linear mixed-effects models revealed a significant interaction between time and ICANS groups ($p<0.05$), such that the patients who developed ICANS performed worse over time compared to those who did not develop ICANS. CARTcog scores were found to distinguish between patients with ICANS (i.e., ICE score<10) and those without ICANS (i.e., ICE score=10) (AUC>0.95 across different scores).

CONCLUSION: CARTcog has the potential to be used in conjunction with ICE scores to improve the detection of ICANS in patients who receive CAR-T. Earlier detection of ICANS, and hence, earlier treatment and management, can lead to improved patient outcomes.

46.
SURGICAL MARGIN RATES AFTER PROSTATECTOMY: INSTITUTIONAL DIFFERENCES HAVE GREATER IMPACT THAN SURGICAL APPROACH — INSIGHTS FROM A GLOBAL REGISTRY

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Aim: Positive surgical margins after prostatectomy for prostate cancer are a strong risk factor for biochemical failure and cancer recurrence. We used a global structured prospective registry of prostate cancer, the TrueNTH Global Registry, to assess the differences in the rate of positive surgical margins depending on stage, institution, or surgical approach.

Method: We developed a mixed-effects logistic regression model to analyse the data. We entered the surgical approach as open, laparoscopic, or robot-assisted, and omitted patients with conversion to open surgery. Patients with pathologic T2 and T3/4 tumours were analysed separately. We also entered biopsy ISUP grade group (GG), prostate specific antigen level ($\log_2$ transformed), and clinical T categories into the model. Institutions were assigned a random identifier and entered as a random intercept. Predicted positive margin rates were generated by biopsy grade group and institution. We used an alpha level of 0.05, with Bonferroni's correction for multiple comparisons, to define statistical significance.

Results: There were 48,022 radical prostatectomies between 2017- 2021, across twelve countries and 197 institutions. There were no differences in the rate of positive surgical margins between open, laparoscopic, and robot-assisted radical prostatectomy (all comparisons $p>0.05$). There were differences in margin positivity between pathologic tumour category (pT2 vs pT3/4) regardless of surgical approach (14.6% in pT2 vs. 36.3% in pT3/4,

p<0.00001). Biopsy GG had little influence on the rate of positive margins between surgical approaches. Patients who had biopsy GG 5, pT3/4 disease, or an open surgical approach had the highest positive margin rates of all groups (51.3%, p=0.025). There was variation between institutions, regardless of pathologic tumour grade or T category.

Conclusion In our global dataset, differences in positive margins for radical prostatectomy were more pronounced between institutions than between different surgical approaches, after adjusting for stage and grade.

47.
ASSOCIATIONS BETWEEN STRUCTURAL TOPOLOGY OF CANCER DRIVERS, AND CANCER EVOLUTION

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Cancer, driven by somatic mutations, disrupts protein function through driver mutations in oncogenes (OCGs) and tumour suppressor genes (TSGs). This study employs structure-based network analysis, a method to understand the structural topology of proteins, to investigate the functional consequences of mutations in cancer driver genes, with a particular focus on lung cancer. By systematically mapping the network properties of each amino acid residue across cancer driver genes using 3D crystallographic proteins structures, and matching these to protein function and cancer mutation frequency in thousands of patients, we found that structural topology of cancer drivers is strongly linked with cancer evolution. Mutations in highly networked residues were strongly associated with significant functional impairments, highlighting the critical role of central residues in protein stability and function. In lung cancer, distinct mutation patterns differentiate TSGs, which mutate in highly networked residues in order to lose function, from OCGs, which preferentially mutate in poorly networked residues to re- tain or gain function, thereby driving cancer. A novel visualisation method developed using PyMOL functionalities facilitates intuitive mapping of network scores onto protein structures, revealing regions of high functional importance and providing insights into structural and functional implications of mutations. Future research should aim to expand to all cancer genes. Beyond cancer research, the visualisation tool can adapt to visualise diverse protein metrics and facilitate comparative structural analyses.

48.
ENGINEERING T-CELL RECEPTORS (TCRS) THROUGH ENHANCED SEQUENCE ANALYSIS AND MODELING

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BACKGROUND
T Cell Receptors (TCRs), play a key role in identifying a variety of threats by recognizing peptides derived from altered self (in cancer) or foreign infections that are presented by the Major Histocompatibility complex. A key challenge in translating TCR's into therapies is the fact that naturally occurring TCR's are of low-moderate affinity, the strength of binding between receptor and antigen. Therefor being able to engineer them to be more stable and of higher affinity is the focus of TCR engineering efforts. Analysing the structural and mechanistic aspects of TCRs is highly challenging due to the extensive diversity of TCR variants in each individual, compounded by the limited availability of experimentally solved TCR-peptide-major histocompatibility complex (pMHC) structures. This gap poses a substantial hurdle in the experimental determination of TCR binding specificities, representing a crucial limitation in the field.

METHODS
This study utilised an innovative method of Structure-Based Network Analysis (SBNA), representing each TCR as a 3- dimensional network of relationships between residues, the building blocks of proteins, to achieve a unified understanding of how TCR's function.

RESULTS
We demonstrate that network scores can uniquely characterize TCR chains and, when integrated with deep learning techniques effectively distinguishing between TCR types (alpha and beta type). We also identified a negative correlation between changes in network scores and the strength (ΔΔG) of TCR-pMHC interactions, highlighting how mutations that enhance network scores can improve TCRs, offering a way to enhance TCRs as drugs. To formally nominate which residues be targeted for engineering purposes we mapped the positional importance of each residue in terms of network metrics Finally, we show how the network scores of residues relate to the evolutionary propensity to conserve that residue in the framework regions of the TCR but not in the antigen recognizing complementarity defining regions (CDR).

CONCLUSION
Collectively, these findings illustrate how SBNA provides a unifying framework for understanding and TCR-pMHC interactions and how this can be exploited to engineer better TCR's, that could be used to treat cancers and infections.

49.
ASSESSMENT OF IMAGE QUALITY ON THE DIAGNOSTIC PERFORMANCE OF CLINICIANS AND DEEP LEARNING MODELS: CROSS-SECTIONAL COMPARATIVE READER STUDY

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Background
Skin cancer is a prevalent and clinically significant condition, with early and accurate diagnosis being crucial for improved patient outcomes. Dermoscopy and artificial intelligence (AI) hold promise in enhancing diagnostic accuracy. However, the impact of image quality, particularly High Dynamic Range (HDR) conversion in smartphone images on model training and diagnostic performance remains poorly understood.

Objective
This study aimed to investigate the effect of varying image qualities, including HDR-enhanced dermoscopic images, on the diagnostic capabilities of clinicians and a Convolutional Neural Network (CNN) model.

Methods
18 dermatology clinicians from 4 different countries and our CNN model assessed 303 images of 101 skin lesions that were categorised into three image quality groups: Low Quality (LQ), High Quality (HQ), and Enhanced Quality (EQ) produced using HDR-style conversion. Clinicians participated in a two-part reader study that required their diagnosis, management and confidence level for each image assessed.

Results
In the binary classification of lesions, clinicians achieved their best diagnostic performance with HQ images, with sensitivity (77.3%;CI 69.1 to 85.5), specificity (63.1%;CI 53.7 to 72.5), and accuracy (70.2%;CI 61.3 to 79.1). The CNN model also performed strongest on HQ images with an AUROC of 0.77 (CI 0.67 to 0.86). Clinicians outperformed (median correct diagnoses) the CNN on LQ ($p<0.01$), and EQ images ($p<0.01$), but their performance was comparable on HQ images ($p=0.2$). Both the model and clinicians had their poorest performance on EQ images.

Conclusion
This study highlights the importance of image quality on the diagnostic performance of deep learning models and clinicians. This has significant implications for AI-based telehealth reporting, triage and public-facing AI mobile applications, as more smartphones adopt automatic HDR conversion for images.

50.

LEVERAGING PROTEIN-PROTEIN INTERACTION (PPI) MODELS FOR T CELL RECEPTOR-PEPTIDE MAJOR HISTOCOMPATIBILITY COMPLEX (TCR-PMHC) BINDING PREDICTION

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High-affinity interactions between T-cell receptors (TCRs) and peptide-major histocompatibility complexes (pMHCs) are essential for TCR-based drugs to be effective. Tebentafusp, the only approved drug of this kind, has an affinity of 24 pM, significantly higher than typical TCR affinities of 30–40 μM. While techniques like phage and yeast display can engineer high-affinity TCRs, they are complex and costly. Computational approaches offer a promising alternative but are hindered by limited experimental data on TCR-pMHC binding affinities.

AIM: To improve the prediction accuracy of mutational free energy changes (ΔΔG) in TCR-pMHC complexes by fine-tuning attention-based geometric deep learning model, and to enhance it further with synthetic data generated through reverse and cross ΔΔG imputations

METHODS: The task-specific (ATLAS) dataset was pre-processed by removing duplicates and missing values. Mutant naming conventions were standardized for consistent PDB retrieval. Data augmentation techniques—including reverse and cross ΔΔG imputations method—expanded the training data to 584 entries (224 original mutations, 136 cross mutations, 224 reverse mutations). Four models were trained using different combinations of these datasets. Training was performed on A100 GPU using the Adam optimizer, employing Mean Squared Error loss and implementing Early-Stopping.

RESULTS: Fine-tuning and synthetic data augmentation significantly improved ΔΔG predictions for TCR-pMHC complexes. The fine-tuned combined mutation model achieved MSE = 1.848 (95% CI: 1.375–2.375), RMSE = 1.359, and correlation (between predicted and actual ΔΔG values) r=0.687, demonstrating enhanced predictive capabilities over the baseline model with MSE = 13.371 (10.998–15.987), RMSE = 3.657, and r=0.209.

CONCLUSION: Fine-tuning the attention-based geometric deep learning model with reverse and cross mutations for data augmentation led to a 62% reduction in RMSE (from 3.657 to 1.359) and increased the correlation coefficient from 0.209 to 0.687. This demonstrates that fine-tuned model captures key interactions and could enable the engineering of TCR therapies against cancer and viral infections.

51.

GENETIC VALIDATION OF IMMUNOPROTEASOME'S CAUSAL ROLE IN IMMUNOTHERAPY FOR NSCLC: MENDELIAN RANDOMIZATION ANALYSIS

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Non-small cell lung cancer (NSCLC) accounts for 80% of lung cancer, and 15%-40% of patients respond to immunotherapy. High expression of immunoproteasome components in advanced NSCLC patients is linked with favourable immunotherapy response.

AIM: To validate causal relationship between immunoproteasome system and immunotherapy response

METHODS: To identify instrumental exposure-SNPs, eQTLGen Phase I cis-eQTL dataset tested on 31,684 blood samples from European ancestry consisting of 10,507,665 cis-eQTL SNPs of 16,987 genes (FDR < 0.05, SNP gene distance < 1 Mb) underwent data processing and linkage disequilibrium (LD) clamping. Outcome-SNPs were extracted from the GWAS dataset (restricting to European ancestry by principal components analysis) presented from survival analysis of Dana-Farber PROFILE cohort (899 immunotherapy-treated NSCLC patients). Exposure- and outcome-SNPs underwent harmonization, and then causal estimation by two sample Mendelian randomization (TSMR) analysis including 12 methods: inverse-variance weighted (IVW), weighted median, simple median, MR-Egger, maximum likelihood (MaxLik), mode-based Estimate (MBE), heterogeneity-penalized (HetPen), contamination mixture (ConMix), MR-Lasso, robust adjusted profile score (dIVW and pIVW), causal mixture model-median absolute deviation (cML-MA-BIC-DP).

RESULTS: LD clamping identified 4 strongly independent, biologically relevant exposure-SNPs in cis-eQTL dataset. Four paired exposure-outcome SNPs post-harmonization underwent TSMR analysis. All 12 methods produced negative causal estimates. The 95% CI of 7 estimates (weighted median, simple median, MBE, HetPen, ConMix, MR-Lasso and cML-MA-BIC-DP) excluded null value (p-value < 0.05), while 5 other estimates (IVW, MR-Egger, MaxLik, dIVM and pIVM) did not (p-value range: 0.18-0.42).

CONCLUSION: The overall pattern of the TSMR analysis suggests causation of immunoproteasome components on immunotherapy response for NSCLC. The negative causal effect estimates indicate a higher expression of immunoproteasome system is causally linked to longer survival outcome. This highlights the potential of biomarker development and genetic drug target. The limitation of results highlights the need for further analysis ideally on more instrumental SNPs or expanded cancer types.

52.

USING THE AUSTRALIAN PROSTATE CANCER OUTCOMES REGISTRY (PCOR) TO IDENTIFY PATTERNS OF VARIATION IN PROSTATE CANCER DIAGNOSIS AND TREATMENT

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Aim: Identify differences in prostate cancer management in Australia within the Prostate Cancer Outcomes Registry - Australia, and to identify areas where the registry can improve capacity to detect disparities and inequalities in potentially disadvantaged populations. We examined differences in rates of transperineal biopsy, (recommended approach) compared to the traditional transrectal biopsy. Timeliness of surgery (prostatectomy) was examined relative to the Australian Optimal Care Pathway recommendation: treatment within 90 days of

diagnosis (1). We assessed data completion and quality to enable improvements in our ability to understand disparities and inequalities.

Method: Data from 73,932 patients diagnosed with prostate cancer in 2018-2022 were analysed. Socioeconomic status (SES) was measured using the Index of Relative Socio-economic Advantage and Disadvantage and rurality of residence was assessed using the Modified Monash Model. Summary statistics and multivariate logistic regressions were utilised to determine factors (institute type, rurality of residence, SES) associated with biopsy method, timely receipt of surgery, and data completeness. Statistics were performed using StataNow 18.5 (StataCorp, USA).

Results: Patients from the most socioeconomically advantaged areas were 1.6 times more likely to receive a transperineal biopsy than those in the most disadvantaged areas, and those diagnosed in a private institution were 2.4 times more likely than those in a public institution. Timeliness of surgery was 6.5 times better for patients diagnosed in a private institution compared to public. Patients outside metropolitan areas were 25% less likely to have timely surgery. Data quality and completeness for country of birth, preferred language, and Aboriginal and Torres Strait Islander status was limited.

Conclusion: The prostate cancer outcomes registry identified significant variation in relation to socioeconomic status, public/private care, and rurality in prostate cancer diagnosis and treatment – highlighting its potential to be a valuable tool in identifying further areas of disparity and inequality, and gaps in data collection.

53.

DEFINING *FOXP4* TRANSCRIPTIONAL TARGETS TO UNDERSTAND THE ROLE OF *FOXP4* IN LUNG CANCER AND LONG COVID

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The Forkhead box P4 (*FOXP4*) gene encodes a transcription factor that regulates gene expression, impacting critical cellular processes. Genetic variants of *FOXP4* are associated with lung cancer and severe and long COVID, though its genetic targets and molecular mechanisms remain poorly understood.

AIMS: To identify *FOXP4*'s genetic targets in lung epithelial cells and understand its role in lung development, lung cancer, and long COVID.

METHODS: We validated a new *FOXP4* antibody and identified *FOXP4* binding sites using ChIP-seq in A549, H441 and iPSC-derived alveolar type II cells, followed by analysis using the Nextflow-core ChIP pipeline. Peak annotation was done with ChIPseeker, and functional clustering was performed using the DAVID database. Results were harmonized with an unpublished ENCODE dataset studying *FOXP4* in HepG2, K562, and WTC11 cells. We identified co-factors of *FOXP4* by immunoprecipitation and mass spectrometry. *FOXP4* targets were validated by siRNA mediated reduction in *FOXP4* and mass spectrometry.

RESULTS: The overall read depth and quality for A549 *FOXP4* ChIP and input samples were good (ENCODE threshold of RSC>0.8). MACS2 called 17,706 and 25,270 peaks for A549 replicates, with 14,421 peaks annotated. Most reads (~90%) for A549, HepG2, K562, and WTC11 were located at transcription start sites and promoter regions. Across the cell lines, 555 genes overlapped, including *E2F6* and *MYC*, both key in non-small cell lung cancer. *FOXP4* binding was enriched for lung cancer-related genes in A549 and HepG2 cells (p=0.02) and for COVID-19-related genes in K562 cells (p=0.05). *FOXP2* and *FOXP4* co-immunoprecipitated confirming heterodimer formation.

CONCLUSION: These experimentally determined *FOXP4* binding maps highlight cell-type specific gene programs regulated by *FOXP4*, validating its role in lung cancer and COVID-19. This resource provides a rich dataset for functional hypothesis generation to identify the mechanisms by which *FOXP4* affects disease risk.

54.

TIMELINESS MATTERS: FACTORS INFLUENCING FIRST SPECIALIST APPOINTMENT AND TREATMENT DELAYS IN PATIENTS WITH NON-SMALL CELL LUNG CANCER.

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Non-small cell lung cancer (NSCLC) comprises 85% of lung cancer cases in Australia. The Australian Optimal Care Pathway recommends a referral to first lung cancer specialist appointment within 14 days and diagnosis to treatment within another 14 days for early treatment and improvement in survival.

AIM: The study aims to identify factors contributing to delays for first lung cancer specialist appointment and treatment for patients with NSCLC.

METHODS: This prospective study utilizes data from the Victorian Lung Cancer Registry between Jan-2012 and Nov-2023 (n=13,304). Factors associated with delays from referral to specialist appointment and diagnosis to treatment were identified through multivariable logistic regression. Survival analyses used Kaplan-Meier estimates of survival.

RESULTS: Factors including primary language other than English, diabetes, history of respiratory or neoplastic comorbidity were associated with referral to specialist appointment exceeding 14 days. In contrast, patients with advanced cancer stage, high SES, loss of weight or treatment at a private hospital had a referral to specialist appointment within 14 days. Delay in diagnosis to treatment beyond 14 days was associated with age >70 years, high socioeconomic status, respiratory comorbidity, less-advanced cancer stage, squamous cell carcinoma histology and treatment at inner-regional hospitals. Patients treated within 14 days of diagnosis had a significantly higher 1-year (0.73 [0.72-075]) and 5-year survival (0.49 [0.48-9.51]) compared to patients experiencing delays (1-year: 0.68 [0.67-0.69], 5-year: 0.33 [0.32-0.35], p<0.001)). Survival did not differ between patients referred to a specialist within 14 days and those experiencing delays.

CONCLUSION: This study highlights the importance of a timely lung cancer specialist appointment and treatment for patients with NSCLC and the various factors influencing time to specialist appointment and treatment. Achieving a diagnosis to treatment within 14 days is particularly important as it is associated with significantly higher survival rates compared to patients experiencing delays exceeding 14 days.

55.

EVOLVING MANAGEMENT OF NON-METASTATIC NODE POSITIVE PROSTATE CANCER IN VICTORIA FROM 2008 TO 2022

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AIM: Historically, men with non-metastatic node-positive prostate cancer (N1M0PC) were considered incurable due to perceived micrometastatic disease. Multi-institutional retrospective/ population studies, and STAMPEDE trial subgroup analysis have suggested that local treatment with surgery or radiation therapy (RT) in N1M0PC improves outcomes and survival. The increased use of PSMA-PET may have led to increased diagnosis of hitherto unsuspected N1 disease. This study examines Victorian temporal trends and factors associated with the primary treatment for N1M0PC.

METHODS: We included men diagnosed with N1M0PC between 2008 and 2022 in the Victorian Prostate Cancer Outcomes Registry (PCOR-Vic). The primary outcome was the temporal trend in the primary management (within the first 12 months of diagnosis).

RESULTS: Among 819 men with N1M0PC, 530 (65%) received local treatment (surgery or RT), 259 (32%) had systemic therapy alone (androgen deprivation therapy +/- chemotherapy), and 30 (4%) had no treatment. Local treatment increased from 52% in 2008-2012 to 72% in 2018-2022 (P-trend<0.001). In multivariable analyses, age, diagnosing institutions, and year of diagnosis were independently associated with the likelihood of having local treatment. Men diagnosed in private institutions were more likely to have local treatment (70% vs 60%; OR=1.6; 95%CI=1.16-2.20; P=0.004), as were those diagnosed in 2018-2022 compared to 2008-2012 (72% vs 52%; OR=3.0; 95%CI=1.74-5.17; P<0.001). Of the 530 men who received local treatment, 169 (32%) had surgery and 361 (68%) had RT. Age and diagnosing institutions were independently associated with likelihood of having surgery. Men diagnosed in private institutions were more likely to have surgery compared to public institutions (56% vs 41%; OR=4.4 times; 95%CI=2.72-7.09; P<0.001).

CONCLUSION: This is the largest cohort of N1M0PC in Australia. We observed increasing use of local treatment for N1M0PC more recently, and noted significant differences in management based on the diagnosing institution, particularly between private and public facilities.

56.

TRAFFIC IS THE CONTRIBUTOR IN THE ACUTE PM2.5 EXPOSURE AND CANCER LINK: A POOLED ANALYSIS OF OVER 9 MILLION CANCER DEATH RECORDS ACROSS A 20-YEAR PERIOD

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Cancer patients, a particularly vulnerable population, may not be able to withstand acute exposure to environmental risk factors. Although the health impacts of short-term $PM_{2.5}$ exposure have been thoroughly investigated, there is a lack of evidence specific to cancer patients.
AIM: To evaluate the effects of acute $PM_{2.5}$ exposure on cancer mortality and explore the need for special attention to traffic-sourced $PM_{2.5}$ ($TSPM_{2.5}$) pollution.

METHODS: We extracted site-specific cancer mortality collected between 2000 to 2019 from eight countries: Australia, Brazil, Canada, Chile, South Korea, Moscow, New Zealand, and Thailand. Daily $PM_{2.5}$ and $TSPM_{2.5}$ were estimated and linked by residential location for each participant. We applied a time-stratified case-crossover design to estimate the impact of $PM_{2.5}$ and $TSPM_{2.5}$ exposure on site-specific cancer mortality. We quantified the attributable cancer burden by acute $PM_{2.5}$ exposure and the addition burden due to the higher risk of $TSPM_{2.5}$ exposure.

RESULTS: In total, 9,223,612 cancer cases were included in the analyses, covering the time period from 2000 to 2019. The pooled results suggested a 10 μg/m³ increase in $PM_{2.5}$ exposure over two days (lag 0-1) corresponds to a 0.8% rise in all-cancer mortality risk [95% confidence interval (CI): 0.6%-0.9%] and each 10 μg/m³ increase in traffic-sourced $PM_{2.5}$ concentration was associated with a 3.9% (95% CI: 3.3%-4.5%) increase in cancer mortality. Assuming causality, around 1.6% (1.4%-1.9%) of cancer mortality were attributable to acute

$PM_{2.5}$ exposure while the contribution of $TSPM_{2.5}$ equal to 1.2% (1.0%-1.4%). No additional vulnerable sub populations were observed but vulnerable cancer sites varied across countries.

CONCLUSION: Acute exposure to $PM_{2.5}$ increased the risks of cancer mortality from multiple sites, and the traffic in a critical contributor in this link. Minimizing $TSPM_{2.5}$ exposure may serve as a practical approach to safeguarding cancer patients from acute environmental hazards.

57.
TIME TO ANTBIOTICS IN ADULT CANCER PATIENTS WITH FEBRILE NEUTROPENIA

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BACKGROUND: Febrile Neutropenia (FN) is a serious oncological emergency that is associated with an increased risk of morbidity and mortality from bacterial infections. Delayed Time to Antibiotic Administration (TTA) is a recognised determinant of increased mortality and length of hospital stay. The recommended TTA at Alfred Health is 30 minutes, regardless of systemic or non-systemic compromise.

AIM: To determine the proportion of Alfred Health inpatients with FN admitted under Haematology/Oncology units administered initial intravenous (IV) antibiotics within 30 minutes of FN.

METHODS: A retrospective review of admitted patients who developed FN between 1st January to 31st December 2023 was performed. Patients were identified using electronic medical records and coded data. Patients were excluded if they had neutrophils > 0.5 x 10^9/L, were afebrile, already on IV antibiotics during their FN episode or if IV antibiotics were administered in the emergency department, intensive care unit or day units. Baseline demographics and clinical variables including time to fever, time to antibiotic administration and all-cause inpatient mortality were collected. Appropriateness of antibiotics was assessed using the National Antimicrobial Prescribing Survey (NAPS) definitions.

RESULTS: 86 patients were identified as having FN. The median TTA was 60 minutes (IQR: 46-84 minutes; range 14-167 minutes), with 8% of patients having antibiotics administered within 30 minutes. In a subgroup of 5 patients with neutropenic sepsis, the median TTA was 50 minutes (IQR:46-60 minutes; range: 21-145 minutes) and only a single patient had antibiotics administered within 30 minutes. Appropriateness of antimicrobial prescriptions was high with 92% of prescriptions considered appropriate. All-cause inpatient mortality was 5.8%.

CONCLUSION: Our results suggest an opportunity to enhance the timely administration of antibiotics in patients with FN. Further work is planned to improve the proportion of patients receiving antibiotics within the recommended 30 minutes.

CARDIOVASCULAR

58.
EXPOSURE TO PM2.5 DURING PREGNANCY AND INFANCY FROM COAL MINE FIRE AND SUBCLINICAL CARDIOVASCULAR DISEASE IN CHILDHOOD: A PROSPECTIVE COHORT STUDY

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BACKGROUND: Chronic exposure to air pollution during early life has been associated with an increased risk of cardiovascular disease (CVD). However, there is limited research on the cardiovascular effects of exposure to acute, high-intensity air pollution events, such as coal mine fire smoke, during early life.

AIM: To investigate the association between exposure to particulate matter (PM2.5) in pregnancy and infancy and subclinical CVD during childhood.

METHODS: A prospective cohort study was conducted among children living in Latrobe Valley, who were exposed to high levels of air pollution from coal mine fire. A total of 298 participants were recruited for clinical follow-ups and classified into three groups: in utero exposed (n=105) and postnatal exposed (n=122) to fire and non-exposed (n=71) controls. Subclinical CVD was assessed using non-invasive tests: pulse wave velocity (PWV), carotid intima-media thickness (CIMT) and resting blood pressure. The clinical follow-ups were conducted at ages 3, 7 and 9 years. Simple and multivariable linear regression were used to evaluate the association between PM2.5 exposure and subclinical CVD at each follow-up, and overall vascular change from 3 to 9 year for participants with data at least two follow-ups.

RESULTS: A total of 241, 167 and 174 participants attended the 3, 7 and 9 year clinical follow-up, respectively. Nearly half of the participants were female, with a mean (±SD) age of 6.3 (±2.9) years. PWV increased in the exposed group at 7 and 9-year follow-ups. Additionally, the overall rate of change in brachial and central blood pressure from ages 3 to 9 was higher among exposed children compared to non-exposed.

CONCLUSION: Exposure to high levels of air pollution during early life was associated with increased PWV and blood pressure. These finding suggest that exposure to air pollution during pregnancy and infancy may contribute to adverse vascular health outcomes during childhood.

59.
SYMPTOMS OF ANXIETY AND DEPRESSION (SAD) IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE IMPLANTATION – THE SAD-TAVI STUDY

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BACKGROUND: Symptoms of anxiety and/or depression (SAD) commonly co-exist in severe aortic stenosis (AS). In patients undergoing transcatheter aortic valve implantation (TAVI), these symptoms are associated with increased morbidity and mortality. Despite this, mental health remains under-researched in the TAVI literature.

AIMS: Drawing from the largest registry in Australia, we aimed to characterise the prevalence of SAD in TAVI patients. We also aimed to identify patient phenotypes at highest risk of these symptoms, examine how they evolve following TAVI and establish factors predictive of improvement and regression in mental health.

METHODS: 1279 patients undergoing TAVI between 2018 and 2023 included in a multi-centre Australian registry were analysed. SAD were assessed using the validated 'anxiety and depression' domain from the EQ-5D-3L questionnaire. Multivariable logistic regression models identifying predictors of change in mental health were developed with excellent calibration and discrimination. Internal validation was performed using bootstrapping (1000 samples).

RESULTS: Median age was 82 (IQR 77, 87), 41% female and median STS score 3.9 (2.3, 5.9). 353 (28%) patients reported SAD at baseline. Of this group, 260 (74%) had complete resolution in symptoms within 30-days. Body Mass Index<25 (adjusted odds ratio [aOR] 3.4, p<0.001), vascular site complications (aOR 3.4, p=0.029) and non-home discharge (aOR 2.4, p=0.036) independently predicted failed improvement in SAD. Only 72 (8%) patients developed new-onset SAD at 30-days following TAVI. Non-home discharge (aOR 2.12, p=0.025) and a composite cardiovascular endpoint including stroke, acute myocardial infarction and heart-failure readmission (aOR 2.55, p=0.028) were independent predictors of new-onset SAD.

CONCLUSION: Symptoms of anxiety and depression are common but under recognised in AS. TAVI is highly effective at improving these symptoms. Regular screening for mental health should be considered in the management of all TAVI patients.

60.

INSIGHTS INTO PULMONARY REMODELING IN HEART FAILURE WITH PRESERVED EJECTION FRACTION THROUGH TRANSPULMONARY BIOMARKER GRADIENTS

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BACKGROUND & AIMS: Pulmonary hypertension (PH) is common in heart failure with preserved ejection fraction (HFpEF), however, the pathophysiology is not well understood. Therefore, we investigated transpulmonary inflammatory biomarker gradients (TPG) and their contribution to invasive haemodynamics.

METHODS: Thirty-four participants (20 HFpEF, 14 healthy controls) underwent exercise hemodynamic testing and concurrent arterial/pulmonary artery blood sampling. A panel of 157 inflammatory biomarkers were analyzed using proximity extension assay technology and subsequent polymerase chain reaction. TPG = [PA]-[arterial], transpulmonary flux =TPG x cardiac output.

RESULTS: HFpEF patients were older (70±9 vs 53±8 years, p<0.001) with higher BMI (34±9 vs 26±9 kg/m², p=0.004). None of the healthy controls had PH, while 55% of HFpEF patients did. Pulmonary vascular resistance was higher (1.95±0.83 vs 0.93±0.50WU, p<0.001), and pulmonary artery compliance (PAC) lower (4.2±1.7 vs 7.1±2.4ml/mmHg, p<0.001) in HFpEF. Principal coordinate analysis revealed significantly different biomarker transpulmonary flux profiles between HFpEF and controls (p=0.002). There was a significant pulmonary contribution from 15 of the 157 biomarkers in HFpEF, with 12 of these correlated with invasive haemodynamics. Correlation between PAC and TPG of follistatin (r=0.10 vs -0.64, p=0.03), agouti-related protein (r=0.223 vs -0.49, p=0.048), lipoprotein lipase (r=0.05 vs -0.59, p=0.03), and thrombomodulin (r=0.26 vs -0.63, p=0.01) significantly differed between HFpEF and controls. Correlation between exercise mean pulmonary artery pressure and TPG of thrombomodulin (r=0.14 vs -0.66, p=0.02), leptin (r=0.31 vs -0.57, p=0.01), ADAMTS13 (r=0.21 vs -0.54, p=0.04), adrenomedullin (r=0.30 vs -0.54, p=0.02), CCL11 (r=0.32 vs -0.48, p=0.03), decorin (r=0.19 vs -0.52, p=0.048),

GDF-2 (r=0.17 vs -0.63, p=0.02), and PD-L2 (r=0.29 vs -0.72, p=0.002) significantly differed between HFpEF and controls.

CONCLUSION: We identified a significantly altered transpulmonary flux profile of inflammatory biomarkers in HFpEF compared to healthy controls. Dysregulation of these biomarker gradients may contribute to adverse pulmonary remodeling, as suggested by correlations with invasive hemodynamics.

61.

FIRING PROPERTIES OF SINGLE AXONS WITH CARDIAC RHYTHMICITY IN THE HUMAN CERVICAL VAGUS NERVE

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Neural activity with both cardiac and respiratory rhythmicity has been documented in the cervical vagus of awake humans. The presence of cardiac rhythmicity is of particular interest, as it suggests that the physiology of vagal neurones that have cardiovascular regulatory function can be investigated using this technique. Here, the activity of single neurons exhibiting cardiac rhythmicity was discriminated from recordings of the human cervical vagus nerve. The functional identification of these neurones was then attempted based on their pattern of firing with respect to the cardiac or the respiratory cycle.

Twenty-two neurones with positive-going spikes (indicative of myelinated axons) and 22 with negative-going spikes (indicative of unmyelinated axons) were isolated across 9 awake participants. Of particular note is the observation of 7 cardiac rhythmic neurones with myelinated axons that showed increased activity during slow, deep breathing. These neurones fired predominantly during expiration, and during the minima in heart rate associated with respiratory sinus arrhythmia. This is consistent with the known firing properties of cardioinhibitory efferent neurones. The remaining 15 cardiac rhythmic neurones with myelinated axons were classified as either cardiopulmonary receptors or baroreceptors based on the average position of their peak in firing with respect to the R wave of the cardiac cycle.

Three neurones with unmyelinated axons showed expiratory rhythmicity, implicating them as cardiac-projecting efferent neurones. Classification of the remaining 19 unmyelinated neurones is challenging, as their slow and variable conduction velocities renders an analysis based on the temporal relationship between their peak in firing and the cardiac cycle futile. However, this population is likely dominated by arterial baroreceptors.

In conclusion, the activity of single neurones with putative cardiovascular function has been discriminated from recordings of the human cervical vagus for the first time, enabling their systematic study in both health and disease.

62.

NURSE-SUPPORTED SEDATION FOR TRANSCATHER AORTIC VALVE IMPLANTS: A RETROSPECTIVE ANALYSIS.

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With the increasing safety and streamlined nature of transcatheter aortic valve implantation, alternative paradigms around sedation have been proposed, including nurse-supported sedation in selected cases, as opposed to routine anaesthetic led care (A-TAVI). There has been limited research into the safety and viability of this model of care.

Aim: To evaluate the quality and safety of nurse assisted sedation for transcatheter aortic valve implantation (NAVI) with the introduction of a new guideline and to investigate the viability of this model of care.

Methods: A retrospective analysis of patients who underwent NAVI in the first 80 days post the introduction of the new guideline. This cohort was compared to A-TAVI for baseline demographics, procedural characteristics, VARC-3 complications, time to procedure, length of stay and post-procedural complications.

Results: In patients undergoing NAVI, there was a significant reduction in fentanyl dose (50 [25-75] vs 75 [50-100], p=0.02) and wait time (27 [11-33] vs 39 [21-57]), p=0.02). Patient and procedural characteristics and length of stay (p=0.6) were similar between groups. There were too few complications amongst either group for comparison, however these were not markedly different.

Conclusion: NAVI patients had a significantly lower wait time to procedure with reduced use of fentanyl and propofol, with no increased risk of complications in carefully selected patients. Translation to a larger cohort will facilitate understanding of program expansion and potential risks.

63.

PRE-DISCHARGE LUNG ULTRASOUND DETECTS SUBCLINICAL PULMONARY CONGESTION IN PATIENTS ADMITTED WITH DECOMPENSATED HEART FAILURE

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BACKGROUND: Pre-discharge pulmonary congestion after heart failure (HF) hospitalisation, detected by lung ultrasound (LUS), predicts worse outcomes.

AIMS: To characterise pre-discharge congestion using LUS as compared with clinical volume assessment in a General Medicine inpatient cohort.

METHODS: We prospectively evaluated pre-discharge volume status both clinically and by LUS in patients admitted under General Medicine with decompensated HF. Clinical assessment was by a modified congestion score evaluating jugular venous distension, rales and peripheral oedema. LUS volume assessment was performed at the bedside with Philips Lumify device (Philips, Cambridge, USA) using an 8-sector scanning protocol, and ≥10 b-lines defined prognostically significant pulmonary congestion. Clinical, laboratory and follow-up data were extracted from the electronic medical record.

RESULTS: 66 patients (52 % female, median age 85 (77-91) years) were enrolled. Common causes of HF decompensation were pulmonary infections (24%), arrhythmia (20%) and non-adherence to self-management (14%). The median admission NT-proBNP was 5696 (3185-8325) ng/L. 13/66 (20%) patients were readmitted with HF within 30 days of discharge.

38/66 (58%) patients had pulmonary congestion on LUS. When assessed independently to LUS, 24/66 (36%) patients were hypervolaemic on pre-discharge clinical examination. Of the remaining 42 patients who were clinically euvolaemic, 20 patients met criteria for pulmonary congestion (i.e., subclinical pulmonary congestion on LUS).

A higher proportion of patients with pulmonary congestion on LUS had HF with reduced ejection fraction (50% vs 14%, p=0.008) and clinical hypervolaemia (47% vs 21%, p=0.03), compared to those without congestion. There were no differences in the incidence of pulmonary infections between the two groups.

CONCLUSION: LUS provides complementary information to the physical examination when assessing volume status. Nearly half of clinically euvolaemic patients exhibit subclinical pulmonary congestion on discharge. More research is warranted to explore the utility of LUS in guiding HF management decisions for General Medicine patients at time of discharge.

64.

USE OF A CUSTOMISABLE CARDIOLOGY DATABASE TO AUDIT PATIENT DOSES IN INTERVENTIONAL CARDIOLOGY

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INTRODUCTION: Since their introduction, regulatory authorities globally have implemented the use of Diagnostic Reference Levels (DRLs), including Australia [1]. DRLs provide a benchmark on what is achievable with good practice, and help identify issues relating to the equipment or clinical practice [2]. In an Australian interventional cardiology context, one DRL has been published in 2020 for diagnostic coronary angiogram (CA) by the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA).

METHOD: The Heart Centre database at Alfred Health was purpose built to record key patient metrics, including the appropriate DRL metric of cumulative kerma-area-product (KAP) for each procedure undertaken. Over 20,000 examinations have been completed since database inception across five catheterisation laboratories. This enabled comparison with the ARPANSA national DRL for CA and the establishment of “target levels” for other common procedures at six-monthly intervals. A cross-disciplinary collaboration comprising of diagnostic medical physicists, cardiologists and radiographers was established to categorise procedures that used the same radiography protocols and were expected to be in a comparable dose range.

RESULTS: Over the six-year data collection period, 18,680 entries were allocated to 15 procedure categories. The most frequent procedure was CA (40%), followed by a CA with a subsequent percutaneous coronary intervention (PCI) (21%). The median KAP value for CA across all catheterisation laboratories was below the respective ARPANSA national DRL. Patient data was sub-filtered for key predictive variables, including body mass index, procedure time, procedure type, fluoroscopic unit model and fluoroscopic unit age. For other procedures, key differences between catheterisation laboratories were noted. Contributory factors explored include age of fluoroscopic unit and case complexity.

CONCLUSION: This analysis enabled a thorough insight into cardiology practices within Alfred Health, particularly from a radiation dose perspective. The establishment of “target levels” for 15 categories highlighted several opportunities for optimisation.

65.

DAPAGLIFLOZIN TREATMENT IMPROVES CARDIAC REMODELING IN A MOUSE MODEL OF HEART FAILURE WITH PRESEVRED EJECTION FRACTION

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INTRODUCTION: Despite global efforts, heart failure with preserved ejection fraction (HFpEF) remains a major issue in modern cardiovascular medicine and is plagued by a paucity of effective evidence-based therapies. Recently, SGLT2 inhibitors (SGLT2i) have demonstrated robust clinical benefits in HFpEF patients, notably via reducing hospitalisations. However, the mechanisms underlying the cardioprotective effects of SGLT2is are not well understand and thought to be distinct from the kidney-mediated pathways of the drug. This study aims to assess the effects of SGLT2i in a clinically relevant mouse model of HFpEF induced by high-fat diet (HFD) and angiotensin II (AngII) infusion in aged female mice.

METHODS: Female C57BL/6J mice (18 months old) were randomly assigned to three treatment groups (n=15-17 per group): (i) Normal chow diet (NCD), (ii) HFD + AngII, and (iii) HFD + AngII + Dapagliflozin (DAPA,1.5/mg/kg/day, in drinking water). AngII infusion (0.75mg/kg/day) began at week 6 via osmotic mini pumps. DAPA treatment started at week 6 in the HFD+AngII+DAPA group and continued for 6 weeks.

RESULTS: HFD+AngII challenge induced a HFpEF phenotype in aged female mice, demonstrating diastolic dysfunction as evidenced by the elevated IVRT and significantly reduced E/A ratio. Concomitantly, the perturbations induced cardiometabolic remodelling including obesity, hypertension, exercise intolerance, inflammation and vascular dysfunction. DAPA treatment did not ameliorate any parameter of the cardiac function or blood pressure. Notably, DAPA treatment attenuated cardiac hypertrophy and overall had mild effects on the metabolic and obese-related HFpEF phenotype.

CONCLUSION: This study highlighted that DAPA treatment only improved aspects related to cardiac remodelling without a significant impact on cardiac function. The minimal benefits in the cardiometabolic HFpEF phenotype may explain, in part, why SGLT2i treatment did not reduce mortality in HFpEF patients. Further investigation is needed to explore the mechanisms underlying the cardioprotective effects of SGLT2i in HFpEF.

66.

A MICROFLUIDIC MODEL TO STUDY THE EFFECTS OF ARRHYTHMIC FLOWS ON ENDOTHELIAL CELLS

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Atrial fibrillation (AF) is the most common type of cardiac arrhythmia and an important contributor to morbidity and mortality. Endothelial dysfunction has been postulated to be an important contributing factor in cardiovascular

events in patients with AF. However, how vascular endothelial cells respond to arrhythmic flow is not fully understood, mainly due to the limitation of current *in vitro* systems to mimic arrhythmic flow conditions. To address this limitation, we developed a microfluidic system to study the effect of arrhythmic flow on the mechanobiology of human aortic endothelial cells (HAECs). The system utilises a computer-controlled piezoelectric pump for generating arrhythmic flow with a unique ability to control the variability in both the frequency and amplitude of pulse waves. The flow rate is modulated to reflect physiological or pathophysiological shear stress levels on endothelial cells. This enabled us to systematically dissect the importance of variability in the frequency and amplitude of pulses and shear stress level on endothelial cell mechanobiology. Our results indicated that arrhythmic flow at physiological shear stress level promotes endothelial cell spreading and reduces the plasma membrane-to-cytoplasmic distribution of β-catenin. In contrast, arrhythmic flow at low and atherogenic shear stress levels does not promote endothelial cell spreading or redistribution of β-catenin. Interestingly, under both shear stress levels, arrhythmic flow induces inflammation by promoting monocyte adhesion via an increase in intercellular adhesion molecule 1 (ICAM-1) expression. Collectively, our microfluidic system provides opportunities to study the effect of arrhythmic flows on vascular endothelial mechanobiology in a systematic and reproducible manner.

67.

IMPROVING HEART FAILURE OUTCOMES WITH THE SMART-HF PROGRAM

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Background
Once discharged from hospital, a person with heart failure (HF) can experience a deterioration in their condition because of poor recognition of important signs and symptoms. People with HF will also need to adhere to complex medication, diet, and exercise regimens, which can be challenging.
Funded by a Targeted Translation Research Accelerator (TTRA) for Diabetes and Cardiovascular Disease grant, a collaboration of Cardihab Pty Ltd, the Baker Heart and Diabetes Institute, and La Trobe University have developed a digital platform (Smart-HF) for people with HF. Smart-HF is initiated by a clinician entering a care plan which then opens a patient-facing app that includes recommendations for input of daily weight, medication reminders, and education on their condition clinicians can monitor patient-reported data.
Built on the successful digital cardiac rehabilitation program, we have. Conforming to Australian HF guidelines, Smart HF is a patient and clinical platform
that helps people with HF 'self-manage'., Smart-HF includes strategies to remind the person to adhere to their care plan, monitor clinical metrics, and undertake education on their condition.
Method
Funded through a TTRA grant, this is a collaboration of Cardihab Pty Ltd, the Baker Heart and Diabetes Institute, and La Trobe University. Building on Cardihab's digital cardiac rehabilitation program, we have developed a digital supported program (Smart-HF) for people with HF. Smart-HF aims to improve the clinical management of HF in the community.
Smart-HF includes recommendations for input of daily weight, medication reminders, and a clinician portal, where clinicians enter care plans and monitor patient-reported data.
Results
We will present findings of a type 2 hybrid RCT evaluating the effectiveness of Smart-HF across three health service sites (Western Health, Melbourne; Royal Hobart Hospital and Launceston General, Tasmania) on improving quality of life and reducing hospital readmission. Findings of feasibility and acceptability of implementation are also presented.

Implications/Key Message
Smart-HF enables support to underserved people with HF, including in regional communities. Smart-HF has potential to deliver a scalable approach and when supported by a health practitioner, Smart-HF can be an effective community-based approach to HF. Offering potential cost-savings via reduced costs to deliver, reduced admissions, and fewer days of hospitalisation, freeing up constrained resources for people with HF who really require in-person healthcare delivery.

68.
MYOCARDIAL EFFECTS OF MULTIPLE PREGNANCIES POST OESTROUS CYCLE CESSATION

Ruth Magaye

Recent data suggests that a history of multiple pregnancies may be associated with an increased risk of heart failure with preserved ejection fraction (HFpEF). The repetitive biological and hemodynamic impact of multiple pregnancies could cause persistent myocardial remodeling, priming the heart for subsequent HFpEF. We investigated effects of multiparity alone on cardiac structure, function & transcriptomic profile.

Method: Multiparous (MP) mice (C57Bl/6J) aged 24 months were compared to age-matched non-parous-virgin mice (NP). We assessed blood pressure, body composition, metabolism, cardiac function, transcriptomics and cardiac markers of fibrosis, hypertrophy, and inflammation at baseline with no experimental intervention.

Results: At 15 months after cessation of oestrous cycle, multiparous mice continued to demonstrate a constellation of myocardial alterations including increased isovolumetric relaxation time ($P<0.005$) and mildly reduced ejection fractions (EF) ($P<0.005$). Accompanied by elevations in mRNA levels of ANP ($P<0.005$), IL-18 ($P<0.05$), fibronectin ($P<0.05$) and significant increase in interstitial fibrosis ($P<0.05$). Additionally, 128 genes were differentially expressed in the MP hearts, with significant upregulation of extracellular matrix related pathway. MP mice also had higher heart weight to tibia length ratio ($P<0.05$), body weight ($P<0.005$), and fat mass ($P<0.005$) compared to NP mice.

Conclusion: Multiparity leads to persistent myocardial remodelling later in life in C57Bl/6J mice, providing a potential foundation for the assessment of HF phenotypes including HFpEF patients with a history of multiple pregnancies.

69.
PIVET-ED: A PROSPECTIVE, RANDOMISED, SINGLE-BLINDED, SHAM-CONTROLLED STUDY OF PELVIC VEIN EMBOLISATION FOR THE TREATMENT OF VENOGENIC ERECTILE DYSFUNCTION – INTERIM RESULTS

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Venogenic erectile dysfunction (ED) caused by venous leakage is an under-recognized but significant contributor to ED, affecting 20% of younger men. This condition impairs sexual function and negatively impacts psychological well-being. Pelvic vein embolisation (PVE) has emerged as a minimally invasive treatment for venogenic ED, though current evidence is limited to small, heterogeneous cohort studies.

AIM: To evaluate the safety and efficacy of PVE for the treatment of venogenic ED in a randomised, single-blinded, sham-controlled trial.

METHODS: Participants were randomised to PVE or a sham procedure. Safety was assessed according to 2017-Interventional-Radiology guidelines; efficacy was measured by improvement in the International-Index of

Erectile Function (IIEF) by ≥4 points and a reduction in penile-Doppler End-Diastolic-Velocity (EDV) to <5 cm/s. Quality-of-Life was assessed using the SF-36-questionnaire.

RESULTS: Thirty-one participants have completed the 6-month follow-up: 16 had PVE and 15 were in the sham group. Baseline characteristics, including demographics, BMI, IIEF-scores, and EDV, were similar between groups. The mean overall: age was 37.6 years and BMI 26.35 kg/m². Seven patients reported depression. No serious adverse events were reported. Two patients experienced minor bruising at the catheter insertion site, which resolved within one week.

At 6 months, the treatment group showed significant improvement in 5/6 IIEF domains, with a 5-point increase in the Erectile Function Domain, meeting the study's efficacy criteria. In contrast, the sham group only demonstrated a 2-point improvement. EDV in the treatment group improved but did not return to normal levels, no change was observed in the sham group.

CONCLUSION: Interim results from this Alfred investigator-initiated RCT suggest that PVE is a safe and effective treatment for venogenic ED. With no major complications and significant improvement in erectile function in the treatment group, PVE shows promise as a therapeutic option. Recruitment is ongoing, and long-term follow-up will continue to five years.

70.

BOTH PLASMA AND MONOCYTE NOX5 EXPRESSION ARE RELEVANT BIOMARKERS OF MULTIMORBIDITY AND COMPLICATIONS IN THE CARDIOVASCULAR KIDNEY METABOLIC (CKM) SYNDROME.

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Aim
To measure NOX5 levels in plasma and circulating immune cells in relation to the occurrence of cardiometabolic complications in a cross-sectional study of subjects undergoing coronary angiography.

Methods
We invited adults having coronary angiograms to provide a blood sample to measure metabolites as well as peripheral blood mononuclear cells (PBMCs). We quantified NOX5 in plasma by ELISA and by flow cytometry on PMBCs (CD45+) and Monocytes (CD45+/CD14+). Cardiac biomarkers and a complete metabolic profile were determined. To estimate the total burden of atherosclerosis, we calculated the Gensini score as a measure of CAD severity, which reflects the number, location, and degree of coronary lesions.

Results
The study population (n=200) consisted of 79% males, with a median age of 67 years (IQR 58-74). People with diabetes (DM=43%) and BMI>30kg/m2 (High-BMI=43%) had significantly higher plasma NOX5 levels compared to those without diabetes (median 246.5 ug/mL vs 174.8 ug/mL, p=0.0049) or normal weight (median 238.3 ug/mL vs. 170.1 ug/mL, p=0.0005).

NOX5+/PBMCs were increased in acute coronary syndromes (ACS=31%) vs. non-acute ACS, (Median 16.0% vs. 7.58 %, p<0.001). NOX5 in plasma was correlated with the severity of the CAD burden (Gensini score) r=0.24 95%CI (0.09-0.36) p<0.001, and eGFR r=0.57 95%CI (0.46-0.66) p<0.0001. A NOX5 concentration >287.3 ug/mL had an AUC=0.83, 95%CI (0.71-0.95) p<0.0001, for the identification of Stage 3 (subclinical CVD) and

Stage 4 (clinical CVD) of the Cardiovascular Kidney Metabolic (CKM) syndrome. A NOX5+/CD14+ cell-count >15.48%, had an AUC=0.74 in distinguishing people requiring CABG vs. PCI. The same was true for CABG vs. medical management, but not CABG vs. PCI.

Conclusion
Plasma and PBMCs NOX5 levels are potential biomarkers for excess CVD risk in diabetes, elevated BMI, CKD and the related CKM stages, detecting patients at risk of adverse coronary outcomes, as well as identifying individuals with unstable CAD requiring non-medical approaches.

71.
ENDOTHELIAL-TARGETED CD39 AS A NOVEL TREATMENT FOR MULTIPLE ORGAN INJURY IN SEPSIS

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Outcomes in sepsis are stubbornly poor and need a new approach. Current treatments do not address the inflammatory cytokine storm, the endothelial activation and thromboinflammation, recognised as common underlying processes contributing to acute organ failure. We have developed a novel therapeutic 'Anti-VCAM-CD39' localising the potent anti-inflammatory, vasodilatory and antithrombotic properties of the ectonucleotidase CD39 to the inflamed microvasculature by binding to the receptor vascular cell adhesion molecule-1 (VCAM-1) expressed on activated endothelial cells (ECs).

In a murine model of lipopolysaccharide (LPS)-induced sepsis (5mg/kg intra-peritoneally) we confirmed that the expression of endogenous CD39 in the lungs decreased, while the expression of VCAM1 significantly increased in lungs, kidneys and brain. Anti-inflammatory adenosine levels in plasma are halved while the expression of inflammatory markers IL-1β, IL-6, MCP1/CCL2 and TNF-α are significantly up-regulated.

Treatment with anti-VCAM-CD39 at 0.8mg/kg, 1-hour post sepsis induction reversed core hypothermia, restored the cytokine storm by dropping significantly plasma levels of IL1β, IL-6 and TNF-α ($p=0.025$, 0.03 and 0.05 respectively, treated versus untreated) at 6h, while increasing adenosine levels at 24h ($p=0.03$).

Locally, anti-VCAM-CD39 treatment was able to inhibit the development of Acute Respiratory Distress Syndrome verified by H&E staining, decrease local thromboinflammation (decreased neutrophil extracellular traps [NETs] formation measured by immunofluorescent staining for citrullinated H3), drop the transcription of endothelial stimulation markers (ICAM, e-selectin), hypoxic drive marker HIF1a, and local pro-inflammatory cytokines (IL-6, MCP1). Heart stress expressed as an upregulation of Atrial Natriuretic Peptide (Nppa) was alleviated at 24h. In regards to the kidneys, anti-VCAM-CD39 significantly decreased the transcription of ICAM1, and pro-inflammatory cytokines IL-6, MCP1, while dropping the expression of Lcn2/NGAL, an early tubular kidney damage marker ($p=0.04$) at 6h.

Collectively, our results show that anti-VCAM-CD39 treatment could be a beneficial addition to antibiotics in the context of sepsis, alleviating the cytokine storm and the resulting tissue damage.

72.
EXAMINING THE MODERATION AND MEDIATION EFFECTS OF DEPRESSION ON POST COVID-19 CONDITIONS AND FUNCTIONAL STATUS

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Background: Post-COVID conditions, including the severity of symptoms, long COVID, and the duration since infection, have been linked to ongoing functional impairments. Despite these associations, the underlying mechanisms remain inadequately understood. This study aims to explore the roles of depressive symptoms in moderating and mediating the relationships between post-COVID conditions and functional capacity.

Methods: A total 1943 participants who were infected with COVID-19 were recruited into the PERCEIVE study. Post-COVID duration and symptoms were recorded. Depressive symptoms and functional capacity were self-reported using the 9-item Patient Health Questionnaire and Duke Activity Status Index (DASI), respectively. The roles of depression were explored using ordinary least squares (OLS) regression, with companion OLS models, Sobel-Goodman tests, and 1000 bootstrap iterations to assess mediation. Additionally, subgroup analyses were conducted.

Findings: Our results showed that severity of post-COVID symptoms associated with higher depression scores (β = 6.31, CI [5.42, 7.21]) and reduced functional capacity (β = -6.40, CI [-9.20, -3.61]), with depression mediating 36.48% of this effect. Long COVID also correlates with higher depression scores (β = 2.06, CI [1.15, 2.97]) and poorer functional capacity (β = -3.99, CI [-6.21, -1.77]), with depression mediating 51.06% of this effect. In individuals with severe symptoms, longer durations since infection are linked to lower functional capacity (β = -1.1448, CI [-1.5207, -0.7689]) and higher depression (β = 2.84, CI [1.41, 4.26]). Depression mediates 39.9% of the effect on functional capacity and moderates the influence of time since infection, with an interaction term of 0.1492 (CI [0.003, 0.296]). Further, subgroup analysis showed that non-vaccinated individuals had worse functional impairment.

Conclusion: Depression plays a key role in exacerbating post-COVID functional impairments, underscoring the need for targeted physical and mental health interventions to enhance long-term recovery for those with severe conditions.

73.

WITHDRAWAL OF HEART FAILURE PHARMACOTHERAPY IN PATIENTS WITH NORMALIZED LEFT VENTRICULAR EJECTION FRACTION AFTER AF RHYTHM CONTROL IN AF-MEDIATED CARDIOMYOPATHY – THE WITHDRAW-AF RANDOMIZED TRIAL

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Background: Atrial fibrillation-mediated cardiomyopathy (AFCM) represents a reversible cause of left ventricular systolic dysfunction (LVSD). Current clinical practice is indefinite heart failure (HF) pharmacotherapy despite LV ejection fraction (LVEF) normalization. However, whether this is necessary to maintain normal LVEF, in addition to rhythm control, is uncertain.

Methods: This multicenter, double crossover randomized trial examined the safety and feasibility of HF therapy withdrawal following AF rhythm control and LVEF normalization in AFCM. Participants were randomized (1:1) to initial staged withdrawal or continued medical therapy for 6 months, followed by crossover to the alternate treatment arm for a further 6 months. The primary endpoint was LVEF maintenance >50% following medication withdrawal. Secondary outcomes included cardiac remodeling, functional status, biomarkers, quality of life and arrhythmia recurrence on and off HF therapy.

Results: Between July 2021 to May 2024, 60 patients were enrolled. Treatment withdrawal and 12-month follow up was completed in all participants. HF therapy was safely withdrawn with LVEF maintenance in the majority (91.7%) 6 months post medication withdrawal compared to continued medical therapy (OR 1.61, 95% CI 0.26-3.86,p=0.609) with no clinical HF or adverse sequelae in 5/60 (8.3%) who experienced a relapse in LVSD. CMR LVEF was comparable between randomization groups and across study time-points (mixed effects p=0.370). TTE parameters, NT-proBNP, functional status, QoL and AF burden were comparable on and off HF therapy.

Conclusions: Withdrawal of HF therapy following AF rhythm control is feasible and safe in the majority with AFCM following LVEF normalization with LVEF surveillance and rhythm control.

74.
BETA BLOCKER THERAPY IS ASSOCIATED WITH DISCORDANT ECHOCARDIOGRAPHIC AND INVASIVE ESTIMATION OF LEFT VENTRICULAR FILLING PRESSURE

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Left ventricular filling pressures provide significant diagnostic and prognostic value when assessing potential cardiac dysfunction. However, estimation of diastolic function via transthoracic echocardiography (TTE), particularly using the E/e' ratio, has limited accuracy compared to right heart catheterisation (RHC). Factors driving discordant TTE and RHC results have not been well-explored.

AIM: To characterise the rate of discordance and identify predictors of this phenomenon.

METHODS: Patients who underwent TTE and RHC within thirty days were retrospectively analysed. The American Society of Echocardiography algorithms using variables including E/e', indexed left atrial volume and peak tricuspid jet velocity were applied to estimate TTE filling pressures. Only those with TTE criteria suggesting normal filling pressures were included. Logistic regression was performed to identify predictors of discordance. A sub-analysis of those with and without beta blocker therapy was also conducted.

RESULTS: Of 104 patients with normal estimated filling pressures on TTE, eleven (11%) demonstrated discordantly high filling pressures on RHC. E/e' was normal in all eleven patients. 27 patients were taking beta blocker medication at the time of assessment. Beta blocker therapy was predictive of falsely normal TTE on logistic regression (p=0.022). Normal E/e' values in the presence of elevated invasive pressures were more common in the beta blocker cohort (p=0.021). Beta blockade was also associated with lower E wave velocity (p=0.009), heart rate (p<0.0001) and cardiac index (p=0.001).

CONCLUSION: Beta blocker therapy is associated with falsely normal estimation of diastolic function on echocardiography. The mechanism driving this may be related to lower E wave velocity secondary to changes in preload. Our data may have significant future implications on non-invasive estimation of filling pressures wherein beta blockers are withheld prior to echocardiographic assessment; however, prospective studies will be vital to validate these findings.

75.

USE OF ARTIFICIAL INTELLIGENCE-GUIDED ECHOCARDIOGRAPHY TO DETECT CARDIAC DYSFUNCTION AND HEART VALVE DISEASE IN RURAL AND REMOTE AREAS: THE AGILE-ECHO TRIAL

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BACKGROUND: Transthoracic echocardiography (TTE) is essential in the diagnosis of cardiovascular diseases (CVD), including but not limited to heart failure (HF) and heart valve disease (HVD). However, its dependence on expert acquisition means that its accessibility in rural areas may be limited, leading to delayed management decisions and potential missed diagnoses. Artificial intelligence-guided (AI)-TTE offers a solution by permitting non-expert image acquisition. The impact of AI-TTE on the timing of diagnosis and early initiation of cardioprotection is undefined.

METHODS: AGILE-Echo (use of Artificial intelligence-Guided echocardiography to assIst cardiovascuLar patient managE- ment) is a randomized-controlled trial conducted in 5 rural and remote areas around Australia. Adults with CV risk factors and exercise intolerance, or concerns regarding HVD are randomized into AI-TTE or usual care (UC). AI-TTE participants may have a cardiovascular problem excluded, identified or unresolved. UC participants undergo usual management, including referral for standard TTE. The primary endpoint is a composite of HVD or HF diagnosis at 12-months.

RESULTS: Of the first 157 participants, 78 have been randomized into AI-TTE (median age 68 [IQR 17]) and 79 to UC (median age 65 [IQR 17], p=0.034). HVD was the primary concern in 37 participants (23.6%) while 84.7% (n=133) experienced exercise intolerance. The overall 10-year HF incidence risk was 13.4% and 20.0% (p=0.089) for UC and AI-TTE arm respectively. Atrial remodeling, left ventricular remodeling and valvular regurgitation were the most common findings. Thirty-three patients (42.3%) showed no abnormalities.

CONCLUSION: This randomized-controlled trial of AI-TTE will provide proof-of-concept for the role of AI-TTE in identifying pre-symptomatic HF or HVD when access to TTE is limited. Additionally, this could promote the usage of AI-TTE in rural or remote areas, ultimately improving health and quality of life of community dwelling adults with risks, signs or symptoms of cardiac dysfunction.

76.

NOVEL VISCOELASTIC COAGULATION TESTS CAN DETECT AND MONITOR THE PRO-THROMBOTIC STATE ASSOCIATED WITH ACUTE EXERCISE

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Exercise is understood to provoke a transient pro-thrombotic state, and this response is heightened in those who have suffered from or are at risk of cardiovascular disease. This has important implications for the planning and implementation of exercise programs such as cardiac rehabilitation. This pro-thrombotic state can be quantified by novel rheologic viscoelastic markers such as Fractal Dimension (df) which quantifies the density and complexity of the fibrin network in the incipient clot and Maximum Contractile Force (CFMax) which measures the force associated with the physiological contraction of a mature clot designed to occur once haemostasis has been achieved.

Aim
Quantify the pro-thrombotic response to exercise in healthy volunteers aged over 40, and ascertain how exercise intensity modulates this effect.

Methods
28 healthy participants aged over 40 who ran at least 3 times per week were recruited to run 10km at a self-selected pace. Viscoelastic tests including df and CFMax were performed before, immediately following, and 1 hour after exercise.

14 participants were invited back to perform a 3km run at maximal intensity with the same measurements.

Viscoelastic tests were compared at each time point, and between the high and low intensity groups.

Results
CFMax was reduced by exercise in both low and high intensity groups and were further reduced 1 hour later when tests were repeated. Low intensity exercise was not sufficient to alter df but a significant increase in df was seen immediately after high intensity exercise(1.68 vs 1.76), this resolved with an hour of rest.

Conclusions
Rheological tests including df and CFMax can detect the pro-thrombotic state seen following exercise, and dz is sensitive to the intensity of the exercise.

Further studies are planned to understand whether this effect differs in patients with past history of cardiovascular disease, and how these tests can be incorporated into prescribed exercise programs.

77.

CANCER SURVIVORSHIP – HEART FAILURE RISK FACTOR OR POTENTIATOR?

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There is an increased incidence of heart failure (HF) in cancer survivorship due to shared risk factors (RF) between cancer and HF. Understanding the interplay of these risks can help risk-stratify which survivors are most vulnerable to the development of HF.

AIM: To investigate the effect of cancer survivorship in relation to subclinical HF (Stage B/SBHF), Global Longitudinal Strain (GLS) and NT-proBNP levels.

METHODS: 275 adult survivors ≥10 years post cardiotoxic cancer treatment were prospectively recruited. All participants were evaluated with clinical review, biochemistry and echocardiography for presence of SBHF. SBHF was defined as the presence of left ventricular hypertrophy, abnormal (GLS) or diastolic dysfunction. Participants were matched 2:1 to non-cancer controls by Atherosclerotic Risk in Communities HF risk (ARIC-HF) score resulting in a group of 550 non-cancer controls selected from 980. Participants were excluded if they were symptomatic, had a prior history of HF or moderate/severe valvular regurgitation.

RESULTS: Once matched, the prevalence of SBHF was not significantly different between groups (27.6% cancer, 23.8% controls, p=0.268). Logistic regression models for the three outcomes - SBHF, reduced GLS and elevated BNP levels were developed. Univariable analysis demonstrated multiple similar variables such as age, gender, BMI, diabetes, atrial fibrillation, hypertension were associated with all three outcomes. On multivariate analysis, once adjusted for variables such as age, gender, atrial fibrillation, diabetes and ARIC-HF score - cancer was significantly associated with SBHF (OR 1.45 [95% CI 1.02-2.05] p=0.04), reduced GLS (OR 2.12 [95% CI 1.45-3.10] p<0.001) and elevated NT-proBNP (OR 3.01 [95% CI 1.98-4.63] p<0.001).

CONCLUSION: This propensity match analysis demonstrates cancer survivorship is significantly associated with SBHF, reduced GLS and elevated BNP levels. Though in isolation cancer does not significantly increase SBHF prevalence, cancer appears to exert a synergistic influence when coupled with established RFs - potentially exacerbating the progression of SBHF.

CLINICAL PUBLIC HEALTH

78.
A NOVEL CONSTRUCT TO HEAL FULL THICKNESS WOUNDS IN PAEDIATRICS– A CASE REPORT

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Introduction: Timely wound closure in massive burns remains an unmet clinical need. Engineered skin substitutes can provide an alternative treatment to split skin grafting. However, since the development of Cultured Epithelial Autograft (Green's method), almost 50 years ago, limited alternatives have been introduced.

Methodology: Here we describe the production of an autologous human skin equivalent (HSE) for the successful treatment of a paediatric patient with a severe burn injury. The HSE was comprised of dermal and epidermal components, including a basement membrane. The epidermis was stratified and semi-matured, providing essential components for a definitive graft. A platelet-derived hydrogel, combined with autologous fibroblasts, acted as a niche for the stem and progenitor keratinocytes, isolated from a small piece of donor skin. The survival of the stem and progenitor keratinocytes in HSE was confirmed by immunofluorescence using Keratin 5, Integrin alpha 5 and beta 1 specific antibodies. Over 500 cm^2 HSE was produced under good manufacturing practice (GMP) guidelines and tested clear of endotoxin, mycoplasma, bacteria and yeast pathogens.

Results and Conclusion: The HSE was grafted on a full thickness wound temporised with NovoSorb ® Biodegradable Temporising Matrix (BTM) and graft take was estimated to be 95% on day 14 post grafting. Histology, at 2 weeks and 6 weeks post grafting, confirmed persistence of a complete and continuous, although hyperproliferative, epidermis.

Applicability to Clinical Care: This study is a proof of concept for the application of HSE as a treatment option in paediatric burn injuries with limited donor skin.

79.
IF PHARMACISTS INCORPORATE "TEACH-BACK" WITH MEDICATION COUNSELLING IS PATIENT UNDERSTANDING IMPROVED?

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Pharmacist counselling promotes safe and effective use of medications. Confirmation of patient understanding after counselling is not routinely undertaken. The "Teach-back" method invites patients to explain information received in their own words.

AIM: To determine the impact of Teach-back training of hospital pharmacists on duration of medication counselling and patient recall of information provided to patients at a pre-admission clinic (PAC) and at discharge from Alfred hospital.

METHODS: In this interventional study, trained students observed medication counselling by pharmacists to patients in PAC and at discharge from acute medical wards in February (standard counselling) and May 2024 (intervention). Alfred Health's Patient Experience team facilitated Teach-back training of pharmacists in April 2024. Counselling details for each new, changed or stopped medication and duration of sessions were recorded. Patients completed a phone survey 3-7 days after counselling to assess recall and understanding of medication information provided using a validated 7-item checklist. Pharmacist counselling was evaluated using a 10-item Teach-back checklist in both groups. Data were analysed using unpaired t-test [STATA].

RESULTS: Of the 262 patients observed (standard:122; intervention:140), 74.8% (n=196, standard:91; intervention:105) completed follow-up. Patient recall was scored for 293 (mean=3.3±2.0) medications in the standard group and 409 (mean=3.9±2.6) medications in the intervention group. Average recall of medication information was greater in the intervention group 82.1±32.0% vs 75.2±33.0%, p=0.006). Counselling duration for PAC patients in the intervention group increased by an average 3.2 minutes (16.6±6.2 vs 19.8±8.9 mins, p=0.018). The Teach-back checklist score was higher in the intervention group (5.7±1.2 vs 7.6±1.5 p<0.0001).

CONCLUSION: Medication information recall was greater in the Teach-back group despite an overall higher average number of medications per patient. Although counselling time increased for PAC patients using Teach-back methods, improved recall and understanding of medication information may result in improved medication safety and effectiveness.

80.

PREDICTING RED BLOOD CELL (RBC) TRANSFUSION NEED USING MACHINE LEARNING

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AIM: To describe early experience from the National Transfusion Dataset (NTD) project in developing a model to predict the need for RBC transfusion in haematology-oncology in-patients.

METHOD: Structured data were extracted from electronic medical records of haematology-oncology patients at The Alfred, and combined with unstructured data, to inform development of a machine-learning model to predict RBC transfusion need. Natural language processing and AI was utilised to extract information.

From 10,286 in-patient episodes with clinical notes, FBE results and ICD code data were classified by transfusion status: 1) Not transfused at all (6,936); 2) Transfused with product other than RBC (1,170); 3) Transfused RBC only (1,158) or 4) Transfused RBC and other product(s) (1,022). Discharge summaries and clinical notes captured after transfusion were excluded.

The K-Best algorithm was used to identify which data fields best distinguished between classifications. A random 5% of episodes were withheld during model training and testing to validate the model later. Stratified five-fold cross-validation was used for training and testing, and Synthetic Minority Over-Sampling Technique (SMOTE) applied to each fold during training to handle group size imbalance. Several classification algorithms were assessed to see which worked best.

RESULTS: With K-Best set at 150 data fields the CatBoost classification algorithm performed best. During testing, it achieved accuracy: 95.37%, precision: 88.9%, recall: 89.5%, F1-Score: 89.2%. During validation on the set-aside data, its results were accuracy: 95.3%, precision: 86.6%, recall: 92.5%, F1-Score: 89.5%.

CONCLUSION: The results indicate the model was able to learn patterns to discern between patients who required RBC transfusion from ones who did not. The consistency between the testing and validation results indicate the model generalised well on unseen data. Further refinement is underway. Future work will explore the potential to deliver real-time alerts, based on the model, on a platform designed in conjunction with hospital staff.

81.

NOX5 IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS: A POTENTIAL PROGNOSTIC BIOMARKER IN CORONARY ARTERY DISEASE

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BACKGROUND:
NADPH oxidase 5 (Nox5) plays a critical role in the pathogenesis of atherosclerosis via reactive oxygen species (ROS) production. It is expressed in peripheral blood mononuclear cells (PBMCs) and is increased in atherosclerotic plaques of diabetic patients with coronary artery disease (CAD), during acute coronary syndrome (ACS), and within diabetic kidney biopsies. Therefore, we assessed the suitability of Nox5 as a prognostic biomarker to identify patients at high risk for cardiovascular events, particularly those with comorbid diabetes and chronic kidney disease (CKD).

METHODS:
200 patients aged 36-94 years underwent elective or emergency coronary angiography/angioplasty at the Alfred Hospital Catheter Laboratory. PBMCs (CD45+/CD14+ cells) from whole-blood were processed for flow-cytometry to measure Nox5 protein and were correlated with patient clinical, biochemical, and angiographic characteristics.

RESULTS:
Nox5 protein expression was increased in ACS with hemodynamically significant CAD versus stable CAD during elective angiography (15.28±1.7 vs 9.77±0.7 AU; p=0.0023), especially in diabetic patients with CKD presenting acutely versus electively (30.35±4.8 vs 11.99±2.0 AU; p=0.0002). Nox5 expression was higher in patients with stable angina who required intervention (PCI/CABG) versus medical management only (12.66±1.8 vs 8.03±0.9 AU; p=0.0014). At time of elective angiography, patients without CAD had lower Nox5 expression compared to those with stable CAD (4.03±1.0 vs 11.61±1.6 AU; p=0.014), with receiver operator characteristic (ROC) curve analysis demonstrating an area under the curve (AUC) of 0.75 (95% CI 0.62-0.88; p=0.0018) in discriminating those with or without CAD.

CONCLUSION:
Nox5 protein expression in PBMCs appears to be associated with the severity and instability of CAD, particularly in patients with diabetes and CKD. Increased Nox5 expression also seems to predict the presence of CAD and need for coronary intervention in patients with stable angina. Prognostic measurement of Nox5 may serve as a useful adjunctive biomarker to consider targeted interventions in those at high cardiovascular risk.

82.

RETROSPECTIVE AUDIT OF CLINICIAN WEIGHT ESTIMATION AND THROMBOLYSIS DOSING FOR ACUTE ISCHAEMIC STROKE AT A MELBOURNE HOSPITAL

Dr Branko Borojević, Dr Sarah El-Naggar

Aims
The accuracy of body-weight estimation and intravenous thrombolysis dosing for ischaemic stroke at a Melbourne hospital over 6-months was evaluated.

Methods
26 patients received thrombolysis for stroke February-August 2022 at Northern Health. 21 had documented estimated body-weight at stroke code and recorded body-weight upon admission. The difference between estimated and actual body-weight and thrombolytic dose was calculated. Age, mRS, admission and day 1 NIHSS, stroke syndrome, and day 1 CT-brain outcome were recorded.

Results
The mean difference between estimated and recorded body weight was 3.496kg (range 0-21.1Kg) with a resultant thrombolytic dose difference of 1.98mg (range 0-8.1mg).

There was a score-difference of 7 between admission NIHSS and day 1 NIHSS in patients with weight estimate error >5.1kg, 5.5 with an error 2.5-5kg and 2.23 with 0-2.5kg (p 0.159). LMCA stroke was associated with a mean 8.33kg error in weight estimation, RMCA stroke 2.74kg, PCA stroke 0.94kg and subcortical stroke 1.93kg (p 0.138). NIHSS >10 at code stroke had a 7.5kg weight estimation error, NIHSS 5- 9 had 3.11kg and NIHSS 0-4 had 1.98kg (p 0.199).

Two patients had intracerebral haemorrhage post-thrombolysis on Day 1 CT brain; one with correct weight estimation and the other 21.1kg weight overestimation.

Conclusions
There was an insignificant relationship between NIHSS change from baseline and body-weight difference from actual and estimated weights. A trend towards significance was seen between stroke syndrome and size and degree of body-weight difference, with greater inaccuracy with larger and LMCA territory stroke, suggesting importance of active patient communication during code stroke. This is consistent with the literature that weight estimates reliant on clinician gestalt are inaccurate (1). Further research is needed to characterize these associations.

83.

RELATIONSHIP BETWEEN PERIVASCULAR SPACES DENSITY WITH EPILEPTOGENIC ZONE IN DRUG-RESISTANT EPILEPSY

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Background

There is a lack of structural imaging biomarkers for epileptogenic zone (EZ) identification in MRI-negative epilepsy. We investigate whether impaired glymphatic systems, characterised by enlarged perivascular spaces (ePVS), are associated with SEEG-defined epileptogenicity.

Methods
We included stereo-electroencephalography (SEEG) patients from 2019-2024 in Alfred Health. We segmented ePVS on pre-implantation non-contrast 3D T1-weighted MRIs using automated PVS identification nnU-net for generalised usage (PINGU) algorithm. We quantified ePVS density on (i) hemispheric level, (ii) sub-lobar level, and (iii) contact level inside a 10mm-radius sphere surrounding each ePVS-labelled voxel. We defined EZ as SEEG contacts proposed for thermocoagulation and high-frequency oscillations (HFO) zone as contacts exhibiting top 10% of spikes, fast ripples (FR), or cross-rate of spikes*HFO. We performed Wilcoxon-sum rank tests for group difference and multi-level logistic regression adjusted for age, sex, cardiovascular risk-factors, voxel size, and contact location.

Results
We analysed 5,953 contacts in 57 patients (male 42.1%, mean age 33.87±10.07 years) from MRI-positive (40.4%) and MRI-negative (59.6%) patients. Hemispheric level: No difference in ePVS density between epileptogenic and non-epileptogenic hemispheres. Sub-lobar level: No difference in ePVS density between epileptogenic and non-epileptogenic sub-lobes. Contact level: Higher ePVS density was observed around epileptogenic contacts ($p<0.001$) particularly in the mesial temporal region ($p=0.024$). Similarly we observed higher ePVS density around contacts displaying top 10% of spikes ($p<0.001$), fast ripples ($p<0.001$), and spikes *HFO ($p=0.002$).

Conclusion
At the contact level, increased ePVS density was observed around epileptogenic SEEG contacts supported by EZ hypothesis and interictal markers. Enlarged PVS density may be a potential imaging biomarker of epileptogenicity that can be incorporated for further machine learning development.

84.
HYPEROXIA AND IN-HOSPITAL MORTALITY FOLLOWING ANEURYSMAL SUBARACHNOID HAEMORRHAGE: A RETROSPECTIVE COHORT STUDY

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Patients in the Intensive Care Unit (ICU) are often treated with supplemental oxygen, and hyperoxia commonly occurs. However, hyperoxia has been associated with harm after cardiac arrest, sepsis, and traumatic brain injury, although its effect after aneurysmal subarachnoid haemorrhage (aSAH) remains uncertain.

AIM*:* To evaluate the association of hyperoxia on relevant patient outcomes following aSAH.

METHODS*:* A retrospective single-centre cohort study was conducted. Data were extracted on adult patients with confirmed aSAH admitted to The Alfred Hospital ICU between 2019 and 2024, who were mechanically ventilated. Hyperoxia was defined as a partial pressure of oxygen ≥200 mmHg on arterial blood gas analysis within 24 hours of ICU admission. The primary outcome was in-hospital mortality. Secondary outcomes were ventilated hours, ICU length of stay (LOS), and hospital LOS. Logistic regression was used to explore the association of hyperoxia with in-hospital mortality.

RESULTS*:* There were 139 patients included, with 99 exposed to hyperoxia. Baseline characteristics between exposure groups were similar. There was no significant association between and in-hospital mortality (odds ratio (OR) 0.75; 95% confidence interval (CI) 0.35-1.60). Additionally, no association between hyperoxia and median ventilated hours (hyperoxia: 98 hours (43-337), no hyperoxia: 58 hours (25-184), p=0.31), median ICU LOS (hyperoxia: 196.8 hours (100.8-331.4), no hyperoxia: 105.8 hours (67.0-259.4), p=0.13), and mean hospital LOS (hyperoxia: 24.2 days (19.1), no hyperoxia: 18.6 days (11.6), p=0.06) was observed.

CONCLUSION: Exposure to hyperoxia within the first 24 hours of ICU admission after an aSAH was not associated with in-hospital mortality, ventilated hours, ICU LOS, or hospital LOS. Any potential harm from hyperoxia requires exploration in larger cohort studies or trials.

85.

ALL-CAUSE, CARDIOVASCULAR, AND RESPIRATORY MORTALITY AND WILDFIRE-RELATED OZONE: A MULTICOUNTRY TWO-STAGE TIME SERIES ANALYSIS

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Wildfire activity significantly contributes to tropospheric ozone (O_3) pollution, yet no study has comprehensively explored its global impact on mortality.

AIM: To systematically analyse the associations between wildfire-related O_3 and daily mortality across various regions and populations worldwide.

METHODS: We did a multicountry two-stage time series analysis. From the Multi-City Multi-Country (MCC) Collaborative Research Network, data on daily all-cause, cardiovascular, and respiratory deaths were obtained from 749 locations in 43 countries/areas from 2000 to 2016. We estimated the daily concentration of wildfire-related O_3 in study locations using a chemical transport model. Using a random-effects meta-analysis, we examined the associations of short-term wildfire-related O_3 exposure (lag period of 0–2 days) with daily mortality, first at the location level and then pooled at the country, regional, and global levels.

RESULTS: Overall, an increase of 1 μg/m³ in the mean concentration of wildfire-related O_3 during lag 0–2 days was associated with increases of 0.55% (95% CI 0.29 to 0.80) in daily all-cause mortality, 0.44% (–0.10 to 0.99) in cardiovascular mortality, and 0.82% (0.18 to 1.47) in respiratory mortality. The associations of daily mortality rates with wildfire-related O_3 exposure showed substantial geographical heterogeneity. Across all locations, estimated annual excess mortality fractions of 0.58% (95% CI 0.31 to 0.85; 31 606 deaths [95% CI 17 038 to 46 027]) for all-cause mortality, 0.41% (–0.10 to 0.91; 5249 [–1244 to 11 620]) for cardiovascular mortality, and 0.86% (0.18 to 1.51; 4657 [999 to 8206]) for respiratory mortality were attributable to short-term exposure to wildfire-related O_3.

CONCLUSION: In this study, we observed an increase in all-cause and respiratory mortality associated with short-term wildfire-related O_3 exposure. Effective risk and smoke management strategies should be implemented to protect the public from the impacts of wildfires.

86.

METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND ITS RELATIONSHIP WITH OLDER ADULT OUTCOMES

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common liver disease in Australia and worldwide. However, its significance in older adults isn't well characterised, which is of importance given the global ageing population.

Aims: To evaluate the risk associated with MASLD on multiple important outcomes in community-dwelling older Australian adults, including persistent physical disability, dementia, death, and major adverse cardiovascular events (MACE).

Methods: Retrospective analysis of the Aspirin in Reducing Events in the Elderly (ASPREE) clinical trial and ASPREE-eXTension cohort study which enrolled 16,703 initially healthy Australians free from dementia, cardiovascular disease, disability, and known life-limiting physical illness. Of the 9,097 adults (all aged ≥70 years) classifiable with the Fatty Liver Index (FLI) and usual diagnostic criteria in terms of the presence/absence of MASLD, 2,998 (33.0%) had MASLD and were eligible for evaluation. FLI<30 represented no-MASLD and was used as a comparator. Death, MACE, dementia, and persistent physical disability were adjudicated end-points.

Results: On univariate analysis, those with MASLD had an increased risk of MACE (HR 1.47 [95% CI 1.22–1.78]) and persistent physical disability (HR 1.87 [95% CI 1.45 – 2.42]), a decreased risk of dementia (HR 0.73 [95% CI 0.57 – 0.94]), but had no significant change in risk of mortality (HR 1.04 [95% CI 0.91–1.19]). When adjusting for multiple known contributors to these outcomes, the relationship between MASLD and MACE was no longer significant (aHR 1.12 [95% CI 0.89 – 1.42)]), but remained strong for both disability (aHR 1.41 [95% CI 1.07 – 1.86]) and dementia (aHR 0.63 [95% CI 0.48 – 0.83]).

Conclusion: MASLD in initially healthy community-dwelling older Australian adults is independently associated with persistent physical disability but not death or MACE. It is also associated with a reduced risk of incident dementia. Further work to understand age-related biological differences in disease outcomes is warranted.

87.

AUTOMATED SEGMENTATION OF EPILEPSY SURGICAL RESECTION CAVITIES: COMPARISON OF FOUR METHODS TO MANUAL SEGMENTATION

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BACKGROUND: Accurate resection cavity segmentation on MRI is important for neuroimaging research involving epilepsy surgical outcomes. Manual segmentation, the gold standard, is labour intensive. Automated pipelines are an efficient potential solution; however, most have been developed for use following temporal epilepsy surgery. Our aim was to compare the accuracy of our previously developed automated segmentation pipeline to other publicly available automated pipelines, following surgical resection in a mixed cohort of subjects following temporal or extratemporal epilepsy surgery.

METHODS: In addition to our algorithm, Epic-CHOP, we identified 3 other open-source automated segmentation pipelines. Epic-CHOP and ResectVol utilise SPM-12 within MATLAB, while Resseg and Deep Resection utilise 3D U-net convolutional neural networks. We manually segmented the resection cavity of 50 consecutive subjects who underwent epilepsy surgery (30 temporal, 20 extratemporal) at the Alfred and Royal Melbourne Hospitals. We calculated Dice similarity coefficient (DSC) for each algorithm compared to the manual segmentation.

RESULTS: No algorithm identified (DSC>0) all resection cavities. ResectVol (n=44, 88%) and Epic-CHOP (n=42, 84%) were able to detect more resection cavities than Resseg (n=22, 44%, P<0.001) and Deep Resection (n=23, 46%, P<0.001). In the overall cohort, the SPM-based pipelines Epic-CHOP (median DSC 0.71) and ResectVol

(median DSC 0.67) performed better than the deep learning-based pipelines Resseg (median DSC 0.00) and Deep Resection (median DSC 0.00). Similarly, in the extratemporal surgery cohort, both SPM-based pipelines had higher detection rates and accuracies than the deep learning-based pipelines (P<0.001). In the temporal cohort, the SPM-based pipelines had higher detection rates (P<0.05), however there was no difference in the accuracy between methods (P=0.13).

CONCLUSION: The SPM-based methods, Epic-CHOP and ResectVol, had high detection rates and accuracy across the cohort. These pipelines could be applied to machine learning studies of outcome prediction to improve efficiency in pre-processing data, however human quality control is still required.

88.

HEALTH-RELATED QUALITY OF LIFE OF ADULT SEPSIS SURVIVORS FOLLOWING CRITICAL ILLNESS: A SYSTEMATIC REVIEW

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BACKGROUND: As survival following sepsis improves, there is increased attention on the health-related quality of life (HRQoL) of survivors following critical illness. Previous systematic reviews which assessed HRQoL post-sepsis included data until 2017, mandating the need for an updated review with studies using the Sepsis-3 definition.

AIM: To systematically review the literature on the HRQoL of adult sepsis survivors following critical illness.

METHODS: Three electronic databases (OVID MEDLINE, EMBASE, and CINAHL) were searched between 2009 and May 2023 (and re-run in June 2024). Studies that assessed the HRQoL of adult sepsis survivors at 90 days or more following critical illness were included. Extracted data from included studies comprised HRQoL findings, the instruments administered, and representation of adult survivors following critical illness. Quality assessment was undertaken using the Cochrane Risk of Bias In Non-Randomised Studies – of Exposure tool. Study selection, data extraction, and quality assessment were conducted independently by two reviewers.
RESULTS: 33 studies were included from 25,611 records, with the sample size among eligible studies ranging from 55 to 2,151 participants. Included studies were conducted all around the world. The EuroQol 5-dimension 3-level instrument was most commonly administered in 19 (58%) studies. Our review found that adult sepsis survivors following critical illness have lower HRQoL than population norms, and no significant difference was found in the HRQoL of adult survivors following critical illness with or without sepsis. High risk of bias in included studies was mostly due to missing data and confounding.

CONCLUSION: Sepsis negatively impacts long-term HRQoL of adult survivors following critical illness. As survival following critical illness improves, future research on improving long-term HRQoL following sepsis is crucial.

89.

LINKING TAU-PET WITH FLUID BIOMARKERS, BRAIN VOLUME, AND COGNITION TO ADVANCE DIAGNOSTICS IN PROGRESSIVE SUPRANUCLEAR PALSY

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AIM: Identifying biomarkers for primary tauopathies such as Progressive Supranuclear Palsy (PSP) is crucial for improving diagnosis and establishing clinical trial endpoints. The novel PET radiotracer ^{18}F-PI-2620 shows promise in detecting tau pathology in PSP. This study investigates associations between tau-PET, fluid biomarkers, brain volume, and cognition.

METHODS: We conducted a cross-sectional analysis of ^{18}F-PI-2620 tau-PET uptake, T1-weighted brain volume, and cognitive performance in 28 patients with clinically diagnosed probable PSP (Richardson's Syndrome). A subset of 23 patients and 10 healthy controls underwent blood and CSF analyses for NfL, GFAP, and t-tau levels. Standardized uptake value ratios (SUVr) were calculated for voxel-wise and region-of-interest analyses. Cognitive assessments included the Digit Span, Hayling, Stroop, Trail Making, Category Fluency, FAS, NIH toolbox, BRIEF-A, and PSP-RS. Mixed-effects models and multiple regression were used to explore relationships across all markers.

RESULTS: Tau-PET uptake correlated positively with NfL and NfL/t-tau in plasma and CSF ($p < 0.05$) and negatively with GFAP and t-tau in plasma ($p < 0.05$) and strong negative correlations were observed for GFAP/NfL ($p < 0.001$), particularly in the basal ganglia and midbrain (e.g., pallidum, putamen, red nucleus, substantia nigra). PSP patients showed significantly higher levels of NfL, GFAP, and GFAP/t-tau in both plasma and CSF, and lower GFAP/NfL in CSF compared to controls. Tau-PET uptake in the basal ganglia and midbrain was associated with lower brain volume, impaired executive functions ($p < 0.05$), and greater disease severity ($p < 0.05$).

CONCLUSIONS: These findings highlight the utility of ^{18}F-PI-2620 as an in-vivo biomarker for tau pathology in PSP. Fluid biomarkers, especially the GFAP/NfL ratio, show potential as surrogate markers, supporting their application in future clinical trials.

90.

THE IMPACT OF CHRONIC RENAL FAILURE ON PERIOPERATIVE OUTCOMES OF NON-METASTATIC COLORECTAL CANCER SURGERY PATIENTS

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Introduction:
The rising prevalence of colorectal cancer (CRC) and chronic renal failure (CRF) due to an aging population poses challenges in the perioperative management of CRC surgery patients. The impact of renal function on

postoperative outcomes remains controversial, with limited data available on their association with morbidity and mortality.

Methods:

A retrospective analysis was conducted using a high-quality, prospectively maintained colorectal neoplasia database from multiple hospitals in Australia. A total of 2,286 patients who underwent CRC surgery between 2010 and 2023 were categorised based on clinically determined CRF status and preoperative estimated Glomerular Filtration Rate (eGFR) levels, with comprehensive data on demographics, comorbidities, surgical details, and both short-term and long-term outcomes. Multivariable logistic and Cox proportional hazards regression analyses examined the associations between CRF, eGFR, and postoperative outcomes, including complications, 30-day mortality, overall survival (OS), and relapse-free survival (RFS).

Results:

CRF, present in 135 patients (5.9%), was independently associated with an increased risk of postoperative complications, 30-day mortality, and prolonged ileus. CRF significantly increased overall mortality (AHR: 1.49, p<0.001) and relapse-free mortality (AHR: 1.51, p<0.001), with 5-year OS and RFS rates of 58.9% and 57.4%, respectively, compared to 83.3% and 82.7% in non-CRF patients. In contrast, in univariate analysis, preoperative eGFR <60 mL/min/1.73m² was significantly associated with medical complications and 30-day mortality in univariate analysis but lost significance in multivariable analysis.

Conclusion:

CRF, defined by persistent serum creatinine elevation, is a strong predictor of increased perioperative morbidity and reduced long-term survival in CRC surgery patients. Comprehensive preoperative renal function assessment is essential for optimizing surgical outcomes in this population.

91.

ASSOCIATIONS BETWEEN IN-MATCH HEAD ACCELERATION EVENTS MEASURED BY INSTRUMENTED MOUTHGUARDS AND POST-MATCH SERUM GFAP AND NFL LEVELS IN AMATEUR MALE AUSTRALIAN FOOTBALL PLAYERS

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BACKGROUND: Advances in instrumented mouthguards (iMGs) allow for the accurate quantification of single high-acceleration head impacts and cumulative head acceleration exposure in collision sports. However, relationships between these measures and risk of brain cell injury remain unclear.

AIM: Quantify measures of non-concussive head impact exposure and assess their association with blood glial fibrillary acidic protein (GFAP), neurofilament light (NfL), and phosphorylated-tau-181 (p-tau-181) levels in male amateur Australian football players.

METHODS: Thirty-one athletes underwent in-season (24h post-match) and post-season (>5 weeks) blood collections and/or wore HITIQ Nexus A9 iMGs measuring peak linear (PLA) and rotational (PRA) acceleration. Match footage was used to verify and code impacts. Blood GFAP, NfL, and p-tau-181 were quantified using Simoa and natural log transformed for analysis. Associations between post-match biomarkers and within-match maximum single impact and cumulative PLA/PRA were assessed with linear mixed models.

RESULTS: In-season versus post-season elevations were found for GFAP (mean dif.=0.14, 95%CI=0.012-0.26, p=0.033), NfL (mean dif.=0.21, 95%CI=0.09-0.32, p=0.001) and p-tau-181 (mean dif.=0.49, 95%CI=0.33-0.65, p<0.001). Post-match GFAP was associated with maximum single impact PLA (B=0.003, 95%CI=0.0002-0.005, p=0.036), cumulative PLA (B=0.001, 95%CI=0.0002-0.002, p=0.017) and PRA (B=0.01, 95%CI=0.002-0.02,

p=0.014), and impact number (B=0.03, 95%CI=0.003-0.05, p=0.029) within a single match. Change in NfL levels between two-matches correlated with cumulative PLA (r=0.80, 95%CI=0.38-0.95, p=0.005), PRA (r=0.71, 95%CI=0.19-0.92, p=0.019), and impact number (r=0.63, 95%CI=0.05-0.89, p=0.038).

CONCLUSION: We found a significant association between iMG-measures of maximum and cumulative non-concussive head impact accelerations during a match and elevated blood biomarkers indicative of brain cell injury. While future research is needed to establish HAE thresholds and to define clinically significant biomarker changes, these findings highlight the potential benefits of integrating both iMGs and blood biomarkers for improved head impact management in collision sports.

92.
VALIDATION OF SERIAS, A NOVEL SELF-REPORT INSTRUMENT TO MEASURE THE IMPACT OF EPILEPSY

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Epilepsy affects 250,000 Australians of all ages. The primary treatment goal is seizure freedom with minimal treatment adverse effects. There is a need for a self-report questionnaire (patient reported outcome measure, PROM) that gives a 'trade off' between seizure- and treatment-related burden to inform treatment decisions.

AIM: In this prospective study, we aimed to create and validate the Seizure-Related Impact Assessment Scale (SERIAS) to address this critical gap in epilepsy PROMs.

METHODS: Adult epilepsy patients attending Alfred Health's Comprehensive Epilepsy Centre (Melbourne, Australia) completed SERIAS at baseline, 3- and 6-month timepoints, along with validated instruments: QOLIE-31 (quality of life), SSS-8 (somatic symptoms), NDDI-E (depression), GAD-7 (anxiety) and WSAS (seizure- and treatment-related functional impairment). A subgroup of patients also completed SERIAS twice within two weeks to investigate test-retest reliability. This study has Alfred Health IRB approval 17/23.

RESULTS: 99 patients (n=67 females) completed baseline SERIAS. Mean age was 42 years (SD=16, range=18-77). Most patients reported >0 days of disability (62%, median SERIAS score=3, IQR=0–24.5). Based on quartiles, 37 (37%) patients reported no disability, 14 (14%) low disability, 23 (23%) moderate disability, and 25 (25%) high disability. Greater disability was negatively correlated with QOLIE-31 total score (r =-0.48, p<0.001), and positively correlated with scores on NDDI-E (r=0.32, p<0.001), SSS-8 (r=0.39, p<0.001), WSAS for seizures (r=0.59, p<0.001), and WSAS for treatment (r=0.58, p<0.001). Psychometric reliability for SERIAS was high (α=0.87). Test-retest reliability was high (n=38 patients, r=0.83, p<0.001).

CONCLUSION: SERIAS shows good psychometric reliability and strong test-retest stability. Greater disability measured with SERIAS was associated with lower quality of life, greater depression, greater general somatic symptoms, and greater functional impairment secondary to seizures and treatment side effects. Overall, these findings strongly support the use of the SERIAS to measure epilepsy related disability.

This study was supported by a LivaNova USA investigator-initiated grant.

93.

'CHART FIRST' - A TARGETED INITIATIVE TO REDUCE MEDICATION ERRORS ASSOCIATED WITH VERBAL ORDERS IN THE EMERGENCY DEPARTMENT (ED): A RETROSPECTIVE COHORT STUDY

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Medication errors commonly occur in the Emergency Department (ED) with most occurring during prescribing. Many cause harm, are preventable and result in significant healthcare costs. Verbal medication orders pose a risk of error and despite strategies to reduce this, the risk and error associated with such orders continues.

AIM: The aim of this study was to determine if a multidisciplinary ED education program was associated with a reduction in medication errors associated with verbal orders.

METHODS: This was a retrospective cohort study of the 'Chart First' Campaign, a multidisciplinary education program launched across two EDs on the 07/02/22, promoting the importance of prescribing medication on electronic medication records prior to administration. Multidisciplinary clinical champions led the initiative and visual cues with the slogan 'Chart First' were displayed across both ED's. The number and severity of errors associated with verbal medication orders were identified from the hospital's incident reporting database, with a blinded expert panel assessing the severity of errors for 12 months before and after the intervention.

RESULTS: A total of 295,107 medications were administered in the pre and 297,421 in the post-intervention period. There were 21 medication errors due to verbal orders; 16 pre and 5 post-intervention. The intervention was significantly associated with a reduction in medication errors from verbal orders (OR 0.31; 95% CI: 0.12-0.81, p=0.016). After expert panel review, 3 errors were classified as 'major' or 'catastrophic' in the pre-intervention while none in the post-intervention period. The most common medication classes were general anaesthetics, opioids, benzodiazepines and neuromuscular blockers followed by antipsychotics

CONCLUSION: A simple and inexpensive intervention comprising of visual cues, multidisciplinary education and clinical champions was associated with a reduction in the number and severity of medication errors from verbal orders in the ED. The intervention is therefore encouraged with ongoing surveillance to measure effectiveness.

94.

KNOWLEDGE AND ATTITUDES TOWARDS SOLID ORGAN TRANSPLANTATION FOR PEOPLE WITH HIV IN AUSTRALIAN HEALTHCARE PROVIDERS AND CONSUMERS

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Background:

Demand for solid organ transplantation (SOT) among people with HIV (PWH) is increasing as co-morbidities increase in this population. Little is known about the obstacles to SOT that PWH in Australia may experience. This study aimed to explore knowledge, attitudes and barriers to organ donation and receipt for PWH from consumers and providers.

Methods:
We conducted two surveys: 1) healthcare providers involved in HIV and SOT recipient care, and 2) consumers with chronic comorbidities and/or HIV. Surveys were developed in collaboration with HIV community-based organisations and hosted in Qualtrics. Survey responses were multiple choice or five-point Likert scale and disseminated via clinics, community organisations, mailing lists, and professional networks throughout Australia.

Results:
In total, 132 providers and 175 consumers were surveyed. Providers included 42 Infectious Diseases, and 28 transplant specialists. While 110 (86%) providers thought PWH could be organ recipients, only 36 (30%) thought PWH could be donors. Sixty-one (57%) providers indicated that comorbidities were the greatest barrier to organ receipt. Consumers included 122 PWH, and 53 controls with comorbidities. Fewer PWH than controls believed they could be organ recipients to prolong life (51% vs 87%). PWH were significantly less likely to believe they were eligible (40% vs 68%) and registered as organ donors (22% vs 44%) than controls, but more frequently willing to be donors (96% vs 82%). The most common concern for PWH about organ receipt from a donor with HIV was HIV superinfection (n=45, 40%), controls were most concerned about safety (n=16, 35%) and HIV infection (n=18, 40%)

Conclusion:
Although most providers were aware that PWH could receive organ transplants, knowledge of the eligibility to donate is limited. Consumers' knowledge about the ability to receive and donate is limited. Opportunities exist to improve knowledge and overcome misconceptions about SOT for PWH in Australia.

Disclosure of Interest Statement:
JH's institution received reimbursement for her participation in Advisory Boards for Gilead Sciences, ViiV Healthcare and Merck, Sharp & Dohme Australia. Jillian Lau is on an advisory board for ViiV Healthcare, and receives unrelated grants from MSD, and Gilead. Remaining authors have nothing to disclose.
This study was approved by the Alfred Hospital ethics committee, project number 680/23

95.
USE OF INTERPRETERS IN AN OUTPATIENT OCCUPATIONAL RESPIRATORY CLINIC

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Interpreters play an important role in ensuring good communication of important clinical information between patients and clinicians. About 4% of the Australian population have poor English proficiency (2021 Census data) and in the 2022/2023 period, approximately 10% of Alfred Health's patients used the interpreter service. However, data on who these patients are is scarce.

AIM: To describe patients who used interpreters in a specialist respiratory outpatient clinic.

METHODS: The Alfred Health Occupational Respiratory Clinic has provided free occupational health assessments for workers in the Victorian artificial stone benchtop industry (aSBI) since 2021. Data are presented from patients who visited the clinic before May 2024. Chi-square tests and Wilcoxon rank-sum tests were used to compare characteristics of patients who required an interpreter vs those who did not.

RESULTS: Over half (352/630, 55.9%) of aSBI workers were born overseas. Of these, 21.6% (n=76) used an interpreter. Those born overseas and used an interpreter were older than those born overseas but did not use an

interpreter (median age=43 vs 38, p-value=0.001). Workers aged 50-59 years were the most likely to use an interpreter (25.4%). Interpreter use varied by country of birth (p<0.001); highest amongst workers born in China (57.1%), Iraq (50%) and Vietnam (31.2%) and lowest in those born in the Philippines (16.7%), Afghanistan (15.6%), Italy (12.5%) and India (7.4%). Over half (51.9%) of those born overseas and did not use an interpreter, spoke a language other than English at home.

CONCLUSIONS: Interpreter use was higher in older workers and also differed by country of birth. While interpreter use in the clinic was comparable to the health service overall, it was higher than the national figure on English proficiency. These data highlight the varying interpreting service needs of patients and the information can assist in planning of interpreting services.

96.

THE AUSTRALIAN BREAST DEVICE REGISTRY (ABDR): INSIGHTS FROM SEVEN YEARS OF FOLLOW UP

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The ABDR is a clinical quality registry that was rolled out across Australia in 2015 with funding from the Commonwealth Department of Health. Over seven years it has provided a valuable resource to monitor the long-term safety and performance of breast implants, tissue expanders and matrix/mesh.

AIM: To report on device performance and outcomes to better facilitate healthcare decision-making, industry based post-market surveillance and academic research.

METHODS: This abstract is based on the findings from the 2022 Annual Report, where the analysis is stratified by indication for surgery: cosmetic and reconstruction. It includes 87,339 patients records, employing descriptive statistics and time-to-revision analysis.

RESULTS: The ABDR reported 100,114 procedures since 2012, with an overall device capture rate in 2022 of 76.3%. All cause revision rates for reconstructive post cancer procedures was 20% at 7 years, with revisions due to device malposition and capsular contracture being 5.7% and 5.9% respectively. Revision rates for post cancer reconstructive procedures have decreased from 3.8% in 2016 to 2.2% in 2022. All cause revision incidence rates for cosmetic implants at 7 years was 6.3%. The ABDR was notified of 5 cases of Breast Implant Associated Anaplastic Large Cell Lymphoma in this reporting period. Cases were most commonly reported 7-10 years post insertion, where the common clinical issues associated was seroma/haematoma.

CONCLUSION: The ABDR has strong support amongst patients reflected in a consistently low opt-out rate of less than 1%. Surgeons are encouraged to report on their device revision and explantation procedures to ensure the ABDR is well placed to map device longevity and emerging trends in device related complications.

97.

RISKS OF INFECTIOUS DISEASE HOSPITALIZATIONS IN THE AFTERMATH OF TROPICAL CYCLONES: A MULTI-COUNTRY TIME-SERIES STUDY

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Background: The proportion of intense tropical cyclones (TCs), the costliest natural disasters, is expected to increase under global warming. However, a consistent and comprehensive assessment of infectious disease risk following TCs across countries and over decades is lacking.

AIM: To quantify the TC-associated hospitalization risks and burden for cause-specific infectious diseases on a multi-country scale.

METHODS: Hospitalization records for infectious diseases were collected from six countries/territories (Canada, South Korea, New Zealand, Taiwan, Thailand and Vietnam) between 2000-2019. The association of monthly infectious diseases hospitalizations and TC exposure days was first examined at location level using a distributed lag non-linear quasi-Poisson regression model, and then pooled using a random-effect meta-analysis.

RESULTS: Overall, 2.2 million hospitalizations for infectious diseases were included in the analysis. The elevated hospitalization risks for infectious diseases associated with TCs tended to dissipate two months after the TC exposure. Overall, each additional TC day was associated with a 9% (relative risk: 1.09, 95% confidence interval: 1.05–1.14) increase in hospitalizations for all-cause infectious diseases, 13% (1.13, 1.05–1.21) for intestinal infectious diseases, 14% (1.14, 1.05–1.23) for sepsis and 22% (1.22, 1.03–1.46) for dengue over the first two months after TC. In total, 0.72% (95% CI: 0.40%–1.01%) of the hospitalizations for all-cause infectious diseases, 0.33% (0.15%–0.49%) for intestinal infectious diseases, 1.31% (0.57%–1.95%) for sepsis and 0.63% (0.10%–1.04%) for dengue were attributable to TC exposures. The TC-attributable fractions decreased in South Korea, while increasing trends were observed in Vietnam, Taiwan, and New Zealand.

CONCLUSION: TCs were associated with elevated hospitalization risks of infectious diseases persisting for months, particularly for sepsis and intestinal infectious diseases. Targeted interventions should be formulated for different populations, regions and causes of infectious diseases based on evidence on TC epidemiology to respond to the increasing risk and burden.

98.

ADVANCES IN GENERATIVE AI FOR POINT-OF-CARE MAGNETIC RESONANCE IMAGING OF THE BRAIN

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Point-of-Care (PoC) mobile MRI has the potential to revolutionize neuroimaging by enhancing the safety and accessibility of MRI for critically ill patients, particularly in intensive care units (ICUs) and resource-limited settings, including rural and remote areas. However, the current limitation of PoC MRI, particularly at ultra-low magnetic field strength (64mT), is the suboptimal image quality that compromises its diagnostic utility.

OBJECTIVE: To enhance the image quality and diagnostic potential of PoC MRI through the application of Generative Artificial Intelligence (GenAI).

METHODS: This study involved pairing conventional high-field MRI (1.5T and 3T) brain scans with PoC MRI (64mT) scans from both healthy volunteers and patients with various neurological conditions, including traumatic brain injury, epilepsy, multiple sclerosis, and cerebral aneurysms. A GenAI model, utilizing Generative Adversarial Networks (GANs), was developed, trained, and validated on these paired datasets to synthesize high-quality synthetic point-of-care (SynPoC) images.

RESULTS: The GenAI model significantly improved the quality of PoC MRI images, enhancing visualization and providing greater clarity and detail. The synthesized SynPoC images demonstrated remarkable similarity to conventional high-field (3T) MRI, as illustrated by T2-weighted and FLAIR images of a 70-year-old patient with normal pressure hydrocephalus. The baseline PoC MRI images exhibited poor, non-diagnostic quality, whereas the SynPoC images closely approximated the diagnostic standards of high-field MRI.

CONCLUSION: The application of GenAI to PoC MRI presents a promising approach for enhancing diagnostic imaging in both normal and pathological brain conditions. SynPoC images offer substantial improvements in image quality, making high-acuity imaging more accessible for diverse clinical settings. Ongoing model refinements aim to further enhance the clinical utility and diagnostic accuracy of this innovative imaging modality.

99.

OPTIMISING THE MANAGEMENT OF PERIPHERAL ARTERIAL DISEASE THROUGH USE OF A CLINICAL DECISION SUPPORT TOOL

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Background: Consensus guidelines on the management of Peripheral Arterial Disease (PAD) recommend antiplatelet and optimal statin therapy alongside optimisation of blood pressure, diabetes management, and smoking cessation. Despite evident reductions in all-cause mortality, cardiovascular events, cerebrovascular and limb events, and disease progression, adoption of these interventions in PAD is suboptimal.

Aim/objective(s): To evaluate the impact of a collaborative medical-pharmacist clinical support tool on the management of patients diagnosed with PAD.

Methods: A retrospective cohort study evaluated the impact of a new clinical decision support tool on optimising the best medical therapy for hospital inpatients with PAD. Eligible inpatients were included in the pre-intervention phase (April-June 2021) and post-intervention phase (September-November 2021) following the implementation phase (July-August 2021). Discharge prescriptions of antiplatelet, statin [atorvastatin≥40mg] and antihypertensive prescribing, HbA1c monitoring and referral to smoking cessation services were reviewed. Descriptive statistics were employed to summarise data, and inferential statistical analyses were performed to assess the impact of the intervention on optimising PAD management.

Results: A total of 168 patients were included: ninety-seven (58%) in the pre-intervention group and seventy-one (42%) in the post-intervention group. In total, Sixty-three patients (38%) had concurrent diabetes (26 pre vs. 37 post) and fifty-five patients (33%) smoked (35 pre vs. 21 post). Post-intervention increased optimal prescribing was observed for antiplatelets (75% vs. 83%, p=0.22), statins (59% vs. 76%, p=0.019) and antihypertensives (67% vs.75%, p=0.29). Monitoring of HbA1c increased from 4% to 65% (p<0.01). All 55 patients currently smoking were referred to smoking cessation services.

Discussion: Implementing a clinical decision support tool improved the in-hospital adoption of best medical therapy for the management of PAD. Notably, there was a statistically significant enhancement in optimal statin dosing and HbA1c monitoring, underscoring the documentation tool's efficacy in improving PAD management.

100.

INTEGRATING A SAME DAY SLEEP APNOEA ASSESSMENT INTO A SURGICAL PRE-ADMISSION CLINIC (PAC)

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Untreated obstructive sleep apnoea (OSA) is often unrecognised pre-operatively and is associated with increased post-operative complications and morbidity. Anaesthetist screening of OSA risk in pre-admission clinic (PAC) prompts referral to a sleep physician to investigate.

AIM: To explore the novel concept of integrating a sleep physician into PAC, and assess its clinical and logistical outcomes.

METHODS: An audit sampling a PAC service was conducted at a tertiary hospital, pre and post integration of a sleep physician into PAC. Pre-integration, anaesthetists who identified patients at risk of OSA based on STOPBANG questionnaire were referred to the sleep clinic on a future date. Post integration, such patients were referred to the sleep physician in PAC on the same day. Demographic variables, times to assessments and hospital outcomes were reviewed.

RESULTS: 382 patients were reviewed in PAC pre-integration (26% bariatric, 31% orthopaedic, 43% other) and 355 post-integration (16% bariatric, 39% orthopaedic, 45% other). Comparing pre-integration with post-integration: 8 (2%) vs 71 (20%) patients were referred for sleep physician assessment. Patients from a broader range of surgical units were also represented post-integration. Mean days to: sleep physician assessment (120 vs 0), sleep study (91 vs 25), OSA management (138 vs 13) and surgery (261 vs 38). The 30-day mortality and unplanned non-invasive ventilation (NIV) post-operatively did not occur in either group referred for sleep assessment.

CONCLUSION: Integration of a sleep physician into PAC resulted in 10 times more referrals for assessment of OSA, and more diversity in surgical units referring. Time to: see a sleep physician, sleep study, management and surgery was reduced. Mortality and unplanned NIV use were not seen. Limitations of this study include a small sample size and confounders affecting clinical wait times.

101.

DEVELOPMENT AND VALIDATION OF A NOVEL SALIVA BETA-HYDROXY-BUTYRATE POINT-OF-CARE TEST FOR CHILDREN RECEIVING KETOGENIC DIET THERAPY FOR EPILEPSY

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BACKGROUND: Monitoring of ketosis is important to ensure ketogenic diet therapy (KDT) is safe and effective. Capillary blood beta-hydroxy-butyrate (BHB) testing is accurate, but causes discomfort. Urine aceto-acetate testing is cheap and less invasive, but correlates poorly with capillary BHB concentration.

AIMS: To determine if saliva BHB testing is an accurate alternative to blood BHB testing by first establishing the biological correlation between serum and saliva BHB concentration. The secondary aim was to validate the MX3 LAB Pro, a novel point-of-care device for saliva BHB testing.

METHODS: Children admitted to Shenzhen Children's Hospital for commencement of KDT were included. A paired serum blood and saliva sample was taken twice during the admission. Paired saliva samples with a capillary BHB measurement were obtained twice daily. Saliva BHB concentration was measured using liquid chromatography mass spectrometry (LCMS) and the MX3 LAB Pro. The primary outcome was the correlation between serum and saliva BHB concentration measured using LCMS. Secondary outcomes included correlation of capillary with saliva BHB measured using LCMS, and the MX3 LAB Pro, and degree of agreement between saliva BHB concentration measured by LCMS, and the MX3 LAB Pro.

RESULTS: A total of 71 serum and 334 capillary blood with paired saliva samples from 42 children were analysed. Saliva BHB measured using LCMS strongly correlated with serum BHB (Spearman's ρ=0.910) and capillary blood BHB concentrations (Spearman's ρ=0.865). Saliva BHB concentration was 6% of serum BHB and 7% of capillary BHB concentration. The MX3 LAB Pro demonstrated excellent test-retest reliability when compared with LCMS (ICC(A,k)=0.983, 95% CI: 0.980 – 0.986).

CONCLUSION: Saliva BHB concentration has a strong correlation with both serum and capillary BHB concentration. The MX3 LAB Pro can accurately measure saliva BHB concentration. Saliva BHB testing may be a suitable method to monitor ketosis for children requiring KDT.

102.
ADVANCES IN GENERATIVE AI FOR POINT-OF-CARE MAGNETIC RESONANCE IMAGING OF THE BRAIN

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OBJECTIVE: To enhance the image quality and diagnostic potential of PoC MRI through the application of Generative Artificial Intelligence (Gen-AI).

METHODS: This study involved pairing conventional high-field MRI (1.5T and 3T) brain scans with PoC MRI (64mT) scans from both healthy volunteers and patients with various neurological conditions, including traumatic brain injury, epilepsy, multiple sclerosis, and cerebral aneurysms. A Gen-AI model, utilizing Generative Adversarial Networks (GANs), was developed, trained, and validated on these paired datasets to synthesize high-quality PoC (SynPoC) images.

RESULTS: The Gen-AI model significantly improved the quality of PoC MRI images, enhancing visualization and providing greater clarity and detail. The synthesized SynPoC images demonstrated remarkable similarity to

conventional high-field (3T) MRI, as illustrated by T2-weighted and FLAIR images of a 70-year-old patient with normal pressure hydrocephalus. The baseline PoC MRI images exhibited poor, non-diagnostic quality, whereas the SynPoC images closely approximated the diagnostic standards of high-field MRI.

CONCLUSION: The application of Gen-AI to PoC MRI presents a promising approach for enhancing diagnostic imaging in both normal and pathological brain conditions. SynPoC images offer substantial improvements in image quality, making high-acuity imaging more accessible for diverse clinical settings. Ongoing model refinements aim to further enhance the clinical utility and diagnostic accuracy of this innovative imaging modality.

103.

VARIATIONAL BAYES MACHINE LEARNING FOR RISK ADJUSTMENT OF GENERAL OUTCOME INDICATORS WITH EXAMPLES IN UROLOGY

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Introduction: Risk adjustment is often necessary for outcome quality indicators (QIs) to provide fair and accurate feedback to healthcare professionals. However, traditional risk adjustment models are generally oversimplified and not equipped to disentangle complex factors influencing outcomes that are out of a healthcare professional's control. We present VIRGO, a novel variational Bayes model trained on routinely collected, large administrative datasets to risk-adjust outcome quality indicators (QIs).

Methods: VIRGO uses detailed demographics, diagnosis and procedure codes from the Victorian Admitted Episodes Dataset (VAED) to provide individualized risk adjustment for outcome QIs length of stay (LOS) and Hospital-acquired complications (HACs) count and explanations of patient factors affecting outcomes via Bayesian variational inference.

Results: VIRGO achieves state-of-the-art on external datasets (Overall root mean square error (RMSE): LOS: 2.217, 95% CI: [1.847 - 2.618], HACs count: 0.184, 95% CI: [0.154 – 0.214]), beating XGBoost (RMSE: LOS: 2.413, 95% CI: [1.885 - 3.042], HACs count: 0.187, 95% CI: [0.157 - 0.217]) and LightGBM (RMSE: LOS: 2.433, 95% CI: [1.89 - 3.091], HACs count: 0.188, 95% CI: [0.16 - 0.215]), two state-of-the-art gradient boosting models. Furthermore, VIRGO features capabilities of uncertainty expression, explainable features, and counterfactual analysis capabilities.

Conclusion: VIRGO facilitates risk adjustment by explaining how patient factors led to adverse outcomes and expresses the uncertainty of each prediction, allowing healthcare professionals to not only explore patient factors with unexplained variance that are associated with worse outcomes but also reflect on the quality of their clinical practice.

104.

TIMING AND VOLUME OF TRANSFUSION FOR ADULT MAJOR TRAUMA PATIENTS WITH HEMORRHAGIC SHOCK: A REGISTRY-BASED COHORT STUDY

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INTRODUCTION: Transfusion of blood components is vital for the resuscitation of injured patients in hemorrhagic shock. Delays in initiating transfusion have been associated with harm, as has excess transfusion. The aim of this study was to evaluate variables associated with hospital mortality, with a focus on the two modifiable risk factors- time to initiate transfusion and volume of blood components-with hospital mortality.

METHODS: This was a registry-based cohort study, including all consecutive adult patients presenting with hemorrhagic shock (systolic blood pressure (SBP) ≤90 mm Hg and transfusion of blood components) to a level 1 adult trauma center during a 5-year period (January 1, 2017-December 31, 2021). Associations with hospital mortality were assessed using multivariable logistic regression analysis, with final models developed using backward elimination.

RESULTS: There were 195 patients included and there were 49 (25.1%) in-hospital deaths. The median time to first transfusion was 10 (IQR 6-16) minutes. Age (adjusted OR (aOR) 1.06; 95% CI: 1.03 to 1.08), initial SBP (aOR 0.96; 95% CI: 0.3 to 0.98), intracranial bleeding or diffuse axonal injury (aOR 2.63; 95% CI: 1.11 to 6.23), and the volume of blood components in the first 4 hours (aOR 1.08; 95% CI: 1.03 to 1.13) were associated with mortality. Time to transfusion was not associated with in-hospital mortality (aOR 0.99; 95% CI: 0.95 to 1.03). Among the 90 patients who underwent urgent transfer to the operating room or angiography suite, the median time to transfer was 2.38 hours (IQR 1.5-3.7). In this subgroup, age (aOR 1.11; 95% CI: 1.05 to 1.18) and volume of blood components (aOR 1.20; 95% CI: 1.08 to 1.34) were associated with mortality.

DISCUSSION: In this setting where times to transfusion are short, further reductions in the time to transfusion are unlikely to improve outcome. In our population, for every unit of blood component transfused, the adjusted odds of death increased by 8%. These findings suggest investigation into strategies to achieve earlier control of hemorrhage.

105.

LONG-TERM EFFECTS OF A COALMINE FIRE ON HOSPITAL AND AMBULANCE USE: AN INTERRUPTED TIME SERIES STUDY

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BACKGROUND: In 2014, the Hazelwood coalmine fire in regional Victoria, Australia shrouded nearby communities in smoke for six weeks. Prior investigations identified substantial adverse effects, including increases in the use of health services. In this study, we examined the effects on hospital and ambulance use in the eight years following the fire.

METHODS: Using Victorian hospital (Jan 2009-Jun 2022) and ambulance (Jan 2013-Dec 2021) data, we conducted an interrupted time series of changes to the rate of hospital admissions, emergency presentations, and ambulance attendances. A categorical exposure model compared two locations, most-exposed Morwell and less-exposed Latrobe Valley, to the rest of regional Victoria. A continuous exposure model used spatial estimates of fire-related $PM_{2.5}$. Analyses were stratified by sex, age group (<65/65+ years), and condition (cardiovascular, respiratory, mental health, injury).

RESULTS: There were small but significant increases in overall hospital admissions and emergency presentations across all analyses, but little evidence of change in overall ambulance attendances. Effects varied considerably by condition, with the biggest relative increases observed among hospital admissions for mental health conditions and injuries. While cardiovascular-related hospital admissions and emergency presentations increased postfire, ambulance attendances decreased.

CONCLUSIONS: Our findings suggest the Hazelwood coalmine fire likely increased hospital usage. However, it is unclear whether this was due to the direct effects of smoke exposure on health, or the disruptive socioeconomic and behavioural impacts of an environmental disaster that affected how communities engaged with various health services.

106.

DETECTION OF GERMLINE COPY NUMBER VARIATIONS IN A SMALL TARGETED-SEQUENCING PANEL: APPLICATIONS FOR POPULATION GENOMIC SCREENING

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DNA Screen is an Australian pilot study of population genomic screening for Hereditary Breast and Ovarian Cancer (HBOC), Lynch Syndrome (LS) and Familial Hypercholesterolemia (FH) involving >10,000 participants, aged 18-40 years. It uses a small panel targeting the coding regions of 9 genes associated with high risk of HBOC (*BRCA1, BRCA2, PALB2*), LS (*MLH1, MSH2, MSH6*) and FH (*APOB, PCSK9, LDLR*). To date, medically actionable variants detected in DNA Screen have consisted of small variants (up to 20bp). Yet, it is estimated that at least 10% of all pathogenic variations across HBOC, LS and FH are copy number variations (CNVs). The analytical validity of the DNA Screen panel (88 kbp total) for the detection of CNVs is still unknown.

AIM: To explore the possibility of detecting CNVs in the DNA Screen participants and develop a customised framework for CNV interrogation.

METHODS: CNVs were simulated in a series of DNA Screen samples, representing various CN states in different genomic locations. VS-CNV (Golden Helix) was used to detect these simulated CNVs, and the output was used to build 95% confidence intervals to distinguish CNV events from technical noise in the data.

RESULTS: Through the application of our custom framework to the entire DNA Screen dataset, we were able to identify a number of potential CNVs. Assays to experimentally validate and further refine this framework are currently being developed.

CONCLUSION: These preliminary results show that there is potential for CNVs to be identified from DNA Screen data. This is likely to lead to the identification of more at-risk individuals in the population, allowing them to access life-saving early interventions, rather than late-stage treatment.

107.

PREVALENCE OF SEXUAL AIDS USE IN MEN WITH PROSTATE CANCER – PCOR-VIC OBSERVATION STUDY

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Aim: To report the prevalence of self-reported sexual aids (SA) use after localised prostate cancer (PCa) treatment and correlate this with patient-reported sexual function at a population-based level.

Methods and Materials: We included men diagnosed with PCa between 2009 and 2022 in the Victorian Prostate Cancer Outcomes Registry, who had active treatment and completed questionnaire on SA use and the Expanded Prostate Cancer Index Composite-26 (EPIC26) 12-months post-treatment. Primary outcomes were SA use prevalence, and correlation of SA use with the EPIC-26 sexual function score.

Results: Of the 8982 men included, 47% reported SA use. Types of SA use included: oral medications (3842/4180, 92%), intra-urethral suppositories (32/4180, 0.8%), penile injections (933/4180, 22%), and vacuum-erection devices (924/4180, 23%). Of the men who reported SA use, 56% reported that the SA were helpful. Men with high-risk PCa were less likely to use SA compared to men with low-risk PCa (30% vs 60%). 57% of men who had surgery, 27% who had radiotherapy, and 9% who had radiotherapy with androgen deprivation therapy reported SA use. 53% and 37% men who had treatment in private and public institutions, respectively, reported SA use. 52% men from highest socioeconomic quintiles and 38% men from lowest socioeconomic quintiles reported SA use. In multivariable analyses, age, NCCN-risk categories, treatment type, treatment institutions and socioeconomic status were independently associated with SA use. Men who reported SA use and found it helpful had significantly better sexual function score (median=43.0; IQR=20.8-66.7), compared to men who did not use SA (median=16.7; IQR=9.7-29.2), with adjusted mean differences of 16.1 (95%CI=14.7-17.4, P<0.001).

Conclusion: This is the largest population-based study on SA use after PCa treatment. 1-in-2 men reported SA use, with half reported SA helpful and had improved sexual function. This highlights the importance of discussion on SA use after treatment for PCa.

108.

SIGNIFICANT CARBON SAVINGS ASSOCIATED WITH THE REUSE AND INCINERATION OF METERED DOSE INHALERS IN LUNG FUNCTION LABORATORIES

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BACKGROUND: Metered dose inhalers (MDIs) are important devices for delivering inhaled medications, however they have an outsized carbon footprint due to their propellant gas. Many short-acting beta-agonist inhalers contain HFA-134a which has a global warming potential >1000-fold higher than carbon dioxide. We aimed to determine the practices around MDI use and disposal within Australia's major lung function testing laboratories and identify the actions that most influence the carbon footprint of bronchodilator responsiveness (BDR) testing.

METHODS: Australia's forty-five accredited lung function laboratories were invited to participate in an online survey asking about their volume of BDR testing, as well as practices around MDI use such as the number of actuations per BDR test, reuse of MDIs between patients, and disposal method. We calculated MDI-associated carbon dioxide equivalent (CO_2e) emissions by combining previously published estimates.

RESULTS: Thirty-nine laboratories completed the survey. Most laboratories used 4 actuations of salbutamol per BDR test for both adults (27/34, 79.4%) and children (17/20, 85%), but this ranged from 2 to 12. Only three (7.7%) laboratories did not routinely reuse MDIs between patients, however they all sent their used MDIs for high-temperature incineration. Based on different combinations of observed MDI practices in Australia, we identified a potential six-fold difference in CO_2e per 100 BDR tests, from as low as 23.3kg CO_2e up to 166kg CO_2e.

CONCLUSIONS: We identified three key practices to reduce the carbon footprint of BDR testing: disposing MDIs via high-temperature incineration, reducing the number of actuations per BDR test and reusing MDIs between patients.

109.

PHARMACIST IN VASCULAR OUTPATIENT CLINIC IMPROVES GUIDELINE ADHERENT MEDICATION PRESCRIBING IN PATIENTS WITH VASCULAR DISEASE

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BACKGROUND*:* International guidelines recommend antiplatelets, high-dose statins (atorvastatin 40-80mg or equivalent) and smoking cessation in patients with peripheral arterial diseases (PAD) to reduce all-cause mortality and cardiovascular events. Despite this, prescribing remains suboptimum. In 2023, a pharmacist was integrated into the vascular outpatient clinic to optimise medications and promote smoking cessation.

AIM: To assess the impact of outpatient pharmacist review on provision of optimal medical therapy in patients with vascular disease.

METHODS: A mixed prospective-retrospective cohort study was performed comparing appropriate statin and antiplatelet prescribing (initiation and/or dose optimisation), and smoking cessation interventions prior to (Jul-Dec 2022) and following pharmacist integration into vascular outpatient clinic (Jun-Dec 2023). Patients attending the clinic with lower extremity arterial disease, carotid artery disease or complex aortic disease were included in statin and antiplatelet analyses and current smokers with PAD in smoking cessation analyses. Univariate and multivariate logistical regression analyses were performed to ascertain the impact of pharmacist review on statin and antiplatelet prescribing and smoking cessation services. Analyses were performed in RStudio.

RESULTS: Of 304 patients included, 211(69%) had vascular pathology requiring both statin and aspirin therapy (no pharmacist: n=137; pharmacist: n=74) and 107(35%) were smokers (no pharmacist: n=44; pharmacist: n=63). Multivariate analysis demonstrated increased prescribing of appropriate statin therapy following pharmacist review compared to without (no pharmacist: 44.53%; pharmacist: 79.73%; adjusted odds ratio [OR] 4.46, 95%CI: 2.14-9.33, p<0.0001). There was no significant difference in antiplatelet prescribing (adjusted OR 0.89,95%CI: 0.39-2.04, p=0.791). Pharmacist review increased the likelihood of referral to intensive smoking cessation counselling (unadjusted OR19.20, 95%CI: 4.14-89.01,p< 0.0001).

DISCUSSION: Patients in vascular outpatient clinic were over four times more likely to be prescribed appropriate statins and more likely to be offered smoking cessation counselling following pharmacist review compared to those without. Pharmacist intervention is markedly effective in an underperforming area of vascular surgery.

110.

SPLENIC ARTERY EMBOLISATION FOR SPLENIC INJURY DURING COLONOSCOPY: A SYSTEMATIC REVIEW

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Splenic injury due to colonoscopy is rare, but has high mortality. While historically treated conservatively for low-grade injuries or with splenectomy for high-grade injuries, splenic artery embolisation is increasingly utilised, reflecting modern treatment guidelines for external blunt trauma.

AIM: This systematic review evaluates outcomes of published cases of splenic injury due to colonoscopy treated with splenic artery embolisation.

METHODS: A systematic review was performed of published articles concerning splenic injury during colonoscopy treated primarily with splenic artery embolisation, splenectomy, or splenorrhaphy from 1977 to 2022. Datapoints included demographics, past surgical history, indication for colonoscopy, delay to diagnosis, treatment, grade of injury, splenic artery embolisation location, splenic preservation (salvage), and mortality.

RESULTS: The 30 patients treated with splenic artery embolisation were of mean age 65 (SD 9) years and 67% female, with 83% avoiding splenectomy and 6.7% mortality. Splenic artery embolisation was proximal to the splenic hilum in 81%. The 163 patients treated with splenectomy were of mean age 65 (SD 11) years and 66% female, with 5.5% mortality. Three patients treated with splenorrhaphy of median age 60 (range 59–70) years all avoided splenectomy with no mortality. There was no difference in mortality between splenic artery embolisation and splenectomy cohorts (p = 0.81).

CONCLUSIONS: Splenic artery embolisation is an effective treatment option in splenic injury due to colonoscopy. Given the known benefits of splenic salvage compared to splenectomy, including preserved immune function against encapsulated organisms, low cost, and shorter hospital length of stay, embolisation should be incorporated into treatment pathways for splenic injury due to colonoscopy in suitable patients.

111.
EVALUATING ACCURACY OF CERVICAL SPINE COMPUTED TOMOGRAPHY INTERPRETATION BY EMERGENCY TRAINEES WITH THE USE OF A STRUCTURED PROTOCOL.

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OBJECTIVE: Radiological evaluation of cervical spine injury with computed tomography (CT) scanning is a fundamental component of the assessment of major trauma. Accurate interpretation of scans is essential for safe clearance or diagnosis of injuries. However, delays in radiologist reporting often result in prolonged spinal immobilisation. The aim of this study was to evaluate a simple, structured reporting tool to improve assessment of CTs of the cervical spine by emergency medicine trainees.

METHODS: A prospective pre- and post-intervention cohort study was undertaken within a major metropolitan emergency department. Participants in the pre-intervention phase interpreted a set of randomly selected cervical spine CTs. The post-intervention phase presented the same task with the additional provision of a structured cervical spine CT reporting template designed in collaboration with radiologists and emergency physicians. Interpretation by trainees was evaluated for concordance with the final radiology report by two blinded assessors.

RESULTS: A total of 155 cervical spine CT scans were reported by the 46 participants. Participants in the cohorts were similar with regards to experience and country of primary medical degree. Concordance with the radiology report in the pre-intervention phase was 60% (95%CI 0.48-0.71), compared with a concordance of 54% (95%CI 0.42-0.65) in the post-intervention phase (p=0.46).

CONCLUSIONS: Interpretation of cervical spine CT scans by trainees was inferior compared to radiologists and did not improve with a structured reporting template. Other innovative strategies towards timely reporting of CT scans by radiologists of the cervical spine are indicated for earlier definitive diagnosis.

112.
BRAIN-DERIVED TAU AS A BIOMARKER OF TREATMENT EFFECT IN ALZHEIMER'S DISEASE AND BEHAVIOURAL VARIANT FRONTOTEMPORAL DEMENTIA

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Background: Novel biomarkers are needed to measure treatment response in neurodegenerative diseases. Brain-derived tau (BD-tau), a cerebrospinal fluid (CSF) protein biomarker specifically from brain-derived sources, has previously been shown to differentiate Alzheimer's disease (AD) from other neurodegenerative diseases.

Aims: This study aimed to determine if BD-tau may also be a potential biomarker of treatment effect in clinical trials of a potential disease modifying drug, sodium selenate which acts by reducing pathological hyperphosphorylated tau, in patients with AD and behavioural variant frontotemporal dementia (bvFTD).

Methods: We investigated BD-tau and p-tau$_{217}$ levels after treatment with sodium selenate in two clinical trials in patients with AD and bvFTD. We also examined the association of these measures with levels of t-tau, p-tau$_{181}$ and Aβ_{42}.

Results: CSF BD-tau levels decreased after treatment with sodium selenate in patients with AD, however they did not change in patients with bvFTD. No change in p-tau$_{217}$ was seen after treatment in either AD or bvFTD cohorts. CSF t-tau and p-tau$_{181}$ correlated with CSF BD-tau in both the AD ($r = 0.9113$ and 0.7746, $p < 0.0001$) and bvFTD ($r=1.0$, $p=0.004$ and $r=0.79$, $p<0.05$) cohorts. In the bvFTD cohort CSF BD-tau did not correlate with serum or plasma BD-tau ($r<0.32$, $p>0.5$).

Conclusions: CSF BD-tau shows potential as a biomarker of treatment effect in patients with AD, however not in patients with bvFTD. Further research is needed to investigate the feasibility of BD-tau as a measure of treatment effect in blood-based samples and its use in other neurodegenerative diseases.

113.

MSREACTOR COGNITIVE SCREENING TESTS CAN DETECT CHANGES IN COGNITIVE FUNCTION IN LATE-ONSET MULTIPLE SCLEROSIS.

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INTRODUCTION: Late-onset MS (LOMS) occurs in up to 12% of people with multiple sclerosis (MS). How cognition changes over time in LOMS is an area of limited research. Digital measures of cognitive function may address this gap.

AIM: To detect differences in computerised cognitive task performance between LOMS and adult-onset MS (AOMS).

METHODS: MSReactor uses reaction times to screen information processing speed (SRT), attention (CRT) and working memory (OBK). Clinical data was collected via the MSBase registry. Participants with at least one test were divided into LOMS (diagnosed over age 50) or AOMS. Regression was used to compare baseline scores, controlling for disease duration. Change in reaction time (at least three tests) is the difference between last and baseline tests. Additionally, we compared those diagnosed above 60 (VLOMS) to those diagnosed under 60.

RESULTS: From 1376 participants with at least one MSReactor test, 132 were LOMS and 1244 were AOMS. Nineteen were defined as VLOMS. LOMS performed worse than AOMS at baseline, independent of disease duration (SRT 479 milliseconds (ms) vs 405ms (p <0.0001); CRT 657ms vs 599ms (p <0.0001); OBK 1018ms vs 939ms (p <0.0001). VLOMS performed worse than the remaining cohort at baseline (SRT 535ms vs 410ms (p <0.0001); CRT 741ms vs 603ms (p <0.0001); OBK 1087ms vs 945ms (p <0.01)). In total, 849 participants completed at least 3 serial MSReactor tests. In LOMS (n=92), CRT slowed over time compared to AOMS (+10 ms vs -12ms). In VLOMS (n=15), OBK slowed compared to the remaining cohort (+114ms vs -74ms).

CONCLUSION: Differences in cognitive function between LOMS and AOMS could be detected using a computerised test. Longitudinal worsening in attention and working memory were detectable in LOMS and VLOMS, compared to younger diagnosis. Understanding cognitive trajectories in older MS patients is essential for better outcomes and improved trial design.

114.
INTERNATIONAL CONSENSUS DEFINITIONS FOR STANDARDISED ENDPOINTS IN PERIOPERATIVE MEDICINE: PATIENT COMFORT

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Enhancing the patient experience and improving comfort during and after surgery is a key concern for all perioperative clinicians.

AIM: To include patients (consumers) and clincian-researchers to develop consensus-based standardised endpoints for clinical trials focussed on patient comfort before and after surgery.

METHODS: Focus groups, workshop and a multi-round international Delphi consensus process that included clinician-researchers and a patient experience and consumer group assessed numerous standardised endpoints focussed on patient comfort. Consensus was defined as a median item score of ≥7 and ≥70% of responses achieving a score of ≥7 on a 9-point Likert scale. An additional rating was completed by the clinician-researchers to determine validity, reliability, feasibility, and patient-centeredness. Qualitative and quantitative analyses were undertaken to identify themes and endpoints.

RESULTS: Including patients (consumers of healthcare) highlighted the importance of clear communication, shared decision-making and a nominated contact person to enhance comfort through the surgical journey. We identified a preliminary list of 37 outcome measures and their definitions. Response rates for Delphi rounds one and two were each 100% (n=24); and for the clinical researcher psychometric evaluations 100% (n=17). A final list of eight defined endpoints was identified: supplementary analgesic use, subjective analgesic effectiveness, pain intensity (at rest and during movement, at 12, 24 and/or 72 h), postoperative nausea and vomiting (PONV, at 0-6 h, 6-24 h, overall), post-discharge nausea and vomiting, severe PONV, quality of recovery (QoR-15), and time to mobilisation. All eight endpoints were assessed by the clinician-researchers as valid, reliable, and feasible measures of patient comfort, and were considered patient-centred having a meaningful impact on a patient's recovery.

CONCLUSIONS: Clear communication and patient supports reduce anxiety and enhance comfort for people undergoing surgery. We recommend that these standardised endpoints be included as outcome measures in clinical trials assessing patient comfort and pain after surgery.

115.

A FUSION ARTIFICIAL INTELLIGENCE MODEL FOR PREDICTION OF RESPONSE TO ANTI-SEIZURE MEDICATIONS IN NEWLY TREATED EPILEPSY

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Rationale: Anti-seizure medications (ASMs) are successful in controlling seizures for approximately 60% of patients newly treated for epilepsy. However, with more than 30 approved ASMs worldwide, there is no reliable way to predict which would be most effective for a given patient. Consequently, it may take several years to find an effective ASM regimen for an individual with epilepsy. We aimed to develop an artificial intelligence (AI) model to predict seizure freedom in response to ASMs and to potentially suggest the most suitable medication at the onset of treatment.

Methods: Consecutive adults (>18 years) with newly diagnosed epilepsy who had been treated with one or two ASMs as monotherapy from 2015 to 2024 were retrospectively recruited from the patient database of the Alfred Hospital (Melbourne, Australia) (Table 1). A second regimen was administered (either as a monotherapy or as an adjunctive medication), if the first ASM failed to yield an effective outcome (at least 12 months of seizure freedom after starting medication). Patients who underwent 3T MRI (Siemens, Skyra) were eligible for inclusion. The fusion AI model consisted of an 18-layer 3D-ResNet (inputs: three baseline MR images), a long short-term memory (LSTM) recurrent neural network (inputs: the two most recent regimens), and a dual linear neural network (inputs: clinical characteristics and EEG findings) to predict the probability of seizure outcome. The ASMs with less than 3 occurrences within the sample population were omitted and the corresponding patients were excluded. Patients without any high quality/resolution MRIs (T1, T2, and FLAIR images) were also excluded. The probability of seizure freedom per ASM was predicted by the fusion model and thresholded to be compared with the ASM seizure outcome. To train the model, 50 iterations of 5-fold cross-validation was performed. The accuracy, F1-score, and AUC (the area under the curve) for the ROC (receiver operating characteristic) curve were calculated and averaged among the 5 folds.

Results: One-hundred and thirteen patients were included in the analysis, of which 68 patients were seizure free and 45 were not. The fusion model accuracy achieved: 84% and 75%, F1-score: 84% and 74%, and AUC: 89% and 73%, on training and test data, respectively. Figure 1 shows the ROC curves for each of 5 folds in training and validating steps with their AUC. It suggests that the proposed fusion model can predict the ASM leading to seizure freedom for roughly as many as 75% of newly diagnosed epilepsy.

Conclusion: Response to initial ASMs may be predicted using a fusion AI model that integrates ASM information with patient's characteristics and MRI images. This approach holds promise for personalized treatment strategies, leading to improved treatment outcomes.

116.

IDENTIFYING PATIENTS AT RISK OF PREVENTABLE DEATH FROM INJURY IN AUSTRALIA: EXPOSING THE BURDEN OF TRAUMATIC SHOCK

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Injury is the leading cause of death for people aged 1-44 years in Australia and 5-29 years globally. Haemorrhage and subsequent traumatic shock accounts for up to 40% of these deaths, the majority of which may be preventable. Despite this, little is known about the burden of traumatic shock (TS) in an Australian context.

AIM: To describe the epidemiology and outcomes of traumatic shock (TS) in Australia and to identify strategies for improving early detection and reducing preventable deaths from injury-related trauma.

METHODS: Data was extracted from the Australia New Zealand Trauma Registry (ANZTR) from July 2017 to June 2022. Variables related to TS identification, management, and outcomes were selected for analysis. After excluding patients with incomplete data, 31,267 adult major trauma patients from 12 trauma centres were included in the final analysis. Comparisons were made between patients identified with TS and those without.

RESULTS: Patients with TS were predominantly male (72.6%), younger (mean age 46 vs. 52 years), and more severely injured than non-TS patients. TS patients were more likely to arrive by helicopter, have penetrating injuries, present with lower Glasgow Coma Scale (GCS) scores, and require assisted ventilation on arrival. Mortality rates were significantly higher in TS patients (20% vs. 8.6%), with a fourfold increase in the likelihood of dying in the Emergency Department (3.6% vs. 0.9%). TS patients also had longer ICU stays (5.4 vs. 2.7 days) and overall hospital stays (17.2 vs. 11.9 days). More than 21 TS-related deaths occur weekly in Australian trauma centres, and an unmeasured burden exists in less-equipped settings.

CONCLUSIONS: Traumatic shock significantly increases the risk of early death in trauma patients. The study suggests that improving data collection, early detection, and standardizing care for TS could reduce preventable deaths from injury-related trauma in Australia.

117.

PREVALENCE OF ALCOHOL EXPOSURE IN BURNS RELATED INJURIES

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The aim of this registry-based cohort study was to quantify the prevalence, injury characteristics, and outcomes of alcohol exposure in burn-related injuries. All patients ≥ 18 years presenting to The Alfred Emergency & Trauma Centre, a major trauma centre in Victoria, Australia between January 1, 2019 and December 31, 2022 and included in the Victorian Adult Burns Service registry were included. An explicit chart review was performed to verify retrieved data with alcohol exposure coded when documented in medical records, laboratory evidence of a blood alcohol concentration > 2mmol/L, or recorded in discharge ICD codes. Among 1587 eligible patients, 251 (15.8%) had been exposed to alcohol prior to injury. Patients with alcohol exposure at the time of burn-related injury had higher rates of admission to the ICU (28% vs 16.4%, $p < 0.001$) and longer hospital admission (10.1 vs 7.7 hours, $p < 0.001$). The significant impact of alcohol exposure on the overall health burden of burn injuries highlight the need and opportunities for targeted preventive strategies to reduce burn injuries.

118.

EFFECTIVENESS OF A DISABILITY LIAISON OFFICER SERVICE IN A METROPOLITAN EMERGENCY DEPARTMENT

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ABSTRACT

People with disability (PWD) often experience difficulties accessing healthcare, are more likely to have frequent and potentially avoidable hospital admissions, delays in discharge and poor hospital experiences. Factors associated with healthcare outcomes and experiences may include limited staff training in disability, poor attitudes and discrimination towards PWD, diagnostic overshadowing, delayed identification of PWD upon presentation and over reliance on support persons. In this project, PWD refers to adults with a communication disability, intellectual disability, or autism. A disability liaison officer service (DLO) was introduced to an adult major referral emergency department (ED) in Melbourne, Australia. Using a retrospective cohort design, effectiveness of the DLO model of care was compared to standard care for the management of PWD. The primary outcome measure was length of stay in the ED. We also examined length of stay among patients discharged from the ED, admitted to the short stay unit and among those admitted to inpatient wards. After adjusting for baseline differences in age, initial Glasgow Coma Scale, and disability type, the DLO service was associated with earlier disposition from the ED (Adjusted hazard ratio (aHR) 1.44; 95%CI: 1.23-1.69, p<0.001). For the subgroup of patients discharged directly from the ED, the association of DLO service and earlier disposition remained statistically significant (aHR 2.47 (95%CI: 1.83-3.33, p<0.001). Among patients admitted to the short stay unit (aHR 1.67 (95%CI: 0.99-2.80, p=0.06), and those admitted to inpatient wards (aHR 0.89; 95%CI: 0.65-1.23, p=0.50), there was no significant association of the DLO service with time to disposition. Disability liaison services appear effective in EDs to enable timely care. Further assessment of the service using patient and carer-reported outcome measures and cost-effectiveness studies are indicated.

119.

UNDERSTANDING POTENTIAL LUNG RECORVERY FROM COAL MINE FIRE SMOKE EXPOSURE

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Introduction

In 2014, residents of Morwell, Australia, were exposed to extreme concentrations of fine particulate matter ($PM_{2.5}$) ≤ 2.5µm diameter as the Hazelwood open cut brown coal mine burned for ~6 weeks. $PM_{2.5}$ exposure was associated with increased ventilation heterogeneity and worse respiratory mechanics at 4yrs, (R1); this was attenuated at 7yrs (R2).

Aim

To assess the impact of medium duration exposure to $PM_{2.5}$ on respiratory function 9yrs later (R3).

Methods

Participants completed spirometry, gas transfer, and oscillometry (respiratory system mechanics). Individual $PM_{2.5}$ exposure was retrospectively modelled and fitted in mixed-effects regression models to analyse associations between $PM_{2.5}$ and lung function.

Results

164 exposed and 80 unexposed participants from a cohort (R1: N=519, R2: N=329) completed R3: 59% female, mean age 58.6±15yrs, 44% had BMI≥30kg/m^2. A trend for decreasing baseline FVC Z-scores with increasing

$PM_{2.5}$ exposure observed at Round 1 was attenuated by Round 2 and maintained at Round 3 (ΔFVC-Z score per 10ug/m^3 increase in $PM_{2.5}$ R1:-0.08,CI -0.16,0.00 vs R3:-0.02,CI -0.13,0.09, p-int=0.02). Exposure to mine fire related $PM_{2.5}$ was not associated with gas exchange at any round. At Round 1 $PM_{2.5}$ exposure was associated with stiffer lungs evidenced by transformed post-bronchodilator reactance (Xrs). This effect was attenuated at Round 2 and recovery was maintained at Round 3 (ΔXrs per 10ug/m^3 increase in $PM_{2.5}$ R1:-0.01,CI -0.03,0.00 vs R3:0.01,CI -0.01,0.03, p-int=0.002). A trend for increased peripheral resistance with $PM_{2.5}$ exposure reduced across assessment rounds, interaction p-value=0.04 at Round 3.

Conclusion

Long-term follow up, 9 years after the fire, showed that resolution of reduced FVC and increased lung stiffness, associated with medium term $PM_{2.5}$ exposure, was maintained. A potential reduction in peripheral resistance, not seen at earlier assessment rounds, was also found. Findings are consistent with slow recovery of lung function after exposure to coal mine fire smoke.

120.

CHLAMYDIA VACCINE FOR ADOLESCENT GIRLS – WHAT DO PARENTS REALLY THINK?

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Chlamydia is a bacterial sexually transmitted infection (STI), that remains a significant public health issue despite the availability of effective treatment. A recent phase I chlamydia vaccine clinical trial depicts it is safe, well tolerated and immunogenic. However, the existence of a vaccine doesn't necessarily lead to its uptake particularly when there are many unanswered questions about how it will work and when it will be rolled out. Ideally, the vaccine is administered to adolescents prior to sexual debut, a time where parents are primary decision makers.

AIM: To explore parents' thoughts of a chlamydia vaccine for their adolescent daughters to guide vaccination roll out in the future.

METHODS: Individual semi-structured zoom interviews were conducted with parents of children with a cervix aged 10-14, living in Victoria, Australia. Topics included parents' attitudes of vaccines, knowledge of chlamydia, important vaccine characteristics and preferences for delivery. Recruitment occurred via physical and online advertising flyers. Interviews were recorded, transcribed and was coded on NVivo using content analysis.

RESULTS: 18 interviews were conducted from July to August 2024. Overall, parents were supportive of a future chlamydia vaccine to reduce the severity and long-term consequences of infection for their adolescent daughters. However, there were mixed opinions about the right age to vaccinate adolescents and if their daughters would be involved in vaccine decision making. This was important if the adolescent is considered a mature minor with the capacity to consent for vaccination. All parents expressed the need for the vaccine to be easily accessible for example free of cost and available at school or a pharmacy if it's missed.

CONCLUSION: Parents will accept a future chlamydia vaccine for their adolescent daughters, however the vaccine roll out must use a multipronged approach to ensure its accessible and provided with evidence-based information to enable widespread uptake.

121.

FIRST IN-HUMAN MICROELECTRODE RECORDINGS FROM THE VAGUS NERVE DURING CLINICAL VAGUS NERVE STIMULATION

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Vagus nerve stimulation (VNS) is an effective treatment for people with drug-resistant epilepsy. However, its mechanisms of action are poorly understood, including which nerve fibres are activated in humans during VNS at typical clinical settings and which fibres are required for clinical efficacy. To date, there have been no studies of vagus nerve fibre activation in awake, ambulant humans undergoing chronic VNS for the treatment of drug-resistant epilepsy.

AIM: In this study, for the first time, we report successful recordings from the left cervical vagus nerve in conscious drug-resistant epilepsy patients with an implanted VNS device.

METHODS: Recordings were made in five participants aged 19-32 years and were performed using a sterile tungsten microelectrode inserted percutaneously into the left cervical vagus nerve under ultrasound guidance. The recording microelectrode was inserted cephalad to the stimulating cathode of the VNS device. The clinical VNS systems were used to deliver stimulation while activity in the vagus nerve was recorded. Stimulation parameters including current intensity, pulse width and frequency were adjusted to determine activation thresholds of specific fibre groups within the vagus nerve.

RESULTS: In addition to activating myelinated fibres at low currents, we provide evidence that VNS can also activate unmyelinated C-fibres in the vagus nerve at currents below 1 mA.

CONCLUSION: There is much debate as to whether C-fibres are responsible for the anti-epileptic effects of VNS even though the majority of the vagus nerve is composed of unmyelinated C-fibres. Our recordings show evidence of C-fibre activation and these results add to our understanding of what pathway VNS is activating, and how it may be exerting its anti-epileptic effects in the context of drug-resistant epilepsy.

122.

EVALUATION OF PATIENT OUTCOMES FOLLOWING IMPLEMENTATION OF AN ALTERNATIVE, COMMUNITY-BASED MODEL OF CARE FOR COMPLEX HIGH RISK FOOT PATIENTS DURING THE COVID-19 PANDEMIC

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BACKGROUND: Extreme pressure on acute healthcare settings during the Covid-19 pandemic resulted in the rapid implementation of alternative service models for many patient groups. In 2020, complex high risk foot patients attending hospital based, podiatry outpatient services at Alfred Health were transferred to community based services to alleviate pressures on acute services and to reduce the risk of infection spread.

AIM: This study aimed to evaluate the impact of this transition on patient outcomes, and identify opportunities to further evaluate the best model of care for this at-risk patient group.

METHODS: A retrospective audit of electronic medical records was conducted for all patients transferred from acute to community based care for the period April 2020 – July 2020. Pre-determined data was collected for the 6 month periodS pre and post transfer. Demographic data including age, gender and language spoken, was

collected alongside clinical data such as peripheral arterial disease, renal status, foot ulcer and amputation history. Outcome data such as emergency department presentations, hospital admissions, amputations and deaths were also collected.

RESULTS: Data analysis is ongoing, however preliminary results indicate of the 57 patients who were transferred: 93% had diabetes, 11% had end stage renal failure, and 60% had peripheral arterial disease. 9% had an acute Charcot foot and 47% had foot ulcers at time of transfer. It is noted that over 30% of the cohort studied are now deceased.

CONCLUSIONS: Results from this study will be used to inform innovative, out of hospital models of care to manage patients with high risk foot complications.

123.

ADMISSION TO SPECIALISED NEUROCRITICAL UNITS AND ASSOCIATION WITH CLINICAL OUTCOMES: A MIXED-METHODS STUDY

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Globally, managing critically ill adults with acute brain injuries (ABIs) in specialised neurocritical units (NCCUs) is associated with improved survival, but this has not been assessed in Australia.'

OBJECTIVE: To determine in adults with ABI, if admission to a general intensive care unit (ICU) or NCCU was associated with a difference in outcomes.

METHODS: A nation-wide survey was undertaken of Australian ICUs surveyed as to their NCCU capabilities via the Australian and New Zealand Intensive Care Society (ANZICS). Linked ABI patient-level outcomes were then extracted from the ANZICS Adult Patient Database (APD) for a retrospective observational cohort study. Adults with an ABI (intracerebral haemorrhage, acute ischaemic stroke, subarachnoid haemorrhage or traumatic brain injury) admitted to ICU between January 2016 and December 2022 were included. The primary outcome of interest was in-hospital mortality, with secondary outcome measures of ICU mortality, ICU length of stay (LOS), hospital LOS and discharge destination other than home.

RESULTS: Responses were received from 78 out of 192 surveyed ICUs. Amongst respondent units, 41 reported routinely caring for ABI patients, of which 8 were specialist NCCUs. There were 14,740 index admissions to participating ICUs over the study period, 7,402 NCCU and 7,338 general ICUs admissions respectively. Crude in-hospital mortality was 18% (1,356/7,402) in NCCUs and 21% (1,514/7,338) in general ICUs. The adjusted odds ratio (OR) for in-hospital mortality was 0.88 (95% confidence interval [CI] 0.81-0.96, p-value 0.003), favouring those cared for in a NCCU. In survivors, those admitted to NCCUs were more likely to remain in hospital longer (relative change in geometric mean = 20.5%, 95% CI 16.2-25.1, p-value <0.001) and be discharged to a rehabilitation facility (OR = 2.01, 95% CI 1.83-2.21, p-value <0.001).

CONCLUSION: In Australian adult ABI patients admitted to ICU, admission to a NCCU was independently associated with lower hospital mortality.

124.
EPIGENETIC AGE ACCELERATION LINKING WITH FRAILTY AND WORSE COGNITIVE PERFORMANCE OVER TIME AMONG OLDER PEOPLE

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Decline in physical and cognitive function occurs with advanced age, and epigenetic age acceleration (AA) may be a useful marker of physical and cognitive decline, beyond chronological age.

AIMS: This study aimed to explore the extent to which different epigenetic AA measures were associated with the change in frailty scores and cognitive function over an average of 7 years, among 560 Australians aged ≥70 years (50.7% female) enrolled in the ASPREE study. We additionally investigated whether epigenetic AA measures were associated with the risk of incident frailty and dementia.

METHODS: Epigenetic AA indices including GrimAge, GrimAge2, and DunedinPACE were estimated in baseline blood samples. Frailty was assessed regularly using the 67-item deficit-accumulation frailty index (FI) and Fried phenotype (Fried). Cognitive assessments included global function, episodic memory, executive function and psychomotor speed. Dementia (DSM-IV criteria) was adjudicated by international experts. Linear mixed models and Cox proportional-hazard regression models were used as appropriate.

RESULTS: The associations between epigenetic AAs (GrimAA, Grim2AA and DunedinPACE) and increased FI-defined frailty burden over time appeared stronger in females (adjusted-beta, approximately 0.0033) than males (adjusted-beta, approximately 0.0020). DunedinPACE was also associated with worsening Fried scores (adjusted-beta, 0.0175) across the entire cohort. GrimAA/Grim2AA was associated with approximately 40% increased risk of incident FI-defined frailty, with no evidence of sex difference. In females only, GrimAA/Grim2AA was associated with worse delayed recall, composite cognition, and composite memory (adjusted-beta ranged from -0.1372 to -0.2034). In males only, GrimAA/Grim2AA was associated with slower processing speed (adjusted-beta, -0.3049) and up to two-fold increased dementia risk.

CONCLUSION: Our study, the first of its kind, indicates that biological ageing is associated with physical and cognitive deterioration in later life but with evidence of sex-specific associations. Our comprehensive findings underscore the importance of developing sex-specific interventions and healthcare strategies in addressing age-related health disparities.

125.
HIGHER SERUM URIC ACID LEVEL AND ALL-CAUSE MORTALITY IN GENERAL POPULATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Data from population-based studies has suggested a relationship between high serum uric acid (SUA) levels and all-cause mortality. However, the results have been inconsistent.
AIM: We investigated whether higher SUA levels were a risk factor for all-cause mortality with general population-based studies by meta-analysis.

METHODS: A systematic search was conducted in PubMed, Ovid Medline, EMBASE, Web of science and Google Scholar to identify papers published till 23 April 2024. Population-based cohort studies which investigated the association between plasma or serum levels of SUA levels and all-cause mortality were included. The risk of bias of included studies was assessed using the Newcastle–Ottawa Quality Assessment Scale. A random effect maximum likelihood model was used to obtain summary risk estimates. Sex-based stratified analyses were performed to assess potential differences between men and women. Heterogeneity was investigated through subgroup analysis and multivariable meta-regression model using study level covariates.

RESULTS: Higher SUA levels were associated with all-cause mortality (Relative Risk (RR): 1.32; 95% Confidence Intervals (CIs);1.25-1.39, p<0.001). The risk of mortality was higher in women (: 1.78; 1.42 -2.14, p<0.001) compared to men (1.15; 1.08-1.23, p<0.001). Per unit changes of SUA levels, the risk of mortality increases combinedly (Hazard Ratio (HR): 1.11; 1.06-1.15, p<1.001) and separately both men (1.08; 1.03-1.14, P<0.001) and women (1.15; 1.07-1.23, P<0.001) respectively. However, no association was observed when further stratified by other factors. A sensitivity analysis excluding studies with a high risk-of-bias, did not alter the association.

CONCLUSION: Higher SUA levels were significantly associated with all-cause mortality, for both men and women, with an increasing trend in women. These findings provide a basis for continuous improvement of response strategies to major public health emergencies of the older people.

126.

A SURVEY OF GAMMA CAMERA AND SPECT/CT QUALITY CONTROL PROGRAMS ACROSS A SAMPLE OF PUBLIC HOSPITALS IN AUSTRALIA

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Performance testing of gamma cameras and single photon computed tomography/computed tomography (SPECT/CT) systems is not subject to regulatory requirements across states and territories in Australia. Internationally recognised testing standards from organisations such as the National Electrical Manufacturers Association (NEMA) describe methodologies for recommended tests. However, variations exist in suggested quality control (QC) schedules from professional bodies such as the Australia and New Zealand Society of Nuclear Medicine (ANZSNM).

In this study, a survey was conducted to benchmark current QC programs across a selected sample of eight standalone and networked Australian public hospitals.

Vendor-specific flood-field uniformity (intrinsic or extrinsic/system) verification without photomultiplier (PMT) tuning and CT QC were performed at all sites. Weekly and monthly PMT tuning followed by intrinsic flood-field verifications were performed at most sites. At least half of the sites performed monthly centre of rotation (COR) offset verifications. SPECT/CT alignment calibrations and verifications were undertaken by service engineers at all sites, and periodic verifications were performed by local staff at varying frequencies. Variations were observed for other periodic QC tests such as spatial resolution and planar sensitivity. Similarly, variations were observed for tests specific to whole-body systems and SPECT systems. Most sites checked daily and periodic QC results

against pass/fail criteria set by vendors. Additional analyses of the QC results, including trend analysis and periodic reviews, were not common practice. The lack of regulatory requirements is likely to have led to variations in QC tests that are generally either harder to perform or are more labour intensive.

127.

WHITE MATTER HYPERINTENSITIES, NOT RETINAL VESSEL CALIBRE, ARE ASSOCIATED WITH COGNITIVE DECLINE IN COMMUNITY DWELLING OLDER ADULTS

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Retinal vessel calibres (RVCs) may serve as accessible biomarkers for cerebral small vessel disease (CSVD) and cognitive impairment in older adults.

AIM: This study investigates the prognostic utility of RVCs in comparison to white matter hyperintensities (WMH), another marker of CSVD, in predicting cognitive decline.

METHODS: We analysed data from 4,114 community-dwelling participants aged 70 and older from the Aspirin in Reducing Events in the Elderly (ASPREE) trial and its sub-studies. Participants underwent baseline fundus photography and global cognitive assessments, including the Modified Mini-Mental State (3MS) examination, over 11 years. Secondary outcomes included the Hopkins Verbal Learning Test-Revised (HVLT-R) for episodic memory and the Symbol Digit Modalities Test (SDMT) for executive function and processing speed. WMH volumes were measured using 3T magnetic resonance imaging in 453 participants at baseline, year 1, and year 3. Full-covariate adjusted linear mixed models (LMMs), incorporating cross-product terms between time and exposure, analysed trajectories of raw cognitive scores in relation to baseline RVCs and WMHs. Additionally, LMMs explored the association between baseline RVCs and WMH trajectories.

RESULTS: No significant relationship was found between baseline RVCs and trajectories in global cognition, memory, or executive function ($p > 0.05$). RVCs also showed no association with WMH volume trajectories ($p > 0.05$). However, higher total baseline WMH volumes were linked to an estimated mean decline in global cognition and delayed memory of 0.35 (95% confidence interval [CI] 0.55, 0.18) and 0.14 (95% CI -0.24, -0.05) points per year in the highest WMH tertile compared to the lowest.

CONCLUSION: Our findings indicate that RVCs do not exhibit the same prognostic potential as WMH volumes in predicting cognitive decline. Future research should explore a broader range of retinal and brain biomarkers to enhance understanding of the temporal relationship between eye and brain indicators of CSVD and their clinical implications.

128.

EPILEPTIC NETWORKS AND COGNITIVE PROFILES: A DATA DRIVE STEREO-EEG APPROACH TO THE LOCALISATION OF NEUROPSYCHOLOGICAL DEFICIT

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Objectives

Whether epileptic networks drive neuropsychologic deficits and the localising value of cognitive profiles is a topic

of debate. We investigated the association between epileptic networks and neuropsychological deficits using SEEG data.

Methods
In this retrospective study at Alfred Health, we analyzed 38 SEEG patients since 2018. Each patient had pre-SEEG neuropsychological evaluation. For each patient, visual analysis of all SEEG seizures was performed, and every channel scored based on seizure involvement within 10s ('ictal-score'). A 20min interictal sleep segment was analysed to calculate the 'cross-rate' (square-root HFO*spike count) per channel. Combined epileptogenic and early-propagation zone ('EZ/ePZ') was quantified for each sublobar region: EZ/ePZ score=(ictal score*cross rate). Hierarchical clustering on EZ/ePZ data was performed, and value testing of the Ez/ePz score and NP scores performed according to cluster classification to characterize the epileptic network and associated NP profiles.

Results
28/38 patients were MRI-negative, 24/38 were female. Four epileptic network clusters were identified, and each exhibited a unique cognitive profile. Cluster1(n=9), a dominant mesiolateral-temporal network, with language, and verbal memory deficits, but preserved visual memory. Cluster2(n=10), a bitemporal network, associated with naming, verbal, and visual memory deficits. Cluster3(n=6), non-dominant temporoparietal network, with executive and visuoconstructional deficits. Cluster4(n=9), dominant frontal network without NP deficits.

Conclusions
In this data-driven approach, distinct epileptic networks were characterised by unique neuropsychological profiles. This study supports the hypothesis that epileptogenic networks disrupt cognitive functions in corresponding regions, supporting the use of cognitive profiles to help localise the EZ.

129.
INTRODUCTION OF THE BROSET VIOLENCE CHECKLIST IN THE EMERGENCY DEPARTMENT: A RETROSPECTIVE COHORT STUDY

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The Broset Violence Checklist (BVC) can stratify the risk of violence and aggression in emergency departments (EDs).

OBJECTIVE: The aim of this study was to report the initial uptake of introducing this checklist and associations with unplanned alerts to potential or actual violence in two EDs.

METHODS: The BVC was recommended in all patient care episodes. This retrospective review included routinely collected data from an adult tertiary referral hospital and a suburban mixed paediatric and adult ED over a 12-month period. The primary outcome variable was completion of at least one BVC score and the secondary outcome was unplanned alerts to potential or actual violence episodes within the EDs.

RESULTS: There were 121,330 presentations, of which 108,274 were included in this study. The BVC was completed for 42,675 (39.4%) presentations. Using a cut-off score of 3, BVC had a specificity of

99.2% (95%CI: 99.1-99.2) and a sensitivity of 15.6% (95%CI: 12.5-19.3) for unplanned alerts to potential or actual violence events. Completion of a BVC was independently associated with more unplanned alerts to potential or actual violence events (adjusted odds ratio 1.37; 95%CI:1.12-1.66).

CONCLUSIONS: The BVC was highly specific for violence and aggression but had low sensitivity. Completion of the BVC was associated with more frequent unplanned alerts to potential or actual violence events, suggesting that high risk patients might be identified intuitively, without formal scoring. Further exploration of the utility of the BVC in the ED is indicated with a focus on strategies to prevent violence and aggression.

130.

SUPPORTING A BARIATRIC SURGERY SHORT STAY MODEL OF CARE THROUGH OPTIMISED ANTIEMETIC THERAPY

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Background**:** Post-operative nausea and vomiting (PONV) is a major concern following bariatric surgery. It causes patient distress, prolongs hospital stay, and is detrimental to the short stay surgical model.

Aim/Objective(s): To determine the impact of optimising post-operative antiemetics through use of a guideline and electronic medical record (EMR) decision support tool (PowerPlan) on PONV incidence following bariatric surgery.

Methods: A retrospective study compared PONV outcomes before and after standardisation of post-operative antiemetic regimens through a guideline and PowerPlan. The pre-intervention group included patients from July 2019-June 2020 and the post-intervention group from September 2023-May 2024. PONV risk was assessed by the Apfel score. Outcome data, including PONV incidence on post-operative days (POD) 0 and 1 were identified from EMR. Impact on PONV was explored in the post-intervention subset with confirmed PowerPlan usage.

Results: A total of 142 patients were included (pre: n=87; post: n=55). Of the post-intervention group, the PowerPlan was utilised in 30(55%) patients. There was no significant change in PONV incidence on POD0 and POD1 between groups (POD0: 16% pre vs 22% post, p=0.37; POD1: 39% pre vs 27% post, p=0.14). Number of patients administered rescue antiemetics on POD1 significantly decreased with PowerPlan use compared to pre-intervention (pre: n=42/87[48%] vs post: n=8/30[27%], p=0.04). Of pre-intervention patients experiencing PONV on POD1, 20% of regular antiemetics were administered as prescribed, compared with 100% with PowerPlan use (p<0.0001). Contributing factors pre-intervention included prescribing errors (e.g. incorrect timing/route, n=17[63%]). PowerPlan use was associated with a significant reduction in median length of stay compared to pre-intervention (2.3 vs 1.7 days, p<0.0001).

Discussion: Optimising post-operative antiemetic therapy with PowerPlan usage is an effective strategy to decrease need for rescue antiemetics, improve medication administration practices and reduce length of stay. Further interventions should target PowerPlan uptake and intraoperative antiemetic regimens to improve PONV on POD0.

131.

ENLARGED PERIVASCULAR SPACES IN THE BASAL GANGLIA ACROSS EPILPESY SUBTYPES

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**BS and CY contributed equally to this work. †TOB and ML joint senior authors*

INTRODUCTION: The glymphatic system is thought to be the brain's primary waste clearance system, eliminatating soluble metabolites and proteins within the central nervous system. It consists of the cerebrospinal fluid, the interstitial fluid, and a conduit between the two, perivascular spaces (PVS). The PVS and glymphatics may be involved in the pathophysiology of epilepsy, potentially via reduced clearance of excito-toxic substances. We developed an AI algorithm to automatically segment the PVS in a large cohort of epilepsy patients and controls to investigate enlarged PVS burden in epilepsy.

METHODS: 267 Temporal-Lobe Epilepsy (TLE) with hippocampal-sclerosis (TLE-HS), 71 TLE without HS (TLE-), 65 Extra-temporal Focal Epilepsy (ETLE), 64 Genetic Generalised Epilepsy (GGE), and 473 healthy controls were scanned on a 3T MRI with a T1-weighted MPRAGE sequence, voxel size: 1.0x1.0x1.0 mm.
A nnUnet was trained (PINGU: Perivascular-space Identification Nnunet for Generalisable Usage) on 40 manually segmented images of PVS from 7 different sites, to maximise generalizability. PINGU was then applied to the epilepsy cohort to segment PVS. PVS volume was summed within white matter (WM) and Basal Ganglia (BG), and divided by volume of respective region to give volume fraction (VF)
General Linear Models were fitted with PVS-VF as the dependent variable, group as the independent variable, and age and sex as covariates, corrected for multiple comparisons with Tukey's method.

RESULTS: All epilepsy groups had substantially enlarged PVS-VF compared to controls in the BG (TLE-HS (101.4%, $p<1x10^{-20}$), TLE- (107.8%, $p=5.24x10^{-13}$), ETLE (139.6%, $p=1.70x10^{-18}$), GGE (123.9%, $p=1.52x10^{-12}$)), but not in the WM.

DISCUSSION: Using an in-house AI algorithm, we have demonstrated that greater volume of PVS in the BG, but not in the WM, is associated with all epilepsy subtypes, which could arise from a common detrimental effect of seizures on the brain's glymphatic system, or potentially that impaired glymphatics contribute to seizure generation across epilepsy subtypes.

132.

VOLUMETRIC BRAIN DIFFERENCES ACROSS GENETIC SUBTYPES OF FRONTOTEMPORAL DEMENTIA: INSIGHTS FROM BASELINE MRI IN THE ARTFL LEFFTDS LONGITUDINAL FRONTOTEMPORAL DEMENTIA STUDY

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Frontotemporal dementia (FTD) describes a cluster of heterogeneous neurodegenerative syndromes associated with genetic mutations including MAPT, GRN, and C9orf72. Such mutations may differentially impact cortical atrophy patterns, suggesting unique neuropathological mechanisms for each genetic mutation.

AIM: This study analysed baseline magnetic resonance imaging (MRI) scans from the ARTFL LEFFTDS Longitudinal Frontotemporal Dementia (ALLFTD) dataset to investigate volumetric differences in brain regions among FTD patients with MAPT, GRN, and C9orf72 mutations. We hypothesised that volumetric differences would be observed in brain regions across the genetic mutations, with distinct patterns of cortical atrophy observed for each subtype.

METHODS: Baseline visit T1-weighted MRI scans from the ALLFTD dataset were analysed using Fastsurfer. A one-way ANOVA compared volumes in multiple regions across mutation subtypes (MAPT n=108, GRN n=90 and C90rf72 n=190), indicating if at least one pair of mutation subtype had significantly different mean volumes. Significant ANOVA results ($p<0.05$) were subjected to post hoc t-tests to explore pairwise differences.

RESULTS: The most statistically significant volumetric ANOVA findings were differences in the left and right amygdala, and left and right entorhinal cortex between mutation subtypes (all $p<0.0001$). Clinically relevant brain regions implicated in FTD that were statistically significant included the left and right thalamus ($p<0.001$), left and right hippocampus ($p<0.01$), left rostral anterior cingulate ($p=0.01$), right rostral anterior cingulate ($p=0.03$) and right inferior temporal cortex ($p=0.005$). Post hoc t-tests revealed volumetric differences could distinguish between pairs of mutations, with MAPT mutations most frequently differentiated from GRN and C9orf72 mutations across brain regions.

CONCLUSION: The findings demonstrate important volumetric differences among genetic subgroups in key brain regions, particularly the thalamus, hippocampus, entorhinal cortex, and amygdala. The ability to delineate between mutations supports the potential of MRI volumetry as a biomarker for understanding FTD's genetic and neuropathological heterogeneity, enhancing diagnostic accuracy and facilitating personalised treatment strategies.

133.

CHANGE FROM SEMI-RIGID TO SOFT COLLARS FOR PREHOSPITAL MANAGEMENT OF TRAUMA PATIENTS: AN OBSERVATIONAL STUDY

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Protection of the cervical spine is recommended following multisystem injury. In 2021, Ambulance Victoria changed clinical practice guidelines to apply soft collars instead of semi-rigid collars for suspected cervical spine injury.

AIM: To describe associated changes in imaging practices and diagnoses of pressure sores, hospital acquired pneumonia, and spinal cord injury.

METHODS: A retrospective pre- and post-intervention study was conducted including all consecutive patients that presented to an adult major trauma centre in Melbourne, Australia with a cervical collar placed by emergency medical services over two 3-month periods.

RESULTS: There were 1762 patients included. A computed tomography (CT) of the cervical spine was performed in 795 (88.4%) patients in the semi-rigid collar period and 810 (93.8%) in the soft collar period ($p = 0.001$). Soft collars were associated with higher rates of clearance of the cervical spine in the emergency department (ED) (odds ratio [OR] 4.14; 95% confidence interval [CI]: 3.36–5.09). There were no differences in diagnosis of pressure sores (0.11% vs. 0.23%, $p = 0.97$) or hospital acquired pneumonia (2.0% vs. 2.7%; $p = 0.44$) or cervical spinal cord injury (0.45% vs. 0.81%; $p = 0.50$).

CONCLUSION: Following a change from prehospital semi-rigid collars to soft collars, more patients were investigated with a CT scan and more frequent clearance of the cervical spine occurred in the ED. There were no differences in the rates of spinal cord injuries, pressure sores or hospital acquired pneumonia, but the study was

underpowered to detect significant differences. The practice of soft collars for prehospital care of patients with suspected neck injury requires ongoing surveillance.

134.

BRAINSTEM AND CEREBELLAR VOLUME LOSS AND ASSOCIATED CLINICAL FEATURES IN PROGRESSIVE SUPRANUCLEAR PALSY

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INTRODUCTION: Progressive Supranuclear Palsy (PSP) is a rare, neurodegenerative tauopathy with rapid progression of motor, oculomotor, speech and cognitive impairments. PSP pathology predominates in the basal ganglia and midbrain, with subsequent spread and neurodegeneration in other brain regions. The cerebellum is increasingly recognized in the pathophysiology of motor and non-motor symptoms across multiple neurological diseases. We hypothesize that volume loss is appreciable in cerebellum and brainstem regions - beyond the midbrain - in individuals with PSP, and linked to motor and nonmotor clinical features.

METHODS: Using structural T1-weighted magnetic resonance imaging (MRI), automated volumetric subsegmentation of the brainstem and cerebellar structures was performed in 38 adults with PSP. Group-level comparisons were made with 41 healthy controls and 39 adults with Parkinson's disease. Regional volumes in the PSP cohort were correlated against disease severity and cognition. Statistical significance thresholds were Bonferroni corrected for multiple comparisons across 13 brain regions of interest (critical $p<0.0038$).

RESULTS: Compared with healthy controls, the PSP cohort had a significantly smaller midbrain; cerebellar white matter, cerebellar dentate nucleus region, and flocculonodular lobe; and superior and inferior cerebellar peduncles. Similarly, compared with Parkinson's disease, PSP was characterized by significantly smaller midbrain and pons; cerebellar dentate nucleus region; and superior, middle, and inferior cerebellar peduncles. There was a significant positive correlation between the frontal assessment battery (FAB) and the superior ($r=0.486$) and inferior ($r=0.469$) cerebellar posterior lobe volumes.

CONCLUSION: Whilst disproportionate midbrain atrophy is frequently seen on MRI, this study reveals significant PSP-related volume loss across multiple additional brainstem and cerebellar regions. The association of worsening frontal cognitive impairment with cerebellar posterior lobe volume loss highlights the crucial role of the cerebellum in cognition, and likely involvement in PSP. These findings are compatible with caudal tau spread and neurodegeneration resulting in broad network alterations in this disease.

135.

BIOPSYCHOSOCIAL AND NEUROPSYCHOLOGICAL OUTCOMES IN WOMEN WHO HAVE EXPERIENCED INTIMATE PARTNER VIOLENCE WITH BRAIN INJURY AND PROBABLE PTSD

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Intimate partner violence (IPV) is significant public health concern effecting one in three women worldwide. IPV is associated with several long-term health challenges such as PTSD, however brain injuries (i.e. mild traumatic brain injury mTBI) within this context have commonly been underdiagnosed and overlooked.

AIM: To better understand the effect of brain injury and PTSD in women who have experienced intimate partner violence.

METHODS: 37 women who have experienced IPV related mTBI (IPV-BI) were recruited. They were compared to 18 IPV controls (with history of IPV but not mTBI); 14 mTBI controls (with history of mTBI but not IPV) and 31 healthy controls (with no history of either mTBI or IPV). Participants completed medical history, psychosocial questionnaires (i.e. Rivermead Post Concussion Symptom Questionnaire; RPQ, PTSD Checklist for DSM-5; PCL-5, Depression Anxiety and Stress Scale 21; DASS-21), neuropsychological assessment (i.e., Digit Span Forwards and Backwards)

RESULTS: Women who had experienced IPV both with and without mTBI (i.e. IPV+/- mTBI) had significantly greater PCL-5 score ($p < 0.005$), RPQ symptom severity ($p < 0.05$), and depression, anxiety, stress symptoms and total score on the DASS-21 compared to healthy controls ($p < 0.05$). IPV-BI alone had significantly greater concussion symptom severity compared to both healthy ($p < 0.0001$), mTBI controls ($p < 0.05$). Interestingly, 51% of IPV+/- mTBI met the criteria for probable PTSD. Preliminary cognitive assessment revealed that irrespective of history of mTBI, women who had experienced IPV with probable PTSD had significantly poorer attention and working memory via the digit span task compared to healthy controls ($p < 0.05$).

CONCLUSION: Early findings support the long-term psychological cognitive implications of IPV. Further understanding on how the exposure of IPV-BI and interaction with probable PTSD may influence biopsychosocial and neuropsychological outcomes is needed.

136.

BLOOD LACTATE AFTER PRE-HOSPITAL BLOOD TRANSFUSION FOR MAJOR TRAUMA BY HELICOPTER EMERGENCY MEDICAL SERVICES

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BACKGROUND AND OBJECTIVES: The appropriate use of blood components is essential for ethical use of a precious, donated product. The aim of this study was to report in-hospital red blood cell (RBC) transfusion after pre-hospital transfusion by helicopter emergency medical service paramedics. A secondary aim was to assess the potential for venous blood lactate to predict ongoing transfusion.

MATERIALS AND METHODS: All patients who received RBC in air ambulance were transported to a single adult major trauma centre, had venous blood lactate measured on arrival and did not die before ability to transfuse RBC were included. The association of venous blood lactate with ongoing RBC transfusion was assessed using multi-variable logistic regression analysis and reported using adjusted odds ratios (aOR). The discriminative ability of venous blood lactate was assessed using area under receiver operating characteristics curve (AUROC).

RESULTS: From 1 January 2016 to 15 May 2019, there were 165 eligible patients, and 128 patients were included. In-hospital transfusion occurred in 97 (75.8%) of patients. Blood lactate was associated with ongoing RBC transfusion (aOR: 2.00; 95% confidence interval [CI]: 1.36-2.94). Blood lactate provided acceptable discriminative ability for ongoing transfusion (AUROC: 0.78; 95% CI: 0.70-0.86).

CONCLUSIONS: After excluding patients with early deaths, a quarter of those who had prehospital RBC transfusion had no further transfusion in hospital. Venous blood lactate appears to provide value in identifying such patients. Lactate levels after pre-hospital transfusion could be used as a biomarker for transfusion requirement after trauma.

137.

HOME WASN'T BUILT IN A DAY – DEVELOPING A GENERAL MEDICINE HOSPITAL IN THE HOME SERVICE

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Background: Alfred Health established General Medicine Hospital In The Home (GM-HITH), a 15-bed acute bed-substitution model of care for older people with chronic and complex health conditions. This multi-disciplinary, medically-led model aimed to replicate acute inpatient ward-based care in the home with patient-centred, individualised care, delivered through a range of modalities including outreach and telehealth.

Results: Between March 2023 and May 2024 GM-HITH delivered 586 episodes and 4,132 bed days of acute care in the home. Patients admitted to GM-HITH from inpatient setting received 71% of their acute care in the community setting, and this consistently reflects 10% of our hospital's acute general medical care delivered outside the hospital walls. Unplanned readmission rate (28-day) is 15%, similar to in-patient care. Patients and clinicians have voiced high levels of satisfaction. Safety incidents are at 1.2% of bed days, and in keeping with the patient cohort include falls and medication issues. 31% of patients transitioned from GM-HITH to HARP. Embedding the project team into the model has allowed implementation of strategies to address safety issues utilising quality improvement methodology.

Conclusion: GM-HITH has been established as a model for the delivery of acute General medical care in the home for a cohort previously limited to inpatient care, in a way that is acceptable to both patients and clinicians. The GM-HITH service exists within an ecosystem of care initiatives including our emergency department streaming team and Hospital Admission Risk Program, to support continuity of care for this cohort. Further evaluation of the economic and environmental impact of delivering care beyond the hospital walls is warranted, as well as the downstream benefits of a holistic, multi-disciplinary model of care.

138.

REDCAP AS A LOW COST SOLUTION FOR ELECTRONIC CAPTURE OF PATIENT-REPORTED DATA IN A LARGE ESTABLISHED CQR

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AIM**:** The Bariatric Surgery Registry (BSR) collects annual outcome data for participants for up to ten years. Historically, this has been collected by calling participants (or direct from surgeons) but with over 160,000 participants this is no longer feasible. The aim of this project was to develop and implement a system to collect annual outcome data via SMS message and an online questionnaire.

METHODS**:** A system for the electronic collection of annual outcome data from participants was created using the REDCap data capture tool with SMS messaging using Whispir. Development of this system involved assessing the security of various telecommunications systems, as well as designing, testing, collecting feedback on the process and questionnaire, and implementing a two-way data transfer system to load into REDCap patients due

for annual outcome data collection and save data collected back into the BSR SQL database. To access the questionnaire participants were sent an SMS message with a link and were required to enter date of birth (DOB).

RESULTS**:** The system was launched for a subset of patients in August 2024, and as of mid-September, of the 1035 participants contacted, 164 (16%) have completed their outcome data, and 19 (2%) have opted out of annual outcome data collection. In an optional feedback survey, 99% of patients found the data entry easy to do, and 95% were comfortable using their DOB to login to the system.

CONCLUSION**:** The BSR can now electronically collect annual outcome data directly from participants, reducing the need for phone calls to participants. The ongoing cost of the system is minimal given REDCap is already in place at Monash University. Future aims include scaling up the system to the entire registry and refining methodology to improve response rates.

139.

SEX DIFFERENCES IN THE TREATMENT AND CONTROL OF HYPERTENSION AMONG OLDER AUSTRALIANS

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BACKGROUND AND AIM: Whether there are sex differences in the management and control of hypertension in older people remains unclear. We aimed to examine sex differences in blood pressure (BP) management and control among older Australians.

METHODS: We analysed baseline data from the STAtins in Reducing Events in the Elderly (STAREE) trial, a randomized placebo-controlled trial investigating the effects of atorvastatin on disability-free survival and major cardiovascular events in Australians aged ≥70 years without cardiovascular disease. Descriptive statistics were used to compare self-reported hypertension, measured BP, and the use of BP-lowering medications between men and women.

RESULTS: The study included 9971 participants (52% women, mean±SD age 74.7±4.5years). Women were more likely than men to report a history of hypertension (45% vs. 42%, p=0.001). Women also had lower measured BP than men, both among those with and without a history of hypertension (137/80mmHg vs. 140/82mmHg, p<0.001 and 131/78 vs. 136/81mmHg, p<0.001, respectively). Among those with hypertension, a greater proportion of women than men achieved the target BP of <140/90mmHg (57% vs. 47%, p<0.001). The number of BP-lowering medications was similar between men and women with hypertension, (~65% taking one agent, ~20% taking two agents, and ~5% taking three or more agents, p=0.37). However, women were more likely than men to take β-blockers (14% vs. 12%, p<0.001) and diuretics (9% vs. 6%, p<0.001), and less likely to take angiotensin-converting enzyme inhibitors (26% vs. 32%, p<0.001) or other BP-lowering agents such as α-blockers (3% vs. 6%, p<0.001).

CONCLUSIONS: Older women with hypertension had better BP control than older men, which may be related to underlying physiological factors, differences in awareness, or variations in BP treatment patterns. Further work is required to understand the factors contributing to these sex differences in hypertension management and control among older Australians.

140.

TESTOSTERONE AND THE RISK OF INCIDENT ATRIAL FIBRILLATION IN OLDER MEN: THE ASPREE STUDY

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Background: Whether testosterone influences cardiovascular risk in older men remains uncertain. A cardiovascular safety trial of testosterone in men with cardiovascular risk factors or disease found no difference in rates of major adverse cardiovascular events (MACE) or deaths, but noted more atrial fibrillation (AF) events in testosterone-treated men.

Aim: To investigate whether endogenous testosterone concentrations are associated with risk of developing AF in healthy older men.

Methods: Post-hoc analysis of 4,570 male participants in the ASPREE study. Men had no history of cardiovascular disease (including AF), thyroid disease, prostate cancer, dementia, or life-limiting illnesses. Total testosterone was measured at baseline using chemiluminescence immunoassay. Incident AF during follow-up was ascertained using self-reported diagnosis, prescription medication and/or medical records. Risk of AF was modelled using restricted cubic splines and Cox proportional hazards regression.

Results: Mean age±SD was 75.0±4.2 years and median (IQR) of follow-up 4.4 (3.3-5.5) years, during which 286 men developed AF (15.3 per 1000 participant-years). Baseline testosterone was higher in men who developed incident AF compared men who did not (17.3±6.7 vs 16.5±6.3 nmol/L). There was a non-linear association of baseline testosterone with incident AF. Higher baseline testosterone was associated with an increased risk of AF (per 1SD increase: fully-adjusted hazard ratio [HR]=1.17; 95% Confidence Interval [CI]=1.05-1.32). Risk of AF was similar across the lowest three quintiles of testosterone values, but higher in men with testosterone in quintiles (Q) 4&5 (Q4:Q3, HR=1.91; CI=1.29-2.83 and Q5:Q3HR=1.98; CI=1.33-2.94). Results were similar after excluding men who had MACE or heart failure during follow-up.

Conclusion: Serum total testosterone is independently associated with higher risk of incident AF in relatively healthy community-dwelling older men. Screening for AF should be considered when assessing testosterone results or testosterone treatment in older men.

141.

COMPARISON FOR THE EFFECTS OF DIFFERENT COMPONENTS OF TEMPERATURE VARIABILITY ON MORTALITY: A MULTI-COUNTRY TIME-SERIES STUDY

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Temperature variability (TV) is associated with increased mortality risk. However, it is still unknown whether intra-day or inter-day TV has different effects.

AIM: To assess the association of intra-day TV and inter-day TV with all-cause, cardiovascular, and respiratory mortality.

METHODS: Data on total, cardiovascular, and respiratory mortality and meteorology from 758 locations were collected from 47 countries or regions from 1972 to 2020. We defined inter-day TV as the standard deviation (SD) of daily mean temperatures across the lag interval, and intra-day TV as the average SD of minimum and maximum temperatures on each day. In the first stage, inter-day and intra-day TVs were modelled simultaneously in the quasi-Poisson time-series model for each location. In the second stage, a multi-level analysis was used to pool the location-specific estimates.

RESULTS: Overall, the mortality risk due to each interquartile range [IQR] increase was higher for intra-day TV than for inter-day TV. The risk increased by 0.59% (95% confidence interval [CI]: 0.53, 0.65) for all-cause mortality, 0.64% (0.56, 0.73) for cardiovascular mortality, and 0.65% (0.49, 0.80) for respiratory mortality per IQR increase in intra-day TV0–7 (0.9 °C). An IQR increase in inter-day TV0–7 (1.6 °C) was associated with 0.22% (0.18, 0.26) increase in all-cause mortality, 0.44% (0.37, 0.50) increase in cardiovascular mortality, and 0.31% (0.21, 0.41) increase in respiratory mortality. The proportion of all-cause deaths attributable to intra-day TV0–7 and inter-day TV0–7 was 1.45% and 0.35%, respectively. The mortality risks varied by lag interval, climate area, season, and climate type.

CONCLUSIONS: Intra-day TV may explain the main part of the mortality risk related to TV and comprehensive evaluations should be proposed in more countries to help protect human health.

142.

RISK OF RE-OPERATIONS AFTER METABOLIC BARIATRIC SURGERY WITHIN 5 YEARS OF FOLLOW-UP – RESULTS FROM THE AUSTRALIAN BARIATRIC SURGERY REGISTRY

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Re-operations following a Metabolic Bariatric Surgical (MBS) procedure are indicated for early and late post-operative complications and suboptimal weight control. The long-term incidence of revisional surgery is scarce and varies (15-50%).
AIM: To provide the incidence of the need for re-operations following MBS.

METHODS: Time-to-revision analysis was conducted on patients in the Australian Bariatric Surgery Registry with a primary procedure and re-operations occurring on/or before 31st December 2022. Cumulative incidences were calculated using Kaplan-Meier method.

RESULTS: There were 117,579 patients who fulfilled inclusion criteria with 29,950 who had completed 5-year follow-up (76.7% female). At 5-years the overall risk of any re-operation was 7% with majority being women. Revisional rates at 5-years were highest for gastric bands (20%; n=3,887). Roux-en-Y gastric bypass (RYGB)

had the highest rate of reintervention in 1-year (4%; n=7,884). The rate of revision for sleeve gastrectomy (SG) appears to be increasing at 5-years with an increase from 2% (4 years) to 4% at (5-years) (n=23,203).

CONCLUSION: This is the first real world data documenting the need for re-operations after MBS. The overall need for re-operations is lower in this real-world registry than other reports. Gastric bands have the highest need for reintervention at 5-years and RYGB within 12-months. The increase in rate of intervention for SG at later time points suggests an emerging need to convert SG and is a trend that will need to be monitored. The data will be important as part of informed consent for consumers and for payers enabling better health service delivery planning.

143.
THE CLINICAL IMPACT OF STEREO-ELECTROENCEPHALOGRAPHY (SEEG) ELECTRODE ACCURACY

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Rationale: Factors influencing inaccuracy in SEEG electrode implantation have been well studied, but the clinical impact of accuracy poorly understood. This study aimed to investigate the influence of electrode accuracy on i) achieving positive outcomes following SEEG and subsequent surgery and ii) intracranial haemorrhage (ICH).

Methods: We included consecutive SEEG patients from two Melbourne epilepsy centres. Post-MRIs were coregistered with pre-implantation-MRI. Target errors were calculated between actual (AT) and planned (PT) electrode trajectories. ATs were classified as "off-target" if they mis-sampled the intended target/s. ICH area was classified as either within/outside the radio-frequency thermocoagulation (RF-THC). Logistic regression assessed the relationship between electrode accuracy and clinical outcomes at patient, electrode and contact levels: (1) Engel I outcomes post-RF-THC and/or (2) post-resection, (3) ICH occurrence and (4) performed RF-THC.

Results: We analysed 913 implanted electrodes in 69 patients (age 34.5+/-10.0 years). Median absolute error at target was 1.9mm [1.3 – 2.7] and 83 (9.0%) electrodes were "off-target. We identified 22 instances of post-explantation ICH (91% asymptomatic, 9% transient symptomatic). A single patient can have multiple areas of ICH. Of the 22 patients, 17 had ICH outside the RF-THC area, and 11 had ICH within it.

At the patient level, there was no significant association between the mean target error with ICH (p=0.77), Engel class I post RF-THC (p=0.36) or surgery (p=0.43). At the electrode level, target error was significantly associated with an electrode being "off-target" (p<0.001) and with ICH outside the RF-THC area (p=0.03). At the contact level, inaccuracy was significantly associated with a lower likelihhod of performing RF-THC (p = 0.011) and ICH occurred outside RF-THC area (p =0.004).

Conclusion: Inaccuracy at electrode and contact level were strongly associated with ICH and negatively associated with the RF-THC chance. Minimising electrode errors may reduce ICH risk and enhance feasibility of RF-THC procedures.

144.
FLOODING EXPOSURE ACCELERATED BIOLOGICAL AGING: A POPULATION-BASED STUDY IN THE UK

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Floods have been the most common type of disaster and are expected to increase in frequency and intensity due to climate change. Limited studies investigated the association between flooding exposure and biological aging acceleration.

AIM: To investigate the association between flooding exposure and biological aging.

METHODS: We collected data from 364,841 participants from the UK Biobank project. Cumulative flooding exposure within four years before the baseline was calculated. We calculated the two biological aging measures at baseline: PhenoAge and Klemera-Doubal method biological age (KDM-BA) and assessed their associations with floods using mixed-effects linear regression models.

RESULTS: Participants exposed to higher levels of floods were more likely to have accelerated biological aging. The risks associated with flooding exposure could last for several years, with the highest cumulative effect observed over 0–4 years. In the fully adjusted model, per interquartile increase in flood index was associated with an increase of 0.24 years (95% CI: 0.14, 0.34) in PhenoAge acceleration and 0.14 years (95% CI: 0.07, 0.21) in KDM-BA acceleration over lag 0–4 years. The associations were consistent regardless of lifestyles, demographics, and socio-economic status.

CONCLUSION: Exposure to floods may lead to accelerated biological aging. Our work provides the basis for further understanding of the flood-related health impacts and suggests that public-health policies and adaptation measures should be initiated in the short-, medium- and even long- terms after flooding.

145.

CIRCADIAN AND MULTI-DAY HEART RATE CYCLES IN PATIENTS RECEIVING VAGUS NERVE STIMULATION FOR DRUG-RESISTANT EPILEPSY

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BACKGROUND: Vagus nerve stimulation (VNS) is a valuable tool in the treatment of drug-resistant epilepsy. Cyclic patterns in seizures have recently gained considerable attention, in particular the potential of using these cycles to tailor neurostimulation therapies. Modern VNS devices detect and respond to rises in heart rate, yet there has been minimal investigation into the presence of cycles in tachycardia detections in VNS.

AIM: To identify cycles in tachycardia detections of VNS in patients with drug-resistant epilepsy.

METHODS: Tachycardia detection data from SenTiva M1000 and Aspire M106 VNS devices were analysed in 42 consecutive outpatients, with 1 exclusion due to insufficient data. Cycles in tachycardia detections were identified using spectral analysis from hourly and daily detection counts.

RESULTS: Cycles in tachycardia detections were present in almost all subjects (40/41). For the 35 subjects with hourly detection counts recorded, circadian (24hr) rhythm was the most common (29/35, 82.9%), followed by 12-hourly cycles (6/35, 17.1%). Phase analysis of the hourly detections revealed an alignment of detections with a certain time of day in 34/35 patients. Significant multi-day (infradian) cycles were present in 22/26 patients with analysable daily detection counts. Common multi-day cycles were approximately monthly (24 - 32 days) (15/22, 68.2%), weekly (6-8 days) (4/22, 18.2%), and bi-weekly (12 - 16 days) (4/22, 18.2%). Unsupervised clustering showed 4 groups of similar multi-day cycles, around 11 days, 29 days, 48 days and 66 days. Magnet swipes, the

manual delivery of stimulations in response to perceived impending seizures, were recorded in 9 patients. Phase analysis revealed alignment of magnet swipe timings with multiday cycles in 8/9 patients.

CONCLUSION: We show for the first time that multi-day cycles in tachycardia detections can be demonstrated using standard implantable VNS systems. These cycles could potentially be used to provide better tailored epilepsy treatment and VNS programming.

146.

ASSOCIATIONS OF TELOMERE LENGTH AND ITS CHANGE OVER TIME WITH RISK FACTORS AND MORTALITY IN TYPE 2 DIABETES: THE FREMANTLE DIABETES STUDY

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AIMS: Relative telomere length (rTL), a marker of aging, is implicated in type 2 diabetes (T2D) complications. We aimed to identify (a) associates of rTL and 4-year rTL change (ΔrTL), and (b) if they predict mortality in Fremantle Diabetes Study Phase II (FDS2) participants.

METHODS: T2D participants (n=819) had baseline and Year-4 (mean±SD: 4.2±0.4 yrs) rTL measured by qPCR (intra- and inter-assay CVs 0.56% and 2.69%, respectively). Baseline mean age was 66 years, 8-years T2D, HbA_{1c} 6.7%, BMI 31.3 kg/m^2. ΔrTL was categorised as: Shortening (<–2.69%), Unchanged (–2.69% to +2.69%), and Lengthening (>+2.69%). Multiple logistic regression identified baseline determinants of rTL Shortening vs. Not Shortening. rTL and ΔrTL (continuous/categorical variables) were added to Cox regression models of baseline predictors of cardiovascular disease (CVD) death and all-cause mortality over 11.5±2.1 years.

RESULTS: rTL inversely correlated with age (r= –0.186, P<0.001) and associated with C-reactive protein and urine albumin:creatinine ratio even after age- and sex-adjustment. rTL shortened in 25.5% subjects, lengthened in 64.0% and was unchanged in 10.5%. rTL shortening associated with older age, male sex, smoking, obesity, lipid drugs, and higher platelet and bilirubin levels (P<0.05).

On unadjusted Cox regression longer baseline and Year-4 rTL associated with reduced risk of all-cause mortality ((HR (95% CI): 0.87 (0.75, 0.996), P=0.043, and 0.914 (0.855, 0.997), P=0.008, respectively). Longer Year-4 rTL and ΔrTL lengthening were associated with lower CVD death ((HR:0.880 (0.807, 0.959), P=0.004, and 0.989 (0.979, 0.9996), P=0.042, respectively). After age and sex adjustment, Year-4 rTL remained a predictor of CVD death (P=0.046). Neither ΔrTL (continuous/categorical variable) nor rTL improved prediction of all-cause mortality (P≥0.268).

CONCLUSION: In T2D adults rTL and ΔrTL were associated with cardiometabolic factors. rTL do not always shorten over time. rTL and ΔrTL were associated with mortality but did not improve mortality prediction in models including traditional risk factors.

147.

THE UTILITY OF IMAGING IN ACUTE PYELONEPHRITIS IN THE EMERGENCY DEPARTMENT

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Acute pyelonephritis (APN) is a common diagnosis among patients presenting to the Emergency Department (ED). The role of imaging for APN in the ED is poorly understood, with variability among clinical guidelines for when patients should be imaged, and the modality of imaging.

OBJECTIVE: To identify the proportion of patients with APN being imaged, the proportion of imaging with abnormal findings, and the association between abnormal imaging and discharge disposition.

METHODS: A single-centre retrospective review of patients with a discharge diagnosis of APN at an adult tertiary referral hospital over a five-year period (2018-2022) was conducted. A chart review was performed to collect variables such as demographics, vital signs, imaging, clinical features, and disposition. The proportion of patients with APN investigated with imaging was calculated, and abnormalities on imaging were extracted and categorised. To assess association with inpatient admission, univariable and multivariable logistic regression analyses were to assess whether imaging was associated with change in disposition from the ED.

RESULTS: There were 778 patients included for analysis (724 females). Among these, 210 (27%) were investigated with ultrasound (US) and/or computed tomography (CT) in the ED. US was the most performed modality of imaging (12%), followed by CT without contrast (9%), and CT with contrast (6%). Of the 214 imaging reports available, 112 (52%) were abnormal. Imaging was associated with inpatient admission (aOR 5.28; 95%Ci: 3.35–8.31) as was abnormal imaging (aOR 4.51; 95%CI: 2.62–7.75).

CONCLUSION: Among patients with APN, abnormalities on imaging were common, and both imaging and abnormalities on imaging were associated with hospital ward admission. This suggests that there is possible utility of early and routine imaging for patients with APN to allow clinicians to efficiently make decisions about patient disposition.

148.

ESTIMATES OF GLOBAL MORTALITY BURDEN ASSOCIATED WITH SHORT-TERM EXPOSURE TO FINE PARTICULATE MATTER ($PM_{2.5}$)

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BACKGROUND AND AIM: Acute health effects of short-term (from hours to days) exposure to fine particulate matter ($PM_{2.5}$) have been well-documented. however, the global mortality burden attributable to this exposure has not been estimated. We aimed to estimate the global, regional, and urban mortality burden associated with short-term exposure to $PM_{2.5}$ and the spatiotemporal variations in this burden from 2000 to 2019.

METHODS: We combined estimated global daily $PM_{2.5}$ concentrations, annual population counts, country-level mortality rates, and epidemiologically derived exposure–response functions to estimate the mortality attributable to short-term $PM_{2.5}$ exposure from 2000 to 2019, in the continental regions and in 13 189 urban centres worldwide at a spatial resolution of 0.1° × 0.1°. We tested the robustness of our mortality estimates with different theoretical minimum risk exposure levels, lag effects, and exposure–response functions.

RESULTS: Approximately 1 million (95% CI 690 000–1.3 million) premature deaths per year from 2000 to 2019 were attributable to short-term $PM_{2.5}$ exposure, representing 2.08% (1.41–2.75) of total global deaths or 17 (11–22) premature deaths per 100 000 population. Annually, 0.23 million (0.15 million–0.30 million) deaths attributable

to short-term $PM_{2.5}$ exposure were in urban areas, constituting 22.74% of the total global deaths attributable to this cause and accounting for 2.30% (1.56–3.05) of total global deaths in urban areas. The sensitivity analyses showed that our worldwide estimates of mortality attributed to short-term $PM_{2.5}$ exposure were robust.

CONCLUSION: Short-term exposure to $PM_{2.5}$ contributes a substantial global mortality burden, particularly in Asia and Africa, as well as in global urban areas. Our results highlight the importance of mitigation strategies to reduce short-term exposure to air pollution and its adverse effects on human health.

149.

LONG-TERM EXPOSURE TO WILDFIRE-RELATED O_3 AND ALL CAUSE MORTALITY IN AUSTRALIA: A DIFFERENCE-IN-DIFFERENCE ANALYSIS

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AIM: This study aimed to examine the associations between long-term wildfire-related ozone (O_3) exposure and all-cause mortality, and to estimate the mortality burden attributable to wildfire-related O_3 exposure.

METHODS: We collected annual all-cause death data from 2,250 statistical areas level-2 (SA2) in Australia during 2016-2019. Area-level annual mean concentrations of wildfire-related O_3 were derived from the three-dimensional chemical transport model GEOS-Chem at a 0.25° × 0.25° resolution. The variant of difference-in-differences method was used to evaluate the causal relationship between annual wildfire-related O_3 and all-cause mortality.

RESULTS: The impacts of wildfire-related O_3 on all-cause mortality were liner and lasted for 0-1 year. Every 1 μg/m3 increase in the moving average wildfire-related O_3 (0-1 year) was associated with 15.9% (95%CI: 6.3-26.5%) increase in all-cause mortality. We estimated that a total of 242,784 (95% CI: 116,852-335,294) all-cause deaths, representing 245 (95% CI: 118-338) per 100,000 population, were attributable to wildfire-related O_3 exposure.

CONCLUSION: Long-term exposure to wildfire-related O_3 was associated with increased risk of mortality. Health promotion strategies are needed to reduce health risks from the increasing wildfires.

150.

A SYSTEMATIC REVIEW ASSESSING INCORPORATION OF PROPHYLACTIC SPLENIC ARTERY EMBOLISATION (PSAE) INTO TRAUMA GUIDELINES FOR THE MANAGEMENT OF HIGH-GRADE SPLENIC INJURY

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Splenic artery embolisation (SAE) has become a vital strategy in the modern landscape of multidisciplinary trauma care, improving splenic salvage rates in patients with high-grade injury. However, due to a lack of prospective data there remains contention amongst stakeholders as to whether SAE should be performed at the time of presentation (prophylactic or pSAE), or whether patients should be observed, and SAE only used only if a patient re-bleeds.

AIM: This systematic review aimed to assess published practice management guidelines which recommend pSAE, stratified according to their quality.

METHODS: The study was registered and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Medline, PubMed, Cochrane, Embase, and Google Scholar were searched by the study authors. Identified guidelines were graded according to the Appraisal of Guidelines Research and Evaluation II (AGREE-II) instrument.

RESULTS: Database and internet searches identified 1006 results. After applying exclusion criteria, 28 guidelines were included. The use of pSAE was recommended in 15 guidelines (54%). This included 6 out of 9 guidelines that were high quality (66.7%), 4 out of 9 guidelines that were moderate quality (44.4%), and 3 out of 10 (30%) guidelines that were low quality, $p = 0.275$.

CONCLUSIONS: This systematic review showed that recommendation of pSAE is more common in guidelines which are of high quality. However, there is vast heterogeneity of recommended practice guidelines, likely based on individual trauma systems rather than the available evidence. This reflects biases with interpretation of data and lack of multidisciplinary system inputs, including from interventional radiologists.

DIABETES

151.

ROLE OF HISTONE METHYL TRANSFERASE EZH2 IN FOAM CELL FORMATION IN DIABETES ASSOCIATED ATHEROSCLEROSIS.

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BACKGROUND: Atherosclerosis involves plaque build-up in arteries, leading to cardiovascular disease, and is accelerated by diabetes. Macrophages play a crucial role in this process by converting into foam cells when they take up oxidized low-density lipoprotein (oxLDL). Epigenetic mechanisms, particularly through Enhancer of Zeste Homolog 2 (EZH2), influence macrophage inflammation. Research indicates that EZH2 deficiency reduces foam cell formation, but its role in diabetes-associated atherosclerosis remains unclear.

AIM: To identify role of EZH2 in foam cell formation in diabetes-associated-atherosclerosis.

METHODS:(i) In an *in-vitro* model, THP-1 derived macrophages were stimulated with ox-LDL+High glucose(HG) for 24hrs to induce foam cell formation. EZH2 mediated trimethylation of lysine 27 on histone 3(H3K27me3) was inhibited using a specific EZH2 inhibitor, GSK126. (ii)Genetic knockdown of EZH2 in THP-1 monocytes was also performed. (iii) Foam cell formation was assessed in atheroprone diabetic mice by performing Sudan IV and Oil Red O(ORO) staining. (iv) H3K27me3 levels were measured in human carotid plaque samples by immunohistochemistry.

RESULTS: Foam cell formation was significantly reduced with GSK-126 in ox-LDL+HG stimulated THP-1 cells as assessed by ORO staining. Western blot analysis confirmed EZH2 knockdown in THP-1 monocytes, which also showed reduced foam cell formation in stimulated cells. In the *in-vivo* model, plaque formation was significantly reduced in the aorta of diabetic mice treated with GSK-126. Activity assays showed reduced EZH2 mediated H3K27me3 in GSK-126 treated diabetic mice. Immunohistochemistry staining showed foam cell formation was significantly decreased with GSK-126 in diabetic mice. Human carotid plaque samples also presented higher H3K27me3 levels in samples from individuals with diabetes when compared to a non-diabetic group.

CONCLUSION: Our study identified that inhibiting EZH2 with GSK-126 is important strategy to inhibit diabetes associated atherosclerosis due to its impact on macrophages and epigenetic regulation. Thus, EZH2 inhibition can be a potential new therapeutic target for the disease.

152.

UV/VISIBLE SPECTROSCOPY FOR RAPID POINT-OF-CARE ALBUMIN/CREATININE RATIO ANALYSIS IN URINE: A NOVEL APPROACH FOR MONITORING KIDNEY DISEASE AND DIABETES

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Albumin/Creatinine Ratio (ACR) is a crucial metric for monitoring diabetic kidney disease (DKD). Abnormal levels can indicate a propensity for progressive renal failure and other complications such as cardiovascular diseases. This study employed UV/Visible spectroscopy to analyze aqueous urine samples spiked with bovine serum albumin (BSA) and creatinine at clinically relevant concentrations and in a small number of urine samples collected from participants of the PREDICT study at the Baker Heart and Diabetes Institute.

UV/Visible spectra of co-spiked samples revealed distinct bands at 229 nm and 249 nm, corresponding to BSA and creatinine, respectively, alongside other amino acid bands. Partial Least Squares Regression (PLS-R) analysis for BSA yielded Root Mean Square Error of Calibration (RMSEC) and Cross-Validation (RMSECV) values of 66.93 and 73.92 mg/L, respectively. For creatinine, RMSEC and RMSECV values were 244.32 and 275.65 mg/L, respectively. Prediction models for both BSA and creatinine compared to ELISA demonstrated robust performance with R^2_{PRED} values of 0.96 and 0.95, respectively, indicating strong model reliability. The Limit of Detection (LOD) for co-spiked samples was 19.82 mg/L for BSA and 58.43 mg/L for creatinine, where the normal physiological range is 0-30 mg/L for albumin and 6-18 mg/L for creatinine.

We subsequently analysed 14 unprocessed fresh urine samples as collected from participants of the PREDICT study. ACR values obtained spectroscopically were compared to the urinary ACR as measured by ELISA (Alfred Pathology), yielding an excellent LOD of 0.2494 mg/mmol, which provides a superior differentiation even in the normo - albuminuric range which is <2.5 mg/mmol for males and <3.5 mg/mmol for females.

These results demonstrate the potential of our UV/Visible spectroscopy-based method as a rapid, cost-effective point-of-care (PoC) tool for ACR measurement, offering promising applications in the early diagnosis, monitoring, and prognosis of diabetic kidney disease and associated cardiovascular complications.

153.

DECREASE IN HEART FAILURE MORTALITY LAGS BEHIND ATHEROSCLEROTIC CARDIOVASCULAR DISEASE MORTALITY IN PEOPLE WITH DIABETES

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Background/Aim: Contemporary trends in cardiovascular disease (CVD) cause-specific mortality by diabetes status, particularly heart failure (HF) mortality, are inadequately described. We performed the first multi-country analysis of trends in mortality due to coronary heart disease, cerebrovascular disease and HF in people with diabetes, compared to people without diabetes, across eight high-income countries worldwide.

Methods: CVD cause-specific mortality data in people with and without diabetes from eight countries were assembled, spanning 2000 to 2021. Using rate models with a Poisson likelihood, we estimated mortality rates and mortality rate ratios for deaths due to coronary heart disease, cerebrovascular disease and HF.

Results: We analysed 2.54 million deaths over 1.14 billion person-years of follow-up. Coronary heart disease, cerebrovascular disease and HF mortality decreased in all countries in both people with and without diabetes, except for HF mortality in people with diabetes in South Korea and France (no change). For coronary heart disease and HF mortality in people with diabetes, the greatest five-year declines occurred in Denmark (32.3% and 25.3% respectively). For cerebrovascular disease in people with diabetes, the greatest five-year decline in mortality was noted in South Korea (35.0%). In 4/6 countries with HF mortality data available, the declines in HF mortality were less than the declines in coronary heart and cerebrovascular disease mortality. Excess coronary heart and cerebrovascular disease mortality associated with diabetes either decreased or remained stable in all countries except France (increased). In all countries, excess HF mortality due to diabetes increased or remained stable.

Conclusions: Declines in HF mortality have lagged behind declines in coronary heart and cerebrovascular disease mortality, and excess HF mortality associated with diabetes has increased or not changed. Greater efforts are required to reduce HF mortality in people with diabetes. This includes targeting existing cardioprotective therapies towards those at high risk of HF death.

154.

PREDICTING CHRONIC COMPLICATIONS IN 1100 ADULTS WITH TYPE 1 DIABETES: HIGH RISK RATES AND CONCORDANCE BETWEEN TYPE 1 DIABETES-SPECIFIC RISK CALCULATORS

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People with Type 1 diabetes (T1D) are at risk of chronic complications. T1D-specific calculators are more accurate than those developed for people with T2D.

AIM: We aimed to determine (i) rates of high risk; (ii) concordance between risk of cardiovascular disease (CVD), end-stage kidney disease (ESKD) and sight threatening diabetic retinopathy (STDR) and (iii) major modulating factors.

METHODS: An ethics-approval audit of data from adults with T1D attending the Baker Heart and Diabetes Institute Diabetes Clinics (Melbourne) in the last decade was conducted. Risk calculators used were: (i) Steno T1 (CVD) Risk Engine (5- and 10-yr), (ii) MSD Cardiovascular Risk Assessment in T1D (5-yr), (iii) QRisk3 for CVD (10-yr), (iv) Steno ESKD (5-yr) and (v) RetinaRisk STDR (5-yr). Concordance (Spearman correlation coefficient) and difference between groups (Kruskal-Wallis or Mann-Whitney test) were assessed.

RESULTS: After excluding patients with missing data or prior CVD, outputs were available for n=1100/1480 (74%); mean±SD age 50±16.2yrs, 24.3±13.5 yrs T1D, HbA1c 7.7±1.35%. 'High' CVD risk differed by calculator: 41.7% Steno-10 yr; 16.2% MSD; 66.5% QRisk3. For STDR 2.4% were high. Concordance was strong between CVD risk calculators (r=0.86-0.93, p<0.0001); modest between CVD and microvascular complications (r=0.25-0.65, p<0.0001), and between ESKD and STDR risk (r=0.37, p<0.0001). Risk increased with age (<40, 40-60, >60 yr) for CVD (p<0.0001) and STDR (p<0.001), but not for ESKD. CVD (except MSD) and ESKD risks were higher in males vs. females (p<0.01-0.001). Insulin pump vs. injection use associated with lower CVD (p<0.0001) and ESKD (p<0.05) risk. Continuous Glucose Monitor (CGM)-use lowers CVD risk (p<0.01-0.001; except MSD).

CONCLUSIONS: There is good concordance between risk calculators for CVD and microvascular complications. Risks increase with age (CVD and STDR) and being male (CVD and ESKD) and are lower with pump- (CVD and ESKD) and CGM-use (CVD risk).

155.

EXPLORING THE GUT-KIDNEY-AXIS IN A MOUSE MODEL OF DIABETIC KIDNEY DISEASE

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Aim: To investigate whether larazotide improves diabetic kidney disease (DKD) through a gut-kidney-axis mechanism in a type 2 diabetes mouse model.

Background: Emerging evidence suggests a link between intestinal barrier integrity and kidney injury, termed the gut-kidney axis. Our previous research has demonstrated an impaired intestinal epithelial barrier in a DKD mouse model (*Lepr*$^{db/db}$). Larazotide, a gut-targeting therapy aimed at improving intestinal permeability, has yet to be explored in DKD.

Methods: Eight-week-old *Lepr*$^{db/db}$ mice were treated with 20 mg/kg/day larazotide in drinking water for 10 weeks. Intestinal permeability was assessed using FITC-dextran *in vivo*. Gut transit time was measured as a marker of gastrointestinal function, while kidney injury was evaluated by urinary albumin-creatinine ratio and structural damage by periodic acid-Schiff staining and glomerulosclerotic index scoring.

Results: Diabetic *Lepr*$^{db/db}$ mice showed increased intestinal permeability compared to non-diabetic controls (4.322±1.081 µg/ml vs 1.597±1.126 µg/ml, p<0.05), which was not improved by larazotide treatment. Gut transit time was prolonged in *Lepr*$^{db/db}$ mice and further delayed by larazotide (247.6±60.47 min vs 295.7±43.06 min, p<0.05). Larazotide unexpectedly exacerbated albuminuria in diabetic *Lepr*$^{db/db}$ mice (81.81±28.38 µg/µmol vs 125.6±34.93 µg/µmol, p<0.05) and increased kidney weight (0.014±0.002 vs 0.013±0.001, p<0.05), although no changes in glomerulosclerosis were observed.

Conclusions: *Lepr*$^{db/db}$ mice demonstrated increased intestinal permeability, albuminuria, and kidney hypertrophy compared to controls. Larazotide did not improve intestinal permeability and, unexpectedly, worsened kidney injury and gastrointestinal motility. This raises the question of whether larazotide is nephrotoxic in a diabetes setting. Further investigations are required to unravel the underlying mechanisms of this observation.

156.

EPIDEMIOLOGY OF DIABETIC KETOACIDOSIS (DKA) AND EVALUATION OF MANAGEMENT AT A MAJOR TERTIARY REFERRAL HOSPITAL IN AUSTRALIA

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Diabetic ketoacidosis (DKA) is a severe metabolic complication that requires emergency care. Patient harm can be minimised through early intervention of appropriate treatment.
Aim: This study describes the epidemiology, management, and outcomes of DKA episodes within a major Australian tertiary referral hospital.

Methods: Retrospective audit of DKA episodes between January 2019-December 2022 using data extracted from the electronic medical record. Episodes were included where blood ketones >3 mmol/L, pH <7.3 or bicarbonate <15 mmol/L, and blood glucose >11 mmol/L (except recent sodium-glucose cotransporter-2 inhibitor [SGTL2i] use within 72 hours). Recurrent episodes of DKA were excluded.

Results: Total 235 episodes of DKA occurred (2019: n=17; 2020: n=56; 2021: n=77; 2022: n=85). Twenty-three episodes occurred ≥24 hours after admission (hospital-onset). DKA occurred in patients with pre-existing type 1 diabetes mellitus (T1DM) (42%), T2DM (40%), other types (4%), and in those with no previous diagnosis (14.5%). Instances of DKA in T2DM patients increased over time (2019: n=5, 29%; 2020: n=21, 38%; 2021: n=31, 40%; 2022: n=36, 42%). A SGTL2i was used within 72 hours prior in 20% of episodes. The median time to commence an insulin infusion from DKA identification was 1.3 hours, 11.6 hours to resolve acidosis, and an overall DKA resolution time of 24.4 hours. The median length of stay (LOS) was 4.25 days. Hypoglycaemia occurred in 5% and hypokalaemia in 17.9% of episodes during treatment. There was a 4% diabetes-related readmission rate within 30 days, and 15 inpatient deaths.

Discussion: There was an increase in DKA episodes between 2019-2022. The higher-than-expected proportion of T2DM cases has important implications for diabetes care. Variable-rate insulin infusion protocols, as used in this study, may result in a longer time to DKA resolution and LOS, albeit with lower rates of hypoglycaemia and hypokalaemia. Future research should compare variable versus fixed-dose protocols on these outcomes.

157.

CONTINUOUS GLUCOSE MONITORING (CGM) AND HEALTH SERVICE UTILISATION IN DIABETIC PATIENTS: A MODELLING STUDY

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Background
Diabetes mellitus is a chronic condition caused when the endocrine system is unable to produce adequate insulin, or the body cannot utilise the insulin available. In 2021, 529 million individuals were living with diabetes and there were 1.70 million diabetes related deaths. Effective blood glucose monitoring guides health seeking behaviours and has been associated with prevention of complications and better health outcomes. This study aims to model Health Service Use (HSU and associated costs when using Traditional Blood Glucose Level Monitoring (TBGLM) and Continues Glucose Monitoring (CGM.

Methods
A HSU model was developed using an Australian diabetic care pathway. Evidence-based HSU rates were input from systematic review to model the 2023 diabetic population HSU and associated costs when using CGM

compared to TBGLM. The model only included type 1 and type 2 diabetes. The model considered 100% of the diabetic population using CGM and scenario analysis of 25%, 50% and 75% of the diabetic population using CGM.

Findings
This study demonstrated that CGM utilisation will reduce HSU in diabetic patients. The total HSU reduction was 259,137 visits per year and health system cost reduction was $805,942,374.4 if everyone diagnosed with diabetes used CGM. GP visits and pathology HbA1c demonstrated an increase in HSU while blood tests for fats, emergency department presentations and hospitalisations demonstrated an overall decrease in HSU. The reduction in health service use suggests that CGM should be subsidised for all diabetic patients.

Conclusion
CGM utilisation is associated with a change in HSU and health service costs. Future research requires data of the prevalence of CGM use in Australia to be publicly available

158.

TITLE: ASSESSING FOR DIABETES DISTRESS AMONG ADULTS ATTENDING A MULTIDISCIPLINARY TYPE 1 DIABETES CLINIC

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Background: Living with type 1 diabetes (T1D) can impact psychosocial well-being and may lead to diabetes-related distress. The five-item Problem Areas in Diabetes (PAID-5) questionnaire is a validated screening tool to assess diabetes distress. PAID-5 scores range from 0–20; scores ≥8 indicate possible diabetes-related distress warranting further assessment. At the newly established Alfred T1D Clinic, specialised care is provided by a team including doctors, diabetes nurse educators, dietitian, and psychologist.

Hypothesis: That there will be a high prevalence of diabetes distress amongst patients with T1D, which may correlate with glycaemic and clinical characteristics.

Aim: To evaluate diabetes distress among adults attending the Alfred's dedicated T1D clinical service.

Methods: Retrospective record review of patients attending the Alfred T1D Clinic since inception in October 2023 to July 2024. Clinical data from the first PAID-5 assessment visit were analysed. Data were analysed using generalised linear modelling.

Results: In total, there were 137 patients assessed (median age 36 years [IQR 29–51]; T1D duration 16 years [4–24]; HbA1c mean±SD 8.6±2.3%; 69 [50%] were men). Current insulin therapy was via injection for n=114 (83%) and pump for n=22 (16%); one patient was not treated with insulin. PAID-5 median score was 8 [IQR 4–12]. Seventy-four patients (54%) had PAID-5 score ≥8. No individual PAID-5 item scored significantly higher than others. PAID-5 scores did not differ by patient age, sex, T1D duration, HbA1c or insulin delivery modality.

Conclusion: High rates of diabetes distress were reported amongst patients attending specialist T1D care, across all clinical characteristics. These findings reflect the challenges of living with and the complexities of T1D daily management, highlighting the importance of assessing for diabetes emotional distress and providing clinical psychology as part of multidisciplinary T1D care.

159.

SHORT-TERM EXPOSURE TO WILDFIRE-SOURCED FINE PARTICULATE MATTERS INCREASED THE RISK OF DIABETES HOSPITALIZATION IN MULTIPLE COUNTRIES AND TERRITORIES

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AIM: To evaluate associations of wildfire-sourced fine particulate matter ($PM_{2.5}$) with diabetes across multiple countries and territories.

METHODS: We collected 3,612,135 diabetes hospitalization data across 1008 communities in Australia, Brazil, Canada, Chile, New Zealand, Thailand, and Taiwan during 2000–2019. Daily wildfire-sourced $PM_{2.5}$ were estimated through chemical transport models and machine learning calibration. Quasi-Poisson regression with distributed lag non-linear models and random-effects meta-analysis were applied to estimate associations between wildfire-sourced $PM_{2.5}$ and diabetes hospitalization. Subgroup analyses were by age, sex, community income level, and country/territory. Diabetes hospitalizations attributable to wildfire-sourced $PM_{2.5}$ and non-wildfire $PM_{2.5}$ were compared.

RESULTS: Each 10 μg/m^3 increase in wildfire-sourced $PM_{2.5}$ over the current day and the previous 3 days of exposure was associated with relative risks of 1.017 (95% confidence interval [CI]: 1.011–1.022), 1.023 (1.011–1.035), 1.023 (1.015–1.032), 0.962 (0.823–1.032), 1.033 (1.001–1.066), 1.013 (1.004–1.022) for all-cause, type 1, type 2, malnutrition-related, other specified, and unspecified diabetes hospitalization, respectively. Stronger associations were observed for all-cause, type 1, and type 2 diabetes in Thailand, Australia, and Brazil; unspecified diabetes in New Zealand; and type 2 diabetes in high-income communities. An estimate of 0.67% (0.16%–1.18%) all-cause and 1.02% (0.20%–1.81%) type 2 diabetes hospitalizations were attributable to wildfire-sourced $PM_{2.5}$ exposure. Wildfire-sourced $PM_{2.5}$ posed greater risks of all-cause, type 1, and type 2 diabetes than non-wildfire $PM_{2.5}$, responsible for 38.7% of $PM_{2.5}$-related diabetes hospitalizations.

CONCLUSION: Our findings highlight a significant, yet often overlooked, linkage between diabetes and wildfire air pollution. We demonstrate that exposure to $PM_{2.5}$ from wildfires can contribute substantially to diabetes hospitalizations. Precision prevention and mitigation strategies should be tailored for individuals in advantaged communities and residents of Thailand, Australia, and Brazil.

160. **10.**

CARDIOVASCULAR RISK MANAGEMENT IN AUSTRALIAN ADULTS WITH DIABETES

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People with diabetes are disproportionately affected by cardiovascular disease (CVD). Specific targeting of key modifiable risk factors is paramount to delay (and ideally prevent) cardiovascular events, and improve the health and quality of life of people living with diabetes However, there is a lack of contemporary data assessing cardiovascular risk management in people with diabetes in Australia.

AIM: To assess cardiovascular risk management in Australian adults with diabetes to better understand current gaps in clinical care.

METHODS: A retrospective analysis of the 2022 Australian National Diabetes Audit (ANDA) was undertaken. ANDA captures cross-sectional data on people with diabetes attending health services providing diabetes care across Australia. Adults (≥18 years) with type 1 (T1D) and type 2 (T2D) diabetes were included. Clinical performance was assessed by benchmarking risk factors against evidence-based clinical targets for the total cohort, with sub-analyses in T1D and T2D patients, and by presence of CVD.

RESULTS: There were 4341 people included; 32.4% with T1D and 67.6% with T2D. Of the total cohort, 25.9% met the HbA1c target (≤7% or 53 mmol/mol), 45.5% met the low-density lipoprotein cholesterol target (<2 mmol/L), 43.4% met the systolic blood pressure target (<130 mmHg), 20.5% met the body mass index target (<25 kg/m^2), 30.2% met the physical activity target (≥150 mins/week of moderate-to-vigorous intensity), and 85.0% were non-smokers. Compared to patients with T1D, patients with T2D were less likely to meet targets. Patients with existing CVD were less likely to meet targets than patients without existing CVD.

CONCLUSION: Cardiovascular risk management in diabetes is sub-optimal, increasing the risk of adverse health outcomes. Improving management could produce substantial health and economic benefits.

INFECTIOUS DISEASES

161.
ASSOCIATION BETWEEN DAPTOMYCIN DOSING AND IN-HOSPITAL MORTALITY IN PATIENTS WITH VANCOMYCIN RESISTANT *ENTEROCOCCUS FAECIUM* BLOODSTREAM INFECTIONS

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INTRODUCTION: Vancomycin-resistant *Enterococcus faecium* (VRE*fm*) bloodstream infections (BSIs) pose a significant challenge for management. There remains a lack of evidence to support the optimal dose of daptomycin for VRE*fm* BSIs. We aimed to describe the association between daptomycin dose and 30-day in-hospital mortality in this patient group.

METHODS: All adult patients receiving ≥ 3 days of definitive daptomycin therapy for a first episode VRE*fm* BSI at The Alfred Hospital between 2015 and 2022 were included. Daptomycin doses were classified as low (≤7.9 mg/kg), medium (8.0 to 9.9 mg/kg) or high (≥10 mg/kg). Associations between daptomycin dose groups and 30-day in-hospital mortality were assessed by Cox regression analysis. Mortality differences between daptomycin and teicoplanin treatment for *vanB* VRE*fm* BSIs were also explored.

RESULTS: A total of 111 patients with VRE*fm* BSI (59% *vanB* genotype) were included. All-cause 30-day in-hospital mortality was 17.1%, with a median definitive daptomycin dose of 10.6 mg/kg (IQR: 9.8 to 11.9 mg/kg). There was no association between low, medium or high daptomycin doses and mortality (p=0.44) or persistence/relapse of infection (p=0.16). No mortality difference was observed between *vanB* VRE*fm* BSIs treated with daptomycin or teicoplanin (15.6% v 17.5%, p=0.76).

CONCLUSION: In a VRE*fm* BSI cohort where the majority of patients received daptomycin doses ≥10 mg/kg against predominantly *vanB* VRE*fm*, we observed no association between dose and 30-day mortality, or between definitive treatment with daptomycin or teicoplanin for *vanB* VRE*fm* BSIs. Overall, 30-day mortality was low, reinforcing the potential efficacy of daptomycin for the treatment of VRE*fm* BSIs.

162.
GLOBAL GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF CRYPTOCOCCOSIS: AN INITIATIVE OF THE ECMM AND ISHAM IN COOPERATION WITH THE ASM

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Cryptococcosis is a major worldwide disseminated invasive fungal infection. Cryptococcosis, particularly in its most lethal manifestation of cryptococcal meningitis, accounts for substantial mortality and morbidity. The breadth of the clinical cryptococcosis syndromes, the different patient types at-risk and affected, and the vastly disparate resource settings where clinicians practice pose a complex array of challenges. Expert contributors from diverse regions of the world have collated data, reviewed the evidence, and provided insightful guideline recommendations for health practitioners across the globe. This guideline offers updated practical guidance and implementable recommendations on the clinical approaches, screening, diagnosis, management, and follow-up care of a patient with cryptococcosis and serves as a comprehensive synthesis of current evidence on cryptococcosis. This Guideline seeks to facilitate optimal clinical decision making on cryptococcosis and addresses the myriad of clinical complications by incorporating data from historical and contemporary clinical trials. This guideline is grounded on a set of core management principles, while acknowledging the practical challenges of antifungal access and resource limitations faced by many clinicians and patients. More than 70 societies internationally have endorsed the content, structure, evidence, recommendation, and pragmatic wisdom of this global cryptococcosis guideline to inform clinicians about the past, present, and future of care for a patient with cryptococcosis.

163.

CHARACTERISATION OF BACTERIAL PATHOGENS USING CRISPR-CAS9 ENRICHMENT AND OXFORD NANOPORE SEQUENCING

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Culture-free DNA sequencing of patient samples has the potential to improve pathogen surveillance and antimicrobial treatment strategies compared to current laboratory-based approaches. Here, we demonstrate a novel CRISPR-Cas9 enrichment strategy combined with Oxford Nanopore sequencing for targeted characterisation of *Klebsiella pneumoniae* strains directly from complex patient samples. We developed 60 CRISPR-Cas9 guides targeting highly conserved transfer RNA (tRNA), MLST and AMR genes in *K. pneumoniae* via population genomics and sequence alignment against the Genome Taxonomy Database. We validated our guides against 21 *K. pneumoniae* isolates each with distinct STs and AMR profiles in pure culture. We then compared this approach to unenriched metagenomic sequencing in human faecal samples spiked with a known *K. pneumoniae* strain. CRISPR-Cas9 guides successfully enriched DNA yield of genomic regions surrounding tRNA genes in all isolates (median 52x vs untargeted regions, IQR 12-126x). Sequence conservation analysis suggested that tRNA guides could also be applied to many common pathogens across *Enterobacterales*, rather than being limited to *K. pneumoniae*. When performed on human faecal samples, enriched sequencing generated 11.3-28.8x higher abundance of reads aligning to MLST genes compared to unenriched metagenomics. Enriched sequencing detected target AMR genes in 6/6 faecal samples compared to 1/6 samples following unenriched sequencing. CRISPR-Cas9 enrichment shows promise for improved pathogen characterisation from clinical samples over traditional unenriched metagenomics, potentially at a lower financial cost due to reduced sequencing requirements. This approach could enable efficient culture-free surveillance screening of patient samples for problematic pathogens, including *K. pneumoniae*.

164.

STATIN USE AMONG PEOPLE LIVING WITH HIV AT A METROPOLITAN SEXUAL HEALTH CENTRE

Imogen Duplessis

Background: People living with HIV (PLWH) face a higher risk of developing cardiovascular disease (CVD). Whilst lifestyle modification remains important, recent REPRIEVE trial highlighted use of statins to reduce incidence of CVD events.

Aim: To determine the proportion of current statin use in PLWH and non-users now indicated for statins, against local guidelines/REPREIVE trial data, to evaluate if a pharmacist-led optimisation role should be established.

Methods:
A retrospective audit of electronic medical records (EMRs) of all PLWH ≥40years presenting for routine HIV care at a large sexual health centre (SHC) in May-June 2023 was conducted. Newly diagnosed/transferred care <1 year ago were excluded. Baseline demographic data and statin use were collected. For statin non-users, Australian CVD risk was calculated for those without established CVD, and with complete documentation of blood pressure, lipids, diabetes and smoking status within the previous year; to determine if a statin would now be indicated based on new local guidelines/REPREIVE trial data (≥5% CVD risk). Data was descriptively summarised in STATA (version17.)

Results: Of 782 PLWH, 399(51.0%) were ≥40 years (mean age 52.7±9.4 years; 85.7% male) and included in the study. A total of 130(32.6%) patients took a statin with 8(2%) patients prescribed for secondary prevention.

CVD risk considerations were documented in EMR by a doctor or nurse for 235(58.9%) and calculated risk score documented for 33(8.3%) patients. Of 269 statin non-users, 133(49.4%) had <5% calculated CVD risk, 53(19.7%) had ≥5% risk (n=15 ≥10% risk) and are recommended statins based on local guidelines/REPREIVE trial data, and 83(31%) had incomplete data.

Discussion: Over a third of PLWH ≥40 years take statins, with 19.7% of non-users recommended a statin based on local guidelines/REPREIVE trial data. Pharmacist clinic roles for improving documentation of CVD risk in PLWH and instigating appropriate statin use are under consideration.

165.

IMMUNE MARKERS ARE PREDICTIVE OF CMV INFECTION IN SEROPOSITIVE LUNG TRANSPLANT RECIPIENTS

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BACKGROUND: Predicting which transplant recipients will develop CMV infection remains challenging. The aim of this retrospective cohort study was to explore two biomarkers of global immunity, the absolute lymphocyte count (ALC) and the mitogen component of the QF-CMV assay, as predictors of CMV infection in CMV seropositive lung transplant recipients (R+LTR).

METHODS: R+LTR with QF-CMV testing performed at prophylaxis discontinuation were included. Cox models evaluated ALC and mitogen values as predictors of CMV infection, controlling for antiviral prophylaxis.

RESULTS: 204 LTR were included (122 D+/R+, 82 D-/R+). Most were QF-CMV positive (155, 91%) with 30 (15%) negative and 19 (9%%) indeterminate. CMV infection occurred in 111 (76%). Patients with a CMV seropositive donor (D+) were more likely to develop CMV infection (HR 2.24, 95% CI 1.48-3.39, p<0.001). Median ALC values (1.1 vs. 1.4 cells/μL, p=0.006) and mitogen values (2.8 vs. 4.6 IU/mL p=0.13) were lower in patients who subsequently developed CMV infection. After adjusting for serostatus and antiviral prophylaxis, both ALC (HR 0.70 per $1x10^3$ cells/μL increase, 0.53-0.94, p=0.016) and mitogen (HR 0.94 per 1.0 IU/mL increase, 0.89-1.00, p=0.03) were independently associated with CMV.

CONCLUSIONS: Within R+LTR, ALC and the mitogen component of the QF-CMV assay could predict post-prophylaxis CMV infection. D+ patients were higher risk, and extending antiviral prophylaxis was protective. These biomarkers could risk-stratify patients and inform duration of antiviral prophylaxis and frequency of virologic monitoring. Additional studies are needed to further explore the role of immune biomarkers in the prediction of CMV and other opportunistic infections.

166.

GUT CARRIAGE OF ESCHERICHIA COLI VIRULENT LINEAGES IS LINKED TO INCIDENT LIVER DISEASE IN A LARGE POPULATION COHORT WITH 18-YEARS OF FOLLOW-UP HEALTH RECORDS

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Background: Infectious events are risk factors for many non-communicable diseases (NCDs), but underlying mechanisms are largely unclear. Liver disease (LD) can be associated with higher *Enterobacteriaceae* antibody levels, and cohort studies highlight their enrichment in the gut of LD patients. Including microbes can improve LD incidence prediction when combined with other risk factors, but no in-depth microbial characterization has been performed.

Methods: We use a combination of metagenomic and microbial genomic analyses to characterise virulence factors (VF) carriage in gut metagenomes from the FINRISK 2002 cohort (n=7,226). We contextualise VF prevalence and specificity using ~400,000 bacterial genomes, and link VF detection in our cohort with taxa and >18y follow-up disease records from national electronic registries.

Findings: We observed a link between *Escherichia coli* VFs at baseline and incident LD (ICD-10: K70-77) up to 18 years later. In 1,764 VF-carrying participants, microbiome diversity was altered, and greater VF diversity and abundance associated with a higher incidence of LD (Cox; HR=2.3, 95% CI=1.3–4.2, p=0.006). *E. coli* ST-73 and ST-95 lineages preferentially harboured LD-associated VFs and were directly detected in metagenomes from individuals with incident LD.

Conclusion: Asymptomatically-carried *E. coli* can be robustly linked to incident (future) NCDs in a lineage-specific manner, which has implications on diagnostics and prevention, and a better understanding of the microbial risk factors for NCDs.

167.

A ONE-STOP-SHOP FOR HEPATITIS C CARE IN THE COMMUNITY CORRECTIONS POPULATION: THE NURSE AND PEER-LED C NO MORE STUDY.

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In-prison hepatitis programs are successful but exclude individuals on community corrections orders such as probation or parole. The community corrections population is likely to have similar risk factors for hepatitis C virus (HCV) infection and similar barriers to accessing healthcare as the incarcerated population.

Aim: To evaluate the clinical efficiency of a same-day nurse and peer-led mobile model of care at community corrections offices in Melbourne, Australia.

Methods: The C No More study enrolled individuals within the vicinity of three metropolitan community corrections offices. Participants were recruited opportunistically by a peer worker. At enrolment, individuals were tested with point-of-care HCV antibody tests and, if positive, point-of-care HCV RNA tests. Participants with self-reported HCV antibody were reflexed to RNA testing. RNA positive participants were assessed for treatment initiation, and prescribed treatment by a nurse practitioner.

Results: Among 579 participants enrolled in the study, 221 (38%) were on community corrections orders. Of those enrolled, 162 (28%) were reflexed to RNA testing due to reported antibody positivity. Of 392 antibody tests conducted, 28 (6%) were positive. Among the 190 RNA tested, 43 (22%) were positive. Of these, 30 (70%) commenced treatment, 9 were in the process of commencing treatment, 2 were treated elsewhere, and 2 chose not to pursue treatment. Of those who commenced treatment, 10 completed treatment, 8 achieved SVR, 2

participants did not achieve SVR due to nonadherence. Overall, prevalence of HCV RNA positivity was 7% (43/579).

Conclusion: This study shows high rates of retention in care and treatment initiation, indicating that a mobile, same-day test and treat model is effective at providing hepatitis C care to the community corrections population. The level of engagement of community members in this clinic and the prevalence of current HCV infection indicates there is a need for hepatitis C care in these community hubs.

168.

STREPTOCOCCUS PYOGENES PHARYNGITIS ELICITS DIVERSE ANTIBODY RESPONSES TO KEY VACCINE ANTIGENS INFLUENCED BY THE IMPRINT OF PAST INFECTIONS.

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While most of the >750M annual global Streptococcus pyogenes infections affect the skin or throat (pharyngitis), the bacterium causes >500,000 deaths every year, largely due to less common autoimmune complications, notably acute rheumatic fever (ARF) and its chronic sequelae, rheumatic heart disease. There is a clear unmet need for a vaccine to reduce the global burden of Strep A diseases. Despite promising vaccine candidates due to begin clinical trials, our current understanding of which antigens induce beneficial (durable and protective) or harmful (autoreactive) immune memory in humans—the sole natural host of Strep A—remains limited. To bridge these knowledge gap, we investigated antibody responses and memory B cells against 19 virulence factors and vaccine antigens using blood samples from a human Strep A pharyngeal challenge model and tonsil tissue from children. Our findings reveal widespread humoral immune memory against Strep A in both adults and children, and that many vaccine antigens can elicit durable antibody responses. However, despite pre-existing antibodies, most adults remained susceptible to clinical pharyngitis. We have identified baseline antibody responses associated with susceptibility or protection from pharyngitis. Notably, this pre-existing immunity inversely correlates with the magnitude of the antibody response to challenge. These insights emphasize that Strep A vaccines will need to contend with, and build upon, pre-existing immunity, a critical consideration for initial clinical trials in adults.

169.

REAL-WORLD EVALUATION OF ARTIFICIAL INTELLIGENCE (AI) CHATBOTS FOR PROVIDING SEXUAL HEALTH INFORMATION: A CONSENSUS STUDY USING CLINICAL QUERIES

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Introduction
Artificial Intelligence (AI) chatbots could potentially provide information on sensitive topics, including sexual health, to the public. However, their performance compared to human clinicians and across different AI chatbots, particularly in the field of sexual health, remains understudied. We evaluated the performance of three AI chatbots - two prompt-tuned (Alice and Azure) and one standard chatbot (ChatGPT by OpenAI) - in providing sexual health information, compared to human clinicians.

Methods
We analysed 195 anonymised sexual health questions received by callers to the Melbourne Sexual Health Centre phone line. Responses to these questions from nurses and the three AI chatbots were evaluated by a panel of experts in a blinded order using a consensus-based approach. Performance was assessed based on overall correctness and five specific measures: guidance, accuracy, safety, ease of access, and provision of necessary information. We conducted subgroup analyses for clinic-specific (e.g., opening hours) and general sexual health questions and a sensitivity analysis excluding questions, Azure could not answer.

Results
Alice demonstrated the highest overall correctness (85.2%; 95% confidence interval (CI), 82.1%-88.0%), followed by Azure (69.3%; 95% CI, 65.3%-73.0%) and ChatGPT (64.8%; 95% CI, 60.7%-68.7%). Prompt-tuned chatbots outperformed the ChatGPT across all measures. Azure achieved the highest safety score (97.9%; 95% CI, 96.4%-98.9%), indicating the lowest risk of providing potentially harmful advice. All chatbots performed better on general sexual health questions compared to clinic-specific queries.

Conclusions
Prompt-tuned AI chatbots demonstrated superior performance in providing sexual health information compared to base ChatGPT, with high safety scores particularly noteworthy. However, all AI chatbots showed susceptibility to generating incorrect information. These findings suggest the potential for AI chatbots as adjuncts to human healthcare providers for providing sexual health information while highlighting the need for continued refinement and human oversight. Future research should focus on larger-scale evaluations and real-world implementations.

170.

STRAIN DIVERSITY OF BACTERIAL BLOODSTREAM INFECTIONS DESPITE HEALTHCARE-ASSOCIATED ACQUISITION: A MOLECULAR EPIDEMIOLOGY STUDY

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BACKGROUND:
Bacterial bloodstream infections (bBSIs) are highly clinically significant events causing substantial morbidity and mortality. Despite this, our understanding of the genomic epidemiology of bBSIs is limited. We aimed to determine the molecular epidemiology of all bBSIs using an unbiased whole genome sequencing (WGS) approach.

METHODS:
We prospectively included all patients with bBSI at Alfred Health from 2018-2023. Patients with coagulase-negative *Staphylococcus* isolates were excluded. All bBSI isolates underwent WGS. We identified multi-locus sequence types (MLST) and antimicrobial resistance (AMR) genes. We conducted phylogenetic analyses in STs with >5 isolates.

RESULTS:
2371 patients and 2982 bBSI episodes were included. 2145/2982 (72%) episodes were healthcare-associated/hospital-acquired infections (HA/HAI). Crude mortality following bBSI episode at 7- and 30-days was 7.6% and 14.1%. We identified 15 genera/93 species/950 strains, with crude 7-day mortality ranging 0% (*Shigella* spp.) to 25% (*Stenotrophomonas* spp.). There was substantial within-species ST diversity, with most STs represented by a single genome. Gram positives frequently carried acquired resistance (15.8% *S. aureus*, *mecA* gene with 80% being HA/HAI, 78.4% *E. faecium* vancomycin resistance *van* operon). In contrast, amongst Enterobacterales and *P. aeruginosa,* most genomes (59%, 955/1627) carried no acquired resistance determinants. Genotypic multi-drug resistance was noted in 18.7% (n=320) genomes, predominantly in Gram negative species (*E. coli* 245/320, 77%). 397/2371 (17%) patients had multiple bBSI episodes, of which 364/397 (92%) were different bacterial strains.

CONCLUSIONS:
The majority of bBSI episodes were HA/HAI. Despite this, WGS indicated high species and strain diversity, with a limited role of outbreaks. Highest mortality was noted in non-fermenting Gram negative bBSI episodes but most Gram negative bBSI genomes carried no acquired resistance genes. The role of routine WGS in investigating bBSI remains to be determined.

171.

PREDICTION OF ANTIMICROBIAL RESISTANCE IN *PSEUDOMONAS AERUGINOSA* USING INTEGRATION OF MULTIPLE GENOMIC REPRESENTATIONS AND GRAPH NEURAL NETWORKS

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Pseudomonas aeruginosa is a significant global pathogen with rapidly emerging antimicrobial resistance (AMR). Traditional resistance gene detection approaches struggle to detect AMR in *P. aeruginosa* due to complex mechanisms. While machine learning models using whole genome sequencing (WGS) data show promise, studies on advanced deep learning models, particularly graph neural networks (GNN), remain limited.

AIM: To predict AMR in *P. aeruginosa* using WGS data and GNN-based models.

METHODS: We developed AMR-GNN, a GNN-based framework incorporating graph convolutional network layers, to predict binary AMR phenotypes of 12 antibiotics. We constructed network graphs using multiple genomic representations (unitigs, single nucleotide polymorphisms and frequency chaos game representation). We used WGS data from 2,515 *P. aeruginosa* isolates from Alfred Hospital and nine public datasets. Population structure was accounted for by removing edges connecting isolates with the same multi-locus sequence type. AMR-GNN was compared with elastic net, traditional approaches, and public models (VAMPr). An ablation study was conducted on external datasets. Integrated gradients identified predictive biomarkers. Performance was evaluated using area under receiver-operator curve (AUROC) or F1 score over 10 random training/testing splits.

RESULTS: AMR-GNN significantly outperformed elastic net models for 11/12 antibiotics (AUROCs: 0.819-0.971). Edge decoupling further improved AUROC for all tested antibiotics (0.837-0.977). AMR-GNN also outperformed traditional approaches and VAMPr with higher F1 scores (0.720-0.908). The ablation study also demonstrated better generalizability of AMR-GNN compared to simpler models, with better AUROCs in tobramycin, amikacin, meropenem, ceftazidime, and aztreonam. When assessing model interpretability, important biomarkers related to fluoroquinolone resistance (*gyrA, gyrB, parC)* and aminoglycosides (*fusA1*) were identified, with significantly increased minimum inhibitory concentrations observed in isolates harboring mutations in these genes.

CONCLUSION: AMR-GNN shows superior performance in predicting AMR in *P. aeruginosa* compared to existing methods and can identify AMR determinants. This demonstrates the potential of GNN-based approaches for AMR prediction using WGS data.

172.

OPTIMISING HIV PRE-EXPOSURE PROPHYLAXIS AND TESTING STRATEGIES IN MEN WHO HAVE SEX WITH MEN IN AUSTRALIA, THAILAND, AND CHINA: A MODELLING STUDY AND COST-EFFECTIVENESS ANALYSIS

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Men who have sex with men (MSM) in the Asia-Pacific region face a significantly higher HIV burden compared to the general population. Although pre-exposure prophylaxis (PrEP) is effective in preventing HIV, its cost-effectiveness across different countries in this region is unknown.

AIM: This study analyzes the economic and health impacts of long-acting injectable cabotegravir (CAB-LA) versus oral PrEP in high-income and low- to middle-income countries in the Asia-Pacific, specifically Australia, Thailand, and China.

METHODS: Using a Markov model, we evaluated PrEP scale-up among 100,000 MSM aged 18 years or older over a 40-year period. The model considered universal PrEP coverage of 80% and varied HIV testing frequencies. The outcomes were measured in quality-adjusted life-years (QALYs) with a 3% annual discount rate.

RESULTS: Expanding oral PrEP to 80% of MSM could prevent 8.1% of new HIV infections in Australia, 14.5% in Thailand, and 26.4% in China. Cost-effectiveness was highest with 6-monthly testing in Australia, annual testing in Thailand, and 3-monthly testing in China. Replacing oral PrEP with CAB-LA could avert more infections, but its high cost made it non-cost-effective. CAB-LA would need a 50–90% price reduction to be viable as an additional strategy to oral PrEP.

CONCLUSION: Scaling up oral PrEP for MSM with tailored testing frequencies is cost-effective in these countries, while CAB-LA requires significant price reductions to be considered a viable option.

173.

LOW CELL METABOLISM AS A CENTRAL ANTIMICROBIAL-RESISTANCE MECHANISM AND THERAPEUTIC TARGET OF STAPHYLOCOCCAL BIOFILMS IN VENTRICULAR ASSISTANT DEVICE DRIVELINE INFECTIONS

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Objective: Ventricular assist device driveline infections are difficult-to-treat diseases due to high antimicrobial resistance (AMR) of associated biofilms. Several mechanisms of biofilm AMR have been proposed; these mechanisms were based on simplified *in vitro* models and have limited clinical implications. This study aimed to re-evaluate mechanisms that may contribute to staphylococcal biofilm AMR encountered in driveline infections and identify translatable therapeutic targets.

Methods: A tunnel-based biofilm assay mimicking deep driveline infections was developed to culture clinically relevant staphylococcal biofilms. Seven first-line antibiotics and six staphylococcal laboratory and clinical isolates were selected. Various mechanisms were evaluated for their roles in biofilm AMR, including the barrier effect of extracellular polymeric substances (EPS) matrix, high-cell-density growth, quorum sensing responses, global stress responses, the presence of persister cells, and particularly repressed cell metabolism.

Results: EPS had a minor role that was strain and antibiotic dependent and unable to decisively explain biofilm AMR. High-density growth and associated cell metabolic repression appeared to be vital for biofilm AMR against all tested antibiotics. Parallel comparisons of cell metabolic activities and AMR at different biofilm developmental stages suggested a negative and significant correlation between cell metabolism and biofilm AMR. Disarming quorum sensing system or stress-responsive alternative Sigma factor SigB did not restore susceptibilities of established staphylococcal biofilms to vancomycin or oxacillin. Population analysis of biofilms found small subpopulations of tolerant and persister cells with low metabolic activities. Enhancing ATP production partially restored biofilm susceptibilities to antibiotics. STIMULAN beads containing gentamicin, of which the lethality is weakly metabolism-dependent, but not the strongly metabolism-dependent vancomycin eradicated staphylococcal biofilms in a simulated driveline tunnel, further supporting the central role of cell metabolic repression in biofilm AMR.

Conclusions: This study identified cell metabolic repression as the central mechanism underpinning biofilm AMR and a promising therapeutic target for biofilm-associated driveline infections.

174.

EVALUATION OF ARTIFICIAL INTELLIGENCE-POWERED SCREENING FOR SEXUALLY TRANSMITTED INFECTIONS-RELATED SKIN LESIONS USING CLINICAL IMAGES AND METADATA

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BACKGROUND: Sexually transmitted infections (STIs) pose a significant global public health challenge. Early diagnosis and treatment reduce STI transmission but rely on recognising symptoms and care-seeking behaviour of the individual. Digital health software that distinguishes STI skin conditions could improve health-seeking behaviour.

AIM: To develop and evaluate AI algorithms to differentiate STIs from non-STIs based on clinical images and metadata (demographics & symptoms).

METHODS: We used 4,913 clinical images of genital lesions and metadata from the Melbourne Sexual Health Centre collected during 2010-2023. We developed two binary classification models to distinguish STIs from non-STIs: (1) a convolutional neural network (CNN) using images only and (2) an integrated model combining both CNN and Fully Connected Neural Network (FCN) using images and metadata. We evaluated the model performance by the Area under the ROC curve (AUC) and assessed metadata contributions to the Image-only model.

RESULTS: Our study included 1,583 STI and 3,330 non-STI images. Common STI diagnoses were syphilis (34.6%), genital warts (24.5%), and herpes (19.4%), while most non-STIs (80.3%) were conditions such as dermatitis, lichen sclerosis and balanitis. In both STIs and non-STIs, the most frequently observed groups were 25-34 years (48.6% and 38.2%, respectively), and heterosexual males (60.3% and 45.9%, respectively). The Image-only model showed a reasonable performance with an AUC of 0.859 (SD 0.013). The Image+Metadata model achieved a significantly higher AUC of 0.893 (SD 0.018) compared to the Image-only model ($p<0.01$). Out of 21 metadata, the integration of demographic and dermatological metadata led to the most significant improvement in model performance, increasing AUC by 6.7% compared to the baseline Image-only model.

Conclusions: The Image+Metadata model outperformed the Image-only model in distinguishing STIs from other skin conditions. Using it as a screening tool in a clinical setting may require further development and evaluation with larger datasets.

175.

CHARACTERISING SEPSIS-ASSOCIATED ENCEPHALOPATHY AND PROPOSAL OF A NOVEL THERAPEUTIC

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Sepsis-associated encephalopathy (SAE) is a neurodegenerative condition seen in 70% of patients hospitalised with sepsis. Current treatments fail to address the activation of the endothelium that leads to the cytokine storm and is a major contributor to blood brain barrier (BBB) disruption, often leaving patients with permanent cognitive dysfunction. Our novel therapeutic, "Anti-VCAM-CD39", is a bifunctional, fusion antibody that localises to the

endothelium by competitively inhibiting vascular cell adhesion molecule 1 (VCAM-1) expressed by activated endothelial cells, and by inducing the anti-inflammatory response facilitated by ectonucleotidase CD39 through the metabolism of pro-inflammatory ATP, to adenosine.

We investigated SAE in a murine, lipopolysaccharide (LPS) model of sepsis (5mg/kg intraperitoneally). Brain tissues were collected at different timepoints and interrogated through real-time polymerase chain reaction and immunoblotting for markers of endothelial activation, local pro-inflammatory cytokine production and BBB integrity. Additionally, Evan's blue measurement was performed to investigate brain albumin extravasation. We found that the brain endothelium was activated at 6 hours post-LPS injection with increased VCAM and e-selectin expression ($p = 0.0267$ and 0.0193 respectively). Pro-inflammatory cytokines production increased locally for pro IL-1β and IL-6 ($p = 0.0011$ and 0.0318 respectively). Angiopoietin 2, one of the main drivers of BBB disruption, was also upregulated ($p < 0.0001$).

Treatment with Anti-VCAM-CD39 at 0.8mg/kg, 1-hour post-sepsis significantly reduced the gene expression of endothelial adhesion molecules VCAM1 and ICAM1 ($p = 0.0006$ and 0.0001 respectively). Activity of the inflammasome, the executor of pyroptotic cell death, were also mitigated, with decreased expression of pro IL-1β ($p = 0.0128$). Our drug also reduced angiopoietin 2, restoring BBB integrity, as measured by Evan's blue where there was decreased albumin extravasation. Our results demonstrate that SAE may be ameliorated with Anti-VCAM-CD39 through the reduction in circulating inflammatory molecules and the restoration of BBB integrity.

NO CATEGORY (OTHER)

176.

BONE HEALTH FOLLOW-UP AFTER DISTAL RADIUS FRACTURE IN THE EMERGENCY DEPARTMENT: A RETROSPECTIVE COHORT STUDY

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Patients experiencing minimal impact distal radius fractures are at high risk of sustaining further osteoporotic fractures, including in the pelvis and spine. Bone health follow-up is recommended post minimal impact fractures in postmenopausal women and men over 50 years of age. Follow-up includes bone health screening and medication initiation which may reduce the risk of serious fractures.

AIM: To determine the rate of bone health follow-up within three months post discharge from the Emergency Department (ED) after presentation with an acute distal radius fracture.

METHODS: This retrospective cohort study included patients aged over 50 years with a minimal impact distal radius fracture discharged from two EDs in Victoria, Australia from July 2021 to December 2022. Patients taking anti-resorptive medications were excluded. Bone Health follow-up included tests (vitamin D level and/or dual-energy x-ray absorptiometry (DEXA) scans) and/or medications (vitamin D, calcium and/or anti-resorptive therapy (e.g., bisphosphonate, denosumab)). Follow-up was confirmed through a national digital patient health record system (My Health Record), hospital electronic medical records or phone follow-up.

RESULTS: There were 143 patients included. The mean age was 68.7 (SD 11.4) years, most (n=129; 90.2%) were female. Bone health follow-up within 3 months of discharge from the ED was reported in 15 (10.5%; 95%CI: 6.0-16.7) patients; 11 (8%) had vitamin D testing; 2 (1%) had DEXA scans and 7 (5%) had commenced bone health medication.

CONCLUSION: Bone health follow-up for patients discharged from the ED after sustaining distal radius fractures was uncommon. Management of fractures in the ED therefore represents a missed opportunity to initiate bone health follow-up to prevent future fractures.

177.

THE INTRODUCTION OF AN INTESTINAL ULTRASOUND SERVICE SIGNIFICANTLY REDUCES DIAGNOSTIC ENDOSCOPY USAGE IN AN INFLAMMATORY BOWEL DISEASE SERVICE – THE SCOPELESS STUDY

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Background and Aim: Increasingly, intestinal ultrasound (IUS) is utilised as a disease monitoring strategy in inflammatory bowel disease (IBD). Our aim was to compare endoscopy usage for evaluation of IBD disease activity before and after the introduction of an IUS service.

Methods: A retrospective single-centre study was performed. Total numbers of endoscopies performed for Crohn's disease (CD) or ulcerative colitis (UC) disease evaluation were collected from the pre IUS era (2010-2014) and the IUS era (2015-2019). The primary endpoint was a comparison of the cumulative number of endoscopies for IBD activity evaluation annually relative to the annual number of patients seen in clinic in the

pre-IUS and IUS eras. Secondary endpoints included the number of endoscopies according to diagnosis (CD vs UC), and the number of IUS performed.

Results: The number of endoscopies performed for IBD disease evaluation decreased from 576 in the pre-IUS era to 474 in the IUS era despite an increase in cumulative annual patient reviews (1985 vs 3337 patient reviews, respectively). The proportion of annual endoscopies relative to patients reviewed reduced from 29 per 100 patients in the pre-IUS era to 14 per 100 patients in the IUS era (OR 2.47, 95% CI 2.15-2.84; p < 0.001). The proportion of annual endoscopies relative to patients reviewed reduced from 30 to 14 per 100 patients in CD (OR 2.60, 95% CI 2.16-3.12; p < 0.001), and 37 to 17 per 100 patients in UC (OR 2.90, 95% CI 2.33-3.59, p<0.001). In the IUS era, a total of 3319 IUS were performed (2673 CD, 646 UC), 1467 for assessment of activity (44/100 patients/year) and 1852 for objective confirmation of remission (55/100 patients/year).

Conclusion: In the 5 years following introduction of an IUS service, the number of endoscopies performed for evaluation of IBD activity per patient review was halved.

178.

CHANGES IN ENERGY EXPENDITURE AND BODY COMPOSITION FOLLOWING ALLOGENEIC STEM CELL TRANSPLANT

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BACKGROUND: Allogeneic haematopoietic stem cell transplant (SCT) is associated with major nutrition-impacting side effects. There is limited information on energy expenditure to guide nutrition support decisions and body composition alterations may further impact utility of prediction equations.

AIM: To evaluate resting energy expenditure and body composition, from pre-SCT conditioning until +100 days post-SCT.

METHODS: Thirty-four adults undergoing allogeneic SCT participated (18-67 years, 56% male, 62% acute leukaemia, BMI 27.0±5.7kg/m^2). Body weight and measured resting energy expenditure (mREE, fasting state, Cosmed Fitmate^R) were measured at five timepoints (pre-conditioning [*t1*], pre-SCT [day -2 to 0, *t2*]; days +5-+10 [*t3*], +15-+30 [post-engraftment, *t4*] and +90-+100 *[t5*]. Fat-free mass (FFM) was measured at t1, t4 and t5 (Seca^R multifrequency bioelectrical impedance analysis). mREE was expressed as absolute, standardised for weight and FFM, and %predicted BMR (Schofield equation, mREE%predBMR). Linear mixed modelling assessed changes over time, accounting for repeated measures.

RESULTS: Absolute mREE increased after conditioning then declined, however mREE standardised for body weight and FFM were stable. mREE was 16-26% above predicted BMR across the SCT journey but was highly individually variable. Marked loss of weight and FFM occurred, even to day +100.

	t1	t2	t3	t4	t5	p value=
mREE(kJ)	8253±282	8488±286	8092±319	7901±296	7458±293	0.0001
mREE/kg(kJ/kg)	110±3	113±3	108±4	110±3	109±3	0.58
mREE/kgFFM(kJ/kg)	150±6	-	-	148±5	148±5	0.46
mREE%predBMR	123±3	126±3	120±4	120±3	116±3	0.10
Weight(kg)	79±3	80±3	80±3	76±3	73±3	0.0001
FFM(kg)	55±2	-	-	54±2	52±2	0.0002

Data show mean±standard error

CONCLUSION: Allogeneic SCT is associated with elevated REE. Decreasing REE over time may be related to ongoing FFM loss. Sequential measurement enables greater understanding of the impacts of SCT on individuals' energy expenditure and body composition, to support personalised nutrition support and nutritional rehabilitation.

FUNDING SOURCE: An AuSPEN grant provided support towards this study.

179.

GENERALIZABLE SEGMENT ANYTHING MODEL VIA SELECTION STRATEGY FOR SKIN LESION SEGMENTATION

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AIM: The Segment Anything Model (SAM) has demonstrated impressive performance in segmenting diverse objects within natural images. With its powerful zero-shot capability, SAM can generalize to segment objects in unseen domains. However, it struggles to process dermatological images effectively due to the significant distribution shift from natural images, as well as the intricate backgrounds and irregular edges present in lesion areas. Despite the aid of point prompts, SAM tends to produce incomplete and over-concentrated segmentation results.

METHODS: To address these challenges, we introduce an innovative point-selection strategy for SAM to improve its generalization in skin lesion segmentation. Specifically, we first identify the uncertain areas by SAM, which may contain lesion parts, and learn the distribution of these uncertain areas. With this learned prior, complementary points are selected as prompts to refine the segmentation results. Furthermore, to avoid segmentation regions overlapping benign areas, we constrain the segmentation results through pseudo-boxes crafted by the selected points.

RESULTS: Our proposed techniques collectively result in skin lesion segmentation with more precise, completed, and compact lesion areas compared to standard SAM and previous methods. Extensive experiments on the ISIC2016, ISIC2017, PH2, Dermofit, and STIAtlas public datasets demonstrate that our method can achieve superior performance. For example, compared to nnU-Net, our model achieves an average improvement

of +0.82% on dermoscopic images and a +5.85% increase in zero-shot capability when segmenting rare skin infection regions captured in clinical settings.

CONCLUSION: Our PSAM introduces a well-designed framework based on SAM to optimize the model's mask output for point prompts. We further improve the model's ability to recognize skin lesions by adding adapters to the transformer module in the mask decoder. We successfully used the SAM in the skin lesion segmentation task. We hope our work can promote further research on community segmentation models for skin images.

180.

A SYSTEMATIC REVIEW OF INTERVENTIONS THAT INCREASE PARTICIPATION IN OLDER ADULTS WHO EXPERIENCE MILD COGNITIVE DECLINE

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With the aging population, rates of cognitive decline are also expected to increase. Occupational therapists play a key role in optimising participation in meaningful activities in those experiencing mild cognitive decline.

Aim: To systematically review the effectiveness of occupational therapy interventions used with older adults experiencing mild cognitive decline to increase participation in daily tasks.

Method: Systematic review following Cochrane methodology. CINAHL, Medline, and Embase databases were searched from inception to April 2023. Studies were included if they were randomised controlled trials published in English that evaluated an intervention to address mild cognitive decline delivered or supervised by an occupational therapist.

Results: 13442 papers were screened for eligibility, and ten papers described nine studies that met the inclusion criteria. Studies were designed to target remediation (n=9) (eg. cognitive stimulation, memory groups, functional task exercise), compensation (n=3) (eg. education, memory support system, coping strategies) or both (n=2). Sessions were mean 71 (SD 32) minutes, once-twice per week, for 10 (SD 3) weeks and followed a standardised treatment protocol. Seven of the nine studies measured participation and were included in a meta-analysis. Findings indicated that a range of occupational therapy interventions could effectively enhance participation in meaningful activities (SMD=0.382, 95% CI 0.118 to 0.645 immediately post-treatment).

Conclusion: Occupational therapists should draw on remediation and compensation intervention approaches and a variety of procedures and materials to address activity participation in older adults with mild cognitive decline. Additional research is required to build stronger evidence to determine the core features of the intervention.

NURSING

181.
THE IMPACT OF NURSING WORKFORCE SKILL-MIX ON PATIENT OUTCOMES IN INTENSIVE CARE UNITS IN VICTORIA, AUSTRALIA

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International studies have shown that the education level and number of nursing staff are associated with patient outcomes, such as mortality and adverse events. The COVID-19 pandemic required an adaptable nursing workforce with nursing redeployment, rapid upskilling, and changed models of staffing.

AIM: To examine the impact of nursing workforce skill-mix (percentage of critical care registered nurses - CCRN) in the Intensive Care Unit (ICU) during a patient's stay.

METHODS: Registry linked cohort study of the Australian and New Zealand Intensive Care Society Adult Patient Database and the Critical Health Resources Information System using real-time nursing workforce data from 15 public and 5 private hospital ICUs in Victoria, Australia.

RESULTS: 16,618 adult patients were admitted between 1st December 2021 and 30th September 2022. 6,563 (39.5%) patients were cared for in ICUs with >75% CCRN, 7,695 (46.3%) in ICUs with 50-75% CCRN, and 2,360 (14.2%) in ICUs with <50% CCRN. In-hospital mortality was 534 (8.1%) vs. 859 (11.2%) vs. 252 (10.7%) respectively. After adjusting for confounders, patients cared for in ICUs with 50-75% CCRN (adjusted OR 1.21 [95%CI 1.02-1.45]) were more likely to die compared to patients in ICUs with >75% CCRN. A similar but non-significant trend was seen in ICUs with <50% CCRN (adjusted OR 1.21 [95%CI 0.94–1.55]) when compared to patients in ICUs with >75% CCRN. In-ICU mortality, delirium, pressure injuries, after-hours discharge, and ICU length of stay were lower in ICUs with CCRN>75%. The impact on mortality was even higher for patients who needed a breathing machine or advanced supports such as renal replacement therapy or extracorporeal membrane oxygenation (ECMO) with a 35% higher chance of dying.

CONCLUSION: The nursing skill-mix in ICU impacts patient outcomes and should be routinely monitored. Addressing CCRN shortages is likely to lead to improved patient outcomes.

182.
FINDING MEANING IN COMPLEX CARE NURSING IN A HOSPITAL SETTING

Felice Borghmans

AIM: Research on nurses' perceptions of "generalist" complex care in hospitals is scarce. This study aimed to broaden our understanding of the field by investigating the experiences of nurses who provide complex care in 'generalist' hospital settings.

BACKGROUND: Complex care is described as care for patients experiencing acute issues additional to multi-morbidity, ageing, or psychosocial complexity. Nurses are the largest professional group of frontline healthcare workers, and patients experiencing complex, chronic conditions are overrepresented in acute care settings.

METHODS: In-depth semi-structured interviews were conducted with four "complex care" nurses, who discussed their daily routines, typical patient interactions, and system-related experiences. Their narratives were analysed using the conceptual framework of complex adaptive phenomenology (CAP) that integrates two synergistic disciplines: Phenomenology and complex adaptive systems theory. CAP thus explores the complexly interdependent and dynamic nature of experience.

FINDINGS: Two overarching themes constituting the 'essence' of complex care nursing were identified: Contextual factors and attribute/values-based elements. Creating meaningful patient outcomes and feeling part of a team were experienced as professionally fulfilling, while time constraints, institutional settings, and systemic barriers to comprehensive caregiving diminished the experience of providing complex care. Overall, work-meaning presented as a dynamic phenomenon, shaped by personal and professional values, local settings, and systemic factors.

CONCLUSION: Clinician experience is a key indicator of health care quality and sustainability. Hence, the quality of the clinician experience needs to be given careful thought in light of impending nursing workforce shortages, partly driven by burnout in a highly pressured health care context, and rising demand for complex care. This study recommends more expansive research be undertaken exploring the nursing experience of complex care in hospital settings. This information will strengthen efforts to attract and sustain an engaged, productive workforce of complex care nurses that can meet the rising tide of hospital based complex care.

183.

BUILDING A SUSTAINABLE NURSING WORKFORCE: FACTORS THAT INFLUENCE FINAL YEAR NURSING STUDENTS' SELECTION OF GRADUATE PROGRAMS

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Aim: To examine factors that influence final year pre-registration nursing student's selection of their graduate year program and explore student experiences of a *clinical school model* in influencing their selection.

Methods: An exploratory descriptive design was implemented using data from four focus group interviews (n=9 participants). Convenience sampling of all final year undergraduate nursing students at one university was conducted from October – December 2023. Participants were recruited from the Alfred/Latrobe clinical school and three other metropolitan health service clinical schools and one regional campus.

Results: Four themes were identified during analysis of focus group interviews. *The impact of clinical placement, Alignment of culture and values, Career aspirations, The student experience of a 'clinical school model'.*

Participant responses indicated the importance of alignment of personal values and the perceived organisational culture. Clinical placement experiences are an important factor in student decision making when choosing graduate programs. The experiences of student peers on clinical placement, family and friends' experiences as consumers of health services are also important factors in decision-making. Participants identified tension between prioritising geographical location or a preferred specialisation and this affected how they viewed their career path. Informed by the interview data, students prioritised organisational culture, geographical location and positive clinical placement experiences as the most important factors in choosing a graduate program.

Conclusion: Findings indicate that consideration of graduate program selection is a high priority for final year nursing students. There is an opportunity for pre-registration nursing programs and health services to work together to support students in their graduate year selection. With the increasing pressure on health services to recruit and retain novice graduates, the findings from this project help in our understanding of how nursing students' select a graduate program in a competitive workforce environment and the importance of partnering with health services in supporting students.

184.

NON-INVASIVE RESPIRATORY SUPPORTS DELIVERY IN AUSTRALIA

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Introduction/Aim: Non-invasive respiratory supports (NIRS) including conventional oxygen (COT), high flow nasal oxygen (HFNO), continuous positive airway pressure (CPAP) and non-invasive ventilation (NIV) are delivered widely in hospitals to treat acute respiratory failure (ARF). Over the last few decades these modalities have been increasingly used in the ward setting most often by respiratory teams. This study aimed to examine respiratory care practices and organisational processes in Australian hospitals for providing NIRS in medical wards and on discharge.

Methods: A cross sectional survey was undertaken of respiratory or general medicine directors (or delegate) who were working in Australian public hospitals (August-December 2023). The questionnaire was developed, piloted and tested for validity with 33 nominal questions and free text options. All relevant hospitals (n=74) were sent the online survey with two automated reminders

Results: Of 74 hospitals, 63.5% participated, most being metropolitan (51.5%), quaternary/tertiary (68.1%) hospitals, delivering acute NIRS (93.6%) in respiratory (HFNO 68.1%, NIV 46.8%) or medical wards (HFNO 59.6%, NIV 19.1%). Specialised respiratory care units were uncommon (25.5%) and variable written NIRS prescriptions utilised (29.8-63.8%). Most had access to medical emergency response teams (87.2%). Local NIRS guidelines (72.3%) were common. NIRS training was provided to nurses (63.8%) and doctors (53.2%), but was not mandatory (51.1%). Site NIRS clinical audits were uncommon (10.6-34.0%). All offered home NIRS on discharge: COT (84.3%); CPAP (70.2%), NIV (61.7%) and HFNO (8.5%). Patients requiring domiciliary NIRS were followed-up in clinic by doctors (85.1%), nurses (42.5%) or physiotherapists (29.8%), with infrequent outreach nurse visits (42.5%) or remote monitoring (17.2%).

Conclusion: NIRS are used commonly on medical wards in Australia to treat ARF. There is substantial variation in practice and organisational processes regarding NIRS delivery which may contribute to variation in health outcomes. There are no Australian NIRS audits or standards of care; these should be considered.

Key words: Non-invasive respiratory supports, oxygen therapy, high flow nasal oxygen, continuous positive airway pressure, non-invasive ventilation, acute respiratory failure, ward

Grant support: Australian Government research training scholarship

Conflict of interest: Nil

185.

EXPLORING THE PERSPECTIVES AND EXPERIENCES OF PEOPLE WITH DRUG-REFRACTORY EPILEPSY IN AUSTRALIA: A QUALITATIVE INSIGHT

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OBJECTIVES: Epilepsy is a chronic, potentially life-threatening disease estimated to affect up to 3.5 percent of Australia's population at some point in their lives. Despite its prevalence, the perspectives and experiences of

people living with epilepsy are underrepresented in the current literature. This study aimed to gain insights into the perspectives and experiences of this population.

METHODS: Utilising a qualitative descriptive design, individual semi-structured interviews containing 11 open-ended questions were conducted via telehealth. Sixteen patients formally diagnosed with drug-refractory epilepsy were recruited from a tertiary hospital's outpatient epilepsy clinic. Data were analysed using thematic analysis.

RESULTS: Four key themes were identified: 'perceptions, knowledge, and attitudes surrounding epilepsy'; 'narratives of seizure experiences'; influences of diagnosis on personal identity'; and 'attitudes towards public awareness and epilepsy-related stigma'. Participants health literacy was limited, particularly regarding status epilepticus or sudden unexpected death in epilepsy. Conversely, various participants feared acquiring knowledge surrounding the associated risks of epilepsy, due to concerns that such information could exacerbate their seizures. Perceptions and experiences of stigma significantly influenced participants' willingness to disclose their condition to others. Participants' independence and self-confidence had declined since receiving the diagnosis, which subsequently impacted their educational attainment, social relationships, and career development.

CONCLUSIONS: This study provides novel and clinically significant information on patient perspectives and experiences of epilepsy. The consideration of patients' preferences for education should be integrated into clinical practice. Further research is needed to determine whether the standardised and ethical provision of information surrounding epileptic mortality is beneficial or influential to patients' seizure susceptibility.

186.

A COST OUTCOME STUDY OF VARICOCOELE EMBOLISATION AND FUTURE PREGNANCY IN AN AUSTRALIAN PUBLIC HOSPITAL SETTING

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Varicocoele is commonly encountered in males with infertility. Studies have shown that varicocoele repair (surgery or embolisation) can improve the rate of subsequent pregnancy. In Australia, there have been no studies assessing the cost of varicocoele embolisation and current practice is based on international data. AIM: This study aimed to assess the cost of varicocoele embolisation and estimate the treatment cost per pregnancy.

METHODS: Retrospective cost-outcome study of patients treated by embolisation between January 2018 and 2023. A bottom-up approach was used to calculate procedure costs whereas a top-down approach was used to calculate costs for all other patient services, including direct and indirect costs. To calculate cost per pregnancy, costs were adjusted according to existing published data on the rate of pregnancy after embolisation.

RESULTS: Costing data from 18 patients were included, of median age 33.5 years (range 26–60) and median varicocoele grade 2.5 (range 1–3). All patients had unilateral treatment, most commonly via right internal jugular (16 patients, 89%) and using a 0.03500 system (17 patients, 94%). The median cost for the entire treatment including procedural, non-procedural, ward and peri-procedural costs was AUD$2208.10 (USD$1405 or EUR€1314), range AUD$1691–7051. The projected cost to the healthcare system per pregnancy was AUD$5387 (USD$3429 or EUR€3207).

CONCLUSION: Total varicocoele embolisation cost and the cost per-pregnancy were lower than for both embolisation and surgical repair in existing international studies. Patients undergoing varicocoele treatment should have the option to access an interventional radiologist to realise the benefits of this low-cost pinhole procedure.

187.

INDIVIDUALISED MUSIC PLAYLIST BASED ON ISO-PRINCIPLE FOR DE-ESCALATING AGITATION OF PEOPLE WITH DEMENTIA: A RANDOMISED CONTROLLED FEASIBILITY STUDY

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Background
Approximately 70% of residential care home residents with dementia presented agitation. Agitation has detrimental consequences on the individuals with dementia and their carers. Non-pharmacological strategies are recommended as the preferred first-line treatment approach. Music listening has been proven effective in reducing the frequency of agitation occurrence. Yet, the feasibility of de-escalating agitation is still less explored.

Objectives
To evaluate the feasibility of the Individualised Music Playlist based on the ISO Principle for de-escalating agitation of people with dementia and to provide preliminary evidence about its efficacy.

Methods
The randomised participants listened to either the 30-minute music playlist or a book reading audio script twice weekly for six weeks, and when agitation occurred. A wireless neckband speaker was used for listening to create an immersive listening environment. The playlist of the intervention group consists of the preferred music genres sequenced by a music therapist based on the ISO-Principle. Their agitation level was observed every 5 minutes from the beginning of an agitation episode for an hour to monitor its trajectory for two weeks. Multilevel models with maximum likelihood analysis were conducted. The frequency of agitation and other behavioural symptoms were assessed at baseline and the 6th week and analysed with Generalized Estimating Equations.

Results
Twenty-four participants were recruited, and 10 presented 36 agitation episodes during the first two weeks of observation. The recruitment and retention rates were 85.7% and 83.3% respectively. 97.2% of the intervention and control conditions were delivered as planned. The intervention was not more effective than the control condition in de-escalating agitation and reducing agitation or other behavioural symptoms. Overall, agitation symptoms were apparently alleviated in the first 10 minutes with a decelerated pace onwards.

Conclusions
The intervention was feasible, and its efficacy in de-escalating agitation has yet to be confirmed.

188.

HOME-BASED ELIGIBILITY ANALYSIS AND RECOMMENDATION TOOL (HEART): USING MACHINE LEARNING TO IDENTIFY IN-HOSPITAL PATIENTS FOR AT-HOME CARE

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AIM: To develop a robust and reliable tool for identifying in-hospital patients who are suitable for at-home care. Utilising machine learning techniques, the HEART tool aims to support clinical areas with identifying and then prompting discharge disposition conversations and planning.

Method: Free text data was extracted from 3,414 Hospital-In-The-Home (HITH) admissions between April-2018 and April-2023. Named-Entity Recognition was performed to extract key biomedical phrases and characteristics.

Modelling these characteristics, revealed four patient phenotypes, which were validated as being accurate through retrospective analysis.

These admissions informed which biomedical characteristics best discerned the four phenotypes, enabling the automation of a daily report which scored patients receiving in-hospital care at the Alfred site against the four phenotypes, ranking them by similarity. The results were then published for clinician review and suitability discussions.

Prospective evaluation against a selection of all patients further validated the model. Initial roll out occurred with General Medicine on Ward 4 East. Patients identified were streamed for suitability to HITH, Hospital-Admission-Risk-Program, or one of many other home-base services.

Results: During the prospective evaluation, 287 patients were reviewed with 33% scored as 'suitable for home-based care', 34% 'monitor and review in 24-hours', 11% 'not feasible due to current service design' and 21% 'not eligible for home-based care'.

When rolled out to General Medicine, a less than 40% suitability cut-off was set, resulting in 104 patients reviewed with 27% scored as 'suitable for home-based care', 38% 'monitor and review in 24-hours' 20% 'not feasible due to current service design' and 8% 'not eligible for home-based care'.

Ward areas and relevant home-based programs were notified of patients who were screened as suitable.

Conclusion: The HEART tool demonstrates a machine learning approach to identify people eligible for home-based care, whilst maintaining clinician decision making. Additionally, this approach quantifies patient groups for new homecare models.

189.

IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH) – INSIGHTS INTO CONSUMER CONCERNS

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BACKGROUND: IIH is increasingly prevalent, with high morbidity and socioeconomic consequences, affecting young, overweight women in the prime of life. The disease is characterised by chronic headaches, visual symptoms and permanent visual loss. The Alfred Neuro-ophthalmology-IIH clinic (2022), established in addition to the general Neuro-ophthalmology clinic (2018), in the Alfred Brain Program has observed that patients struggle to maintain daily activities and employment resulting in loss of productivity and quality of life. This study consults a group of patients and explores their lived experience of IIH and the health service.

METHODS: Seven patients participated in two online focus groups (women aged 26-77 years), with a Neuro-ophthalmologist, Nurse and two Patient Experience/Consumer Group Facilitators. Patients gave their perspective on five key areas: concerns around the condition; symptom management and side effects, information and education; access to care and coordination of care between healthcare settings and supports to relieve fear and anxiety.

RESULTS: Concerns included symptom management and poor coping mechanisms for headaches, tinnitus, fatigue and medication side effects leading to isolation, loss of "normality", decreased motivation and increased risk of depression and mental health struggles. Lacking information, inadequate access to care, uncertainty of who to rely on to deal with symptoms and time to diagnosis were concerning and needed improvement in the community, particularly country regions. Patients were glad to have found/been referred to a bulk-billed IIH specialty service and had a positive experience with clinic and set-up (orthoptist appointment one day and doctor-telehealth another day), preferring this to long wait times on same day appointments.

CONCLUSION: The focus group was valued and patients were keen on more support and information on other platforms. Outcomes include increased communication awareness strategies and development of community education sessions. . Information gathered highlights the importance and urgent need for dedicated IIH services in Australia.

190.

THE EPIDEMIOLOGY OF PRESSURE INJURIES IN ADULT ICU PATIENTS SUPPORTED WITH EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO).

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Pressure injuries (PIs) are a common complication in intensive care, which can result in significant morbidity, mortality, and cost. There is a limited body of research on PIs specific to the adult extracorporeal membrane oxygenation (ECMO) population.

AIM: To describe the epidemiology of pressure injury (PI) development in adult patients supported with ECMO in a single centre specialist intensive care unit (ICU).

METHODS: Retrospective, observational, cohort study from January 2018 to May 2023. Exposure: Any PI developing more than 24 hours after ICU admission.

RESULTS: 500 ICU patients were supported with ECMO during the study period. Excluding those < 18 years of age, and with an ICU length of stay < 24 hours, 466 patients were included in the analysis. One hundred and thirty-five (29.0%) acquired at least one PI during their ICU stay, with this occurring in 80 patients (17.2%) while supported on ECMO. The PI incidence rate was 1.7 per 100 ECMO patient-days (CI 1.3 – 2.0). Patients with a PI were mechanically ventilated for longer, received more renal replacement therapy, manifest more delirium, and stayed longer in ICU and hospital. A higher proportion of veno-venous ECMO was also noted in those with a PI, a reflection of the COVID-19 pandemic. ICU and in-hospital mortality were lower in the PI group. Factors independently associated with the acquisition of a PI were male gender, oral dietary intake, renal replacement therapy, and prolonged mechanical ventilation. The majority of the PIs acquired during ECMO were stage two and most commonly located on the neck and head (*n* = 25/96 PI's, 26.0%), and sacral region (*n* = 31/96 PI's, 32.3%). Only 3 PIs were in relation to the ECMO cannula, circuit or dressing.

CONCLUSION: A significant proportion of patients developed PI's while receiving ECMO. This was higher than reported in general ICU populations.

191.

SURVEY OF FACTORS INFLUENCING NURSES MANAGING MENTAL STATE DETERIORATION IN ACUTE HOSPITAL SETTINGS

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Introduction
Caring for patients presenting with mental state deterioration (MSD) in acute hospital settings presents complex challenges, impacting patient outcomes including poor patient outcomes, traumatic use of restrictive practices and negative impact on staff. Consequently, ensuring that patients who present with MSD receive timely and appropriate care is a key concern for healthcare organisations. The Alfred piloted DIvERT (De-escalation, InterVention, Early, Response), a tailored rapid response model for managing in two clinical settings. However,

the effectiveness of DIvERT depends on evaluating and understanding the underlying causal generative mechanisms including exploring and addressing the factors that influence the staff's ability to manage patient MSD effectively.

Aim
As part of realist evaluation of DIvERT, this study aims to refine program theories and explore the factors influencing nurses' ability to manage MSD in acute hospital settings.

Method
A survey instrument based on initial program theories was developed to collect quantitative and qualitative evidence for theory testing and refinement.

Results
In total, 60 from a convenience sample of 120 nurses completed the survey. The results showed that, 80% of respondents reported receiving mental health training, with 56% indicating the training lasted less than one hour. De-escalation skills were rated as low by 53% of respondents. Overall, 30% of participants activated DIvERT for assistance, while 16% formally reported MSD incidents. From free text responses, staff highlighted the need for tailored training, implementing daily mental status assessment forms, improving teamwork, communication, and better organisational support for high-risk patients.

Conclusion
The study emphasises the importance of addressing the challenges faced by staff to address mental state deterioration. It is essential to improve clinical skills through tailored training, teamwork, and communicating safety effectively. Additionally, organisational factors such as standardised response team models, and improving risk assessment and reporting processes play a key role.

192.

HOME ALONE ON MILRINONE: A NOVEL WAY TO DELIVER HOME INOTROPES AS A BRIDGE TO HEART TRANSPLANTATION

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Background: Alfred Hospital's home inotropes program has successfully cared for advanced heart failure patients as a bridge to decision/heart transplantation since the year 2000. Traditionally patients have been discharged with ambulatory pumps under the Hospital in the Home program (HITH) involving daily home nursing visits and weekly cardiology appointments, During COVID 19 our patient led, independent model was developed where patients managed their inotropes independently, without daily nursing visits. Independent at home patients completed ambulatory intravenous inotrope education, passed competency testing and had implantable cardioverter-defibrillators inserted prior to discharge. Patients independently managed their ambulatory pump and PICC line care, attended their own haemodynamic assessments and daily inotrope bag changes. Reportable haemodynamic limits, and emergency action plans were provided. Weekly nursing and medical clinic reviews were scheduled.

Methods: Over a 5yr period, 15 consecutive patients treated under the previous Hospital in the Home model were retrospectively compared to 15 independent at home patients. Results: Independent at home patients had a mean time of 112 days compared to 77 days on the program. Despite this, the independent cohort had a reduction in planned outpatient reviews by 79% (16 vs 77). All- cause hospitalisations were 50% (16 vs 32) lower in the independent group and PICC line related sepsis was also lower in the independent cohort (1 vs 2), together fewer PICC line changes (3 vs 6). There were no significant differences between either groups for outcomes. Reasons for cessation of inotropes across both arms: 30% (9) were transplanted, 23% (7) required an LVAD, 30% (9) weaned off therapy, 13% (4) patients progressed to palliative care and there was 3% (1) death due to intractable arrhythmia.

Conclusions: The independent home inotrope program in selected patients is feasible, safe and associated with reduced medical encounters and hospital admissions as compared to a traditional Alfred HITH program.

193.

AN EDUCATIONAL EVALUATION OF A PRECEPTORSHIP PROGRAM FOR REGISTERED NURSES

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The current Australian Nursing workforce is challenged in meeting the vacancy demands (Health Workforce Australia, 2014 & Mannix, 2012). As a result, a greater number of graduate nurses are being employed to increase the nursing workforce (Government of South Australia, 2024). These graduate nurses require education, support and clinical supervision from skilled registered nurses (RNs) to safely transition to competent team members.

AIM: The aim of this study was to evaluate a preceptorship education program implemented by a metropolitan heath service to upskill RNs in providing this support to graduate nurses.

METHODS: RNs were encouraged to undertake a short online learning package introducing the concepts of adult learning and contextualising the roles of the learner and preceptor. RNs were enrolled centrally to attend a 90 minute face to face session. Sessions were run twice per day in double staffing time. Sessions were interactive and covered the concepts of teaching a clinical skill & providing effective feedback. Participants self-rated their confidence pre & post workshop using an online survey in the following areas: Giving feedback, understanding teaching methods, teaching a clinical skill & using questioning to identify a learning need.

RESULTS: 668 RNs were invited to complete the course. 503 RNs (75.3%) completed the course over a six-week period. 621 RNs (93%) have completed the online package, 882 RNs (132%) have completed the face to face workshop. Participants reported an increase in confidence of all outcome measures: Preceptor role (59.9%), providing feedback (78.9%), understanding teaching methods (80.9%), teaching a clinical skill (54.1%), using questioning to identify learning needs (60.0%).

CONCLUSION: This study reviewed the impact of a hybrid preceptor education program across a large metropolitan nursing workforce. Data shows an effective improvement in all learning outcomes. The learning package supports RNs to preceptor graduate nurses as they transition into the workforce.

194.

USING ELECTRONIC MEDICAL RECORDS IN IMPROVING COMMUNICATION BETWEEN HOSPITALISED PATIENTS AND HEALTH PROFESSIONALS ACROSS TRANSITIONS OF CARE

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Introduction

Electronic medical records (EMRs), which contain definitive information about managing patient care, have been implemented in many Australian hospitals. However, little is known about how clinicians use EMRs to facilitate communication with patients. This project aimed to address challenges to achieve better communication in health care services, by investigating current and new engagement strategies to enhance communication with patients and families in using the EMR.

Methods
A qualitative exploratory design included interviews with patients, families and clinicians (*n=114*); observations with clinicians (*102 hours*); and focus groups with digital health experts including chief information officers and IT leaders (*n=34*). Transcripts were analysed inductively using reflexive thematic analysis.

Results
Patients reported that clinicians often did not relay clinical information noted in EMRs back to them in hospitals, except when complex planning requiring patient input was involved, such as discharge planning. Most patients and families desired more transparency and consistency in sharing details in EMRs since it would help them manage their medications and communicate their conditions to general practitioners' post-discharge. Clinicians viewed EMRs primarily as tools for documenting clinical information and communicating between multidisciplinary teams within/across hospitals. They rarely shared their notes or screens with patients unless specifically requested, which was uncommon. Observations confirmed that most clinical notes were filled with medical jargon and acronyms, which were partially simplified during verbal interactions with patients and families. Digital health experts noted that clinicians' use of EMRs for communication still mimicked the paper-based system. Despite their potential to support communication with families and patients, patient portals had inconsistent design and adoption in Australian hospitals.

Implications
Change management is needed to improve clinicians' use of EMRs for better communication with patients and families at the point of care. Patient-centric portal designs are also needed in supporting patient education and autonomy across care transitions.

195.

A DELPHI SURVEY TO DEVELOP INTERNATIONAL CONSENSUS ON THE TIMEFRAME FOR DEFINING A HOSPITAL-ACQUIRED PRESSURE INJURY (HAPI)

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Pressure Injuries (PI) significantly impact the patient and healthcare organisation. Early detection is crucial to implement strategies for managing and preventing harm. PIs are monitored to drive improvements by reviewing data. Previous inconsistencies in hospital-acquired pressure injury (HAPI) definitions have impacted incident reporting, hospital coding, and funding penalties. Many studies discuss the prevalence rate of a HAPI but few define the time frame used to measure this harm.
AIM: To develop an international consensus on the timeframe for defining a hospital-acquired pressure injury (HAPI).
METHODS: This research used a Delphi survey design. Expert participants were identified through national and international organisations. A total of 43 individuals from 11 countries were recruited, 42 were nurses. Three rounds were conducted from September 2022 to June 2023. A percentage level agreement or consensus was set at >70%. Items with less were removed.
RESULTS: This research highlighted a wide variation among international experts on a HAPI definition and a variation in the timeframe used in guidelines within healthcare organisations. Expert interpretations for defining a HAPI had 10 variations, ranging from zero hours on admission to 96 hours after admission. After three Delphi

rounds, a 100% agreement was reached by expert consensus. A HAPI was defined as occurring after the first 24 hours following admission. Deep Tissue Injury/unstageable PIs were defined as occurring after 72 hours

CONCLUSION: This study reached consensus with experts in defining a timeframe for a HAPI. Previous inconsistencies in HAPI definitions have impacted incident reporting, hospital coding, and funding penalties imposed by some governments. A standard definition will support international comparison. Future PI reporting of prevalence and incidence data will allow benchmarking to support quality actions, future research activities, and improve patient outcomes. It is only at this time that this data will represent the true definitive measure of quality.

196.

ENHANCING PATIENT SELF-MANAGEMENT IN SUBCUTANEOUS NATALIZUMAB DELIVERY: A NURSE-LED TRANSITION CLINIC MODEL UTILISING SCAFFOLDING THEORY

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Background: Natalizumab, a monoclonal antibody used to treat multiple sclerosis (MS), is typically administered intravenously. In February 2024, a subcutaneous (SC) formulation was approved for administration in the community via a healthcare professional. Patients transitioning from intravenous receive one administration, and those naïve receive two administrations of SC natalizumab at the site before continuing in the community.

Methods: In this retrospective study, we analysed the demographics of patients with MS receiving SC natalizumab through a nurse-led transition clinic. All patients received education on the ongoing administration process and the importance of compliance. Data was collected on age, sex, neurological score, weight, prior venous access, adverse events together with safety and compliance in the community.

Results: The nurse-led transition clinic commenced in May 2024. To date, 13 patients expressed interest in transition to SC natalizumab. Of these, eight (61%) patients have received SC natalizumab. Five patients explored the transition to SC natalizumab but declined due to the dispensing/GP fees. Of the patients who completed the transition to natalizumab SC, seven (87%) were female and the mean age was 48.25 years [min-max, 30-57.] Patients lived on average 26.5km from Alfred Hospital [range 8-55]. The average EDSS was 2.25 [range 1-5.5]. The average weight of participants was 87.25 kilos [range 70-148]. Five (62%) of patients had difficult intravenous access. Two patients required a port for previous infusion, and three were difficult cannulations. Nil adverse events occurred post-administration. Since transition to community GP management, no adverse events or relapses have occurred. Compliance with administration has been maintained in the community. John Cunningham virus surveillance was maintained at 100%.

Conclusion: The transition to SC natalizumab administration within a nurse-led transition clinic is safe and effective. Nurse scaffolding theory supports patient self-management and safety. No adverse events were reported during or after the transition.

197.

THE RELATIONSHIP BETWEEN NURSING SKILL-MIX AND SEVERITY OF ILLNESS OF PATIENTS ADMITTED IN AUSTRALIAN AND NEW ZEALAND INTENSIVE CARE UNITS

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Nursing is the largest health profession within Australian and New Zealand Intensive Care Units (ICUs) and there is a need to better understand the impact of specialist critical care registered nurses (CCRNs) on patient-centred outcomes.

AIM: To describe the variation in the nursing skill-mix of CCRNs across different hospital types and to determine its association with the severity of illness and survival of critically ill patients admitted to Australia and New Zealand ICUs.

METHODS: A retrospective cohort study using the Australia and New Zealand Intensive Care Society Adult Patient Database to provide information on patient demographics and outcomes, and the Critical Care Resources Registry to provide information on annual nursing staffing levels from July 2014 to June 2020. Four hospital types (metropolitan, private, rural/regional and tertiary) and three patient groups (elective surgical, emergency surgical and medical) were examined.

RESULTS: During the six-year study period 770,747 patients were admitted from 184 ICUs in Australia and New Zealand. The median percentage full-time equivalent (FTE) of CCRNs for each ICU was 59.1% (IQR 48.9 - 71.6). Predicted and observed ICU mortality were maintained across all hospital and patient group types. Multivariable linear regression demonstrated after adjusting for confounders of the severity of illness and hospital type, including private hospitals that patients with the greatest illness severity are being cared for in those centres with the highest percentage of CCRNs.

CONCLUSION: In Australian and New Zealand ICUs, the nursing teams with the highest percentage FTE of CCRNs care for the most critically ill patients. The healthcare system in Australia and New Zealand has a critical care nursing workforce that adjusts to meet the acuity and complexity of ICU patients. With future predictions of global nursing shortages, the challenge of maintaining nursing workforce standards is imperative to meet patient and healthcare organisations' expectations.

198.

A MIXED METHODS STUDY PROTOCOL TO IDENTIFY RESEARCH PRIORITIES FOR PERIOPERATIVE MEDICINE IN AUSTRALIA

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Background: Clinical research in perioperative medicine requires the perspectives of patients and caregivers to increase its relevance and quality, benefiting both researchers and the community. Identifying these priorities will enable researchers, funders, and governing bodies to efficiently use scarce funding and resources. We aim to identify the top 10 research priorities in perioperative medical research in Australia.

Methods: A mixed-methods, exploratory-sequential design will be conducted. The study will include five phases. Initially, a published open-ended survey gathered responses from the population (researchers, healthcare workers, and consumers) regarding uncertainties/questions relevant to the population about perioperative medical research. We

collected 544 questions and quantitatively analysed and grouped them according to the Standardised Endpoints in Perioperative Medicine Core Outcomes Measures in Perioperative and Anaesthetic Care (StEPeCOMPAC) endpoints. Using multicriteria decision-making software, workshops combining the population will be conducted to determine the top 10 priorities for perioperative medicine research for the Australian population.

Ethics and dissemination: Ethical approval to conduct the study was obtained from the Alfred Health (Australia) Human Research Ethics Committee (ID: 171/19). The findings will be disseminated in peer review publications, conferences, and dissemination across perioperative research networks. The top 10 priorities will be available to inform research funders, grant submissions, guidelines, and the population.

Wallace SKA, Bucknall TK, Forbes A, Myles PS. A mixed methods study protocol to identify research priorities for perioperative medicine in Australia. BJA Open. 2023 Oct 25;8:100235. doi: 10.1016/j.bjao.2023.100235. eCollection 2023 Dec. BJA Open, 8 (C): 100235 (2023)

199.

CONSUMER ENGAGEMENT IN PERIOPERATIVE CLINICAL TRIALS

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Consumer engagement (patient and public involvement) in perioperative medicine research is in its infancy. The patient experience and family/carer perspectives can provide an extra layer of insight to give more understanding as to what, why, and how we do research. Patients who have undergone surgery have a unique understanding of the issues, concerns, wants, and needs that they learned as a patient-they, therefore, can be considered as a professional given their experience(s)-thus warranting recognition as a partner in research. Knowledge of the consumer engagement literature and availability of resources should support anesthesia researchers aiming to include these perspectives in their research. This includes several existing engagement frameworks and assessment tools. We provide a framework for consumer engagement for adoption into anesthesia and other perioperative research. By incorporating the patient or caregiver into the design, funding application(s), data collection, and interpretation of the findings can be beneficial to all. This includes promoting knowledge and access to clinical trials, the wording of participant consent and information forms, methods of data collection, selection of important outcomes, and dissemination of results.

PSYCHIATRY

200.
HOW CAN WE IMPROVE THE WELLBEING OF YOUNG PEOPLE? PERSPECTIVES FROM 24,111 AUSTRALIAN ADOLESCENTS

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Background: Mental disorders represent the leading burden of disease among youth. Adolescence is a particularly vulnerable period, comprising the peak life stage for the onset of mental disorders. This necessitates effective strategies promoting adolescent mental health and wellbeing. The lack of adolescent involvement in the co-creation of these strategies, however, raises the possibility of a mismatch between existing strategies and the real-world needs, preferences and interests of adolescents. Our study thus sought to explore the suggestions of Australian adolescents on strategies to improve youth wellbeing. Methods: We analysed 2022 data from the Resilient Youth Survey, where Australian adolescents anonymously responded to the open-ended question: "If you could magically do anything, what is one thing you would do to support the wellbeing of young people?". Two reviewers independently applied content analysis to 50% of the free-text responses each, with a 10% overlap to assess inter-rater reliability. Subgroup analyses were conducted to investigate whether coding frequency differed by sociodemographic variables, including grade, gender, nationality, state, socioeconomic and rurality status. Findings: Following the removal of blank and non-responsive fields, 24,111 responses were coded. Inter-rater reliability was returned as substantial (0.66). We will present an overview of the suggested strategies mapped against the socio-ecological model of health, and a detailed breakdown of strategies for the most frequently coded categories (interpersonal relationships 31%, mental health and wellbeing 27% and school-level factors 11%). We will additionally present the salient trends identified by subgroup analyses. Conclusion: Our findings emphasise the complex amalgam of factors influencing youth wellbeing. We urge stakeholders including schools, researchers, public health and policy-makers to prioritise the suggestions of adolescents when formulating strategies to enhance youth wellbeing. We advocate for the ongoing integration of adolescent voice into the co-creation of promotive and preventive measures.

201.
THE PREVALENCE OF EARLY LIFE TRAUMA IN ENDOMETRIOSIS

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Endometriosis is a common chronic inflammatory gynaecological condition characterised by the abnormal presence of endometrial tissue outside the uterus. Different risk factors for endometriosis have been proposed, with some research finding a significant relationship between endometriosis and early life trauma.

AIM: To determine the prevalence of childhood trauma in a clinical sample of women with existing diagnosis of endometriosis compared with the prevalence of early life trauma in the general Australian female population. Furthermore, we aimed to evaluate the relevance of age and type of early life trauma experience.

METHODS: Participants were recruited from the MAPrc Women's Mental Health Clinic (WMHC). Women who self-reported a diagnosis of endometriosis were identified from the WMHC patient database, established in 2017. The

experience of early life trauma was determined by clinicians informed by, but not directly using, the Child Trauma Questionnaire. In patients who reported a presence of early life trauma, information regarding the type and age(s) of the early traumatic experience(s) was recorded. Type of trauma was classified as childhood emotional abuse, physical abuse, sexual abuse, or neglect. The age of trauma experience was classified by fixed age groups. The prevalence of each type of early life trauma in our participants was compared to the general female population in Australia.

RESULTS: Of 53 included participants, the mean (SD) age was 40.7 (10.2) years. 90.6% of participants (n=48) reported experience of early life trauma, most commonly within ages 6-10 (77.4%). The most reported type of trauma was emotional abuse. Prevalence was higher across all types of trauma in this cohort compared to the general female population: emotional abuse (81.1% vs 35.6%), neglect (45.3% vs 10.8%), sexual abuse (49.1% vs 37.3%), and physical abuse (34.0% vs 31.5%).

CONCLUSION: These preliminary findings suggest that early life trauma, in particular emotional abuse, is associated with endometriosis.

202.

PERSPECTIVES OF MENTAL HEALTH CLINICIANS ON PHYSICAL HEALTH OF YOUNG PEOPLE WITH EARLY PSYCHOSIS

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The aim of this study is to explore the views and understanding of youth mental health clinicians with regard to the physical health of young people with early psychosis and their perspectives on lifestyle interventions improving the health and well-being of young people with early psychosis. Physical health disparities leading to premature mortality among people with mental illness are well evident in the literature. Mental health and physical health are directly correlated. The risk of poor physical health often begins before the onset of mental ill health. Young people with early psychosis are highly susceptible to poor physical health. A co-designed integrated approach focusing on early prevention and intervention in overall well-being and health is imminent for this targeted population to prevent poor physical health trajectory across the lifespan. Ten clinicians were recruited and participated in this study through semi-structured interviews. Five themes were identified: (i) Impact of early psychosis, (ii) Focus of care, (iii) Conversations around physical health, (iv) Co-location of specialist roles and (v) Health literacy. The findings of this study confirm the dimensional impact of early psychosis on the well-being and health of young people through the vicious cycle of early psychosis. Promotion of health literacy along with social connectedness and elements of self-determination, as well as having a prime focus on the individuals' experience in the journey of health promotion through participation in lifestyle interventions, has been identified as critically prominent.

203.

CORTICAL THICKNESS IN TEN-YEAR-OLDS TWO YEARS PRIOR TO ONSET OF NON-SUICIDAL SELF-INJURY: RELATIONSHIP TO IMPULSIVITY

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Non-suicidal self-injury (NSSI) is the deliberate destruction of bodily tissue without suicidal intent. NSSI is associated with negative outcomes including increased impulsivity and suicide.

AIM: To identify biomarkers of NSSI risk in a prospective dataset that can inform development of novel treatments such as non-invasive brain stimulation.

METHODS: This was a secondary analysis of data from the Adolescent Brain Cognitive Development (ABCD) Study. Participants were 241 youths who reported no NSSI, suicidal ideation or attempt at baseline (aged 10), but who reported NSSI at 2-year follow-up (Y2). Individually demographically matched controls were 241 youths without NSSI at baseline or Y2. T1w baseline MRIs were preprocessed using the ABCD-HCP-pipeline. Impulsivity was measured using the Urgency, Perseverance, Premeditation and Sensation-Seeking, Positive Urgency scale (UPPS-P). Vertex-wise cortical thickness was calculated for each subject and groups compared using Permutation Analysis of Linear Models (10,000 permutations), covarying sex and ICV, using threshold-free cluster enhancement. Significance was $p < .05$, corrected.

RESULTS: The NSSI group had greater cortical thickness than controls in left posterior cingulate cortex, precuneus, cuneus, and superior parietal lobe and right superior temporal gyrus and bilateral parahippocampal gyrus. The NSSI group had lower cortical thickness than controls in right dorsal anterior cingulate cortex and gyrus rectus. In males with NSSI, this reduced thickness correlated negatively with UPPS-P Lack of Perseverance but in male controls this thickness correlated positively with Lack of Planning.

CONCLUSION: In the first study of structural brain changes that precede NSSI, we found reduced cortical thickness in regions involved in reward and inhibition in NSSI and increased cortical thickness in posterior default mode regions. Although associations with behaviour require disambiguation, disruption of the normal relationship between reward, inhibition and default mode circuits could be a mechanism of future NSSI suggesting non-invasive brain stimulation could be used to treat NSSI.

204.

EVALUATION OF THE CHILD AND YOUTH HOPE (CY HOPE) SERVICE AT ALFRED HEALTH USING A COHORT, MIXED-METHOD APPROACH

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Suicide is now the leading cause of death among young Australians aged 15-25 years. Following the success of the adult HOPE (Hospital Outreach Post Suicide Engagement), a similar model for young people was introduced at Alfred Health in 2022.

AIM
The aim was to determine to what extent the 3-month psycho-social outreach CY HOPE service was successful in reducing suicide risk and distress and improving well-being outcomes for the young people.

METHOD
A mixed methods approach was undertaken using age-appropriate standard measures. Quantitative data was collected at admission, discharge, 3-months and 6-months follow-up with qualitative data being collected via semi-structured interviews after discharge. Twenty-eight young people participated ranging from 12-25 years.

RESULTS
Linear Mixed Model analyses was conducted to test for significant changes in these measures over time, with an assumption of normality for the residuals. From entry to discharge the results found those age 12-16 years (N=5) there was a 16% increase in Life Quality (QoL), 13% increase in a sense of hope, 10% increase in resilience and 11% increase in wellness. For those age 17-25 years (N-23) there was a 20% increase in QoL, 17% decline in depression, 15% increase in resilience and 31% decline in suicidal ideation. Qualitative data indicated young people felt, there were benefits such as the provision of outreach, feeling supported and understood *"they let me be me…. I felt like I was seen and heard"*, practical supports, support for parents, and a less clinical approach, but some thought the period of engagement too short *"I'm still searching for help".*

CONCLUSION
This evaluation showed that the CY Hope model of care is effective in meeting the needs of young people and their families. However, the findings are limited due to the small sample size and future research should consider a longer data collection period.

205.
BAZEDOXIFENE PLUS CONJUGATED ESTROGEN TO TREAT MENOPAUSAL DEPRESSION – A PILOT STUDY

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BACKGROUND: Gonadal hormone fluctuations in the menopausal transition, particularly the decline in brain estrogen levels, significantly contribute to menopausal depression. Although hormone replacement therapy, known as 'menopause hormone therapy (MHT)', effectively manages physical symptoms, it is not routinely used for mental health disturbances due to limited large-scale clinical trial evidence comparing MHT with standard antidepressants. Concerns about the long-term safety of estrogen and progestins have prompted the exploration of alternative hormone therapies. Bazedoxifene, a selective estrogen receptor modulator, in combination with conjugated estrogens, is a newer, safe option for physical menopause symptoms.

AIM: To evaluate the effects of combined MHT (bazedoxifene plus conjugated estrogen) on menopausal depression.

METHODS: Thirty-seven women participated in our 12-week double-blind, randomised, placebo-controlled pilot study. Twenty participants received bazedoxifene plus conjugated estrogen, while 17 received placebo. The primary measures were the Montgomery-Asberg Depression Rating Scale and Meno-D. These were administered at baseline and week 12.

RESULTS: Both treatment groups had a decrease in the standard depression rating scale (Montgomery-Asberg Depression Rating Scale) scores from baseline to week 12. However, the decrease was not significantly different between groups. When we used our specific menopause depression rating scale – the Meno-D - we found that women receiving bazedoxifene plus conjugated estrogen improved significantly more compared to women taking the placebo.

CONCLUSION: Combined hormone therapy effectively targets the unique symptoms that constitute menopausal depression. Further research is needed to develop targeted treatments for menopausal depression – which appears to be a different type of depression that responds to hormone therapy.

206.

ADHD IN FEMALES: HOW DO SYMPTOMS RELATE TO HORMONAL LIFE STAGES?

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Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition associated with excessive levels of inattention, hyperactivity and/or impulsivity. Symptoms usually persist into adulthood and negatively impact functioning and quality of life. Although sex differences in ADHD are commonly reported, ADHD remains under-recognised in females (including women and people assigned female at birth) with limited knowledge about ADHD in the context of the unique hormonal environment.

AIM: This study aimed to investigate the experience of females with ADHD across hormonal life phases and menstrual cycle phases.

METHOD: A cross-sectional sample of 607 female participants who identified as having an ADHD diagnosis and ADHD symptoms, completed an online survey between June and November 2023. Symptoms of ADHD, depression, anxiety and stress using validated scales and self-reported symptoms at different hormonal life stages were explored.

RESULTS: Retrospective self-reports suggested the majority of participants experienced worsening of ADHD symptoms during the postpartum period and menopause. A cross-sectional analysis of scores on the Adult ADHD Self Report Scale (ASRS) indicated similar symptom severity in all hormonal life phases. A large percentage (84%) of premenopausal participants not taking hormonal therapy reported a change in their ADHD symptoms across the menstrual cycle, with most reporting a worsening during the luteal phase.

CONCLUSION: Findings provide novel evidence of ADHD symptom profiles in hormonal contexts unique to females, confirming anecdotal clinical experiences and suggest a need for further research. Understanding how ADHD symptoms may be associated with hormonal experiences of females is integral to ensuring effective care.

RESPIRATORY MEDICINE

207.

LACK OF DIVERSITY IN CLINICAL TRIAL POPULATIONS FOR MAINTENANCE INHALER THERAPY IN PEOPLE WITH COPD

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Introduction/Aim: Social determinants of health (SDH; sex, socioeconomic status, ethnicity, occupation, and education) play a key role in disease prevalence and progression in chronic obstructive pulmonary disease (COPD) and may impact acceptability or effectiveness of treatments. To date there have been no studies examining the reporting and inclusion of SDH in clinical trials of long-acting muscarinic antagonists (LAMA) and long-acting beta agonists (LABA) inhalers. This review aimed to 1. examine recruitment strategies to target diverse populations in COPD clinical trials of LAMA +/- LABA inhalers, and 2. determine if SDH are reported in primary trial documents or published results.

Methods: Four clinical trials databases (CENTRAL, Clinicaltrials.gov, ISRCTN and ANZCTR) were searched to identify LAMA and/or LABA clinical trials in adults with COPD between 01/01/2000 and 08/05/2023. Extracted data included: study location(s), targeted SDH, recruitment strategies, study outcomes, and eligibility criteria. Reporting of SDH was examined from trial database records and associated published papers from 01/01/2018 to 08/05/2023.

Results: Of 1822 trials identified, 491 primary trials were included, 407 of which had results available and 341 had associated publications. Age (n=387 trials, 95.1%) and sex (n=386 trials, 94.8%) were well reported in published results. Of 256,271 participants in published results describing sex, there was a male preponderance (n=176307, 68.8%). 207 (50.9%) trials reported on race, which demonstrated an overrepresentation of white individuals (n=130,086, 83.2%). Only one trial reported either SES or occupation. No trials reported on education or rurality. Trials were mainly conducted in high or upper-middle income countries (95.8%).

Conclusion: SDH, other than age and sex, were under-reported in LABA and/or LAMA COPD trials, and when reported, lacked diversity in ethnicity among trial participants. Future trials must include and report on diverse populations to demonstrate efficacy for all people in all contexts.

208.

LUNG TRANSPLANT SURVIVAL FROM DONORS ≥65 YEARS IS EQUIVALENT TO THAT OF YOUNGER DONORS

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Although the demand for allografts continuously surpasses the supply, the majority of lungs offered for transplant (LTx) are declined based on various factors, including donor age. In the US, more than 15000 lungs consented for LTx were discarded in the last two decades based on donor age (>60) alone.
Aim: To compare the outcomes of LTx recipients from a large single centre cohort stratified according to the donor age < and ≥65 years.

Methods: In this single-centre, longitudinal study we included 1101 LTx performed at The Alfred between January 2010 and December 2023. Univariate Cox proportional hazards regression was used to assess the timing and distribution of graft survival after LTx. Multivariate Cox proportional hazards regression was used to assess donor risk factors (donor age ≥65, FiO2 >300, X-ray changes, diabetes, and smoking history).

Results: The median age of LTx recipients was 58 years (IQR 45-64), 57% were male and the median follow-up was 4 years (IQR 2-7). The most prevalent LTx indication was COPD (38%). Donors ≥65 years were used in 146/1101 (13%) of all LTx. LTx recipients of older donors were themselves older (60 years [IQR 56-65] vs 58 years [IQR 43-64], p<0.001). The proportion of graft failure was similar between groups (41% vs 34%, p=0.109). Most importantly, graft survival was similar irrespective of donor age ≥65 years (HR 0.84, 95% CI 0.62-1.13, p=0.24). Survival remained similar between groups also when older donor age was paired with an ischemic time >7h (p=0.254). The multivariate analysis showed that the X-ray abnormalities were the only donor risk factor associated with increased mortality (HR 1.26, 95%CI 1.01-1.58, p=0.04).

Conclusion: Contrary to earlier US reports, graft survival is similar for lungs retrieved from donors <65, compared with donors ≥65. Appropriately assessed age-extended lungs should be routinely considered for clinical LTx.

209.

SOCIAL DETERMINANTS OF HEALTH AND ACCESS TO CLINICAL TRIALS FOR PEOPLE WITH IDIOPATHIC PULMONARY FIBROSIS

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Introduction/Aim: Social determinants of health (SDH; age, sex, race/ethnicity, socioeconomic status, and rurality) can influence development, progression, and patterns of care for people with interstitial lung disease (ILD). Failure to include diverse participants in clinical trials can hinder generalisability. It is unclear whether clinical trials investigating anti-fibrotic therapies for people with ILD have been conducted in diverse and representative populations. This study aimed to investigate the active consideration and reporting of SDH in clinical trials of anti-fibrotic therapies for people with ILD.

Methods: A search of four registries (clinicaltrials.gov, ANZCTR, ISRCTN, and CENTRAL) was conducted for clinical trials investigating anti-fibrotic therapies for people with ILD registered from 01/01/2000 until 03/09/2023. Data were extracted regarding trial phase and status, recruitment strategies, and eligibility criteria. If trial results were available, reporting of SDH data from participant demographics and subgroup analyses were extracted.

Results: Of 313 records identified, 70 trials were included. The majority of trials were phase II or III (77%); 56% were completed and 61% had published results. Of 70 registered trials, all specified age and sex but no other SDH within recruitment strategies or eligibility criteria. Of 43 trials reporting results, all reported age and sex of participants and 40 (95%) reported race/ethnicity. Descriptors for race/ethnicity varied considerably. No other SDH were reported. 10,387 participants were described, of which 74% were male, 77% were White, 16% were Asian and <1% were Black. Five trials (12%) included only White participants and three (7%) included only Asian participants. Four trials (9%) reported subgroup analyses by race/ethnicity and three (7%) reported subgroup analyses by sex.

Conclusions: Consideration and reporting of SDH beyond age, sex, and race/ethnicity were absent. Trial populations were predominantly male and White. There is a need to actively consider SDH to ensure diverse and representative clinical trial populations.

210.

INVESTIGATION OF EXERTIONAL DYSPNOEA BY CARDIOPULMONARY EXERCISE TESTING WITH CONTINUOUS LARYNGOSCOPY

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AIM: Abnormal breathlessness at maximal exercise may be caused by a range of conditions, including exercise-induced bronchospasm (EIB), breathing pattern disorder (BPD), or exercise-induced laryngeal obstruction (EILO). These three disorders may not be detected on standard cardiopulmonary exercise testing (CPET). The aim of this study was to describe diagnostic outcomes of an expanded protocol during CPET.

METHODS: Patients presenting with abnormal breathlessness on maximal exercise underwent continuous laryngoscopy with CPET (CL-CPET) on stationary cycle ergometer. BPD was evaluated by video and ventilatory data. Pre and post-exercise spirometry was performed.

RESULTS: 24 adult patients were evaluated, 10 were professional athletes. Mean age was 40 years (range 18-73). Nine of 24 (38%) were diagnosed with EILO and referred for speech pathology. Six of these had supraglottic EILO; all were aged < 30 years; five were professional athletes. One patient had BPD and was referred for physiotherapy; one had EIB, requiring escalation of asthma medication; one had muscle tension dysphonia resulting in referral to an otolaryngologist who administered a laryngeal injection of botulinum toxin. A further four patients had unexplained lower maximal oxygen consumption with cardiac limitation and were referred for further cardiac investigation.

CONCLUSION: In patients reporting abnormal breathlessness at maximal exercise, this expanded exercise protocol provided diagnostic information in 66.7% cases which contributed to further personalised management.

211.

SINGING FOR BREATHING IN PEOPLE WITH COPD AND ILD: LONGITUDINAL QUALITATIVE INTERVIEW STUDY

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INTRODUCTION: During the COVID-19 pandemic, many international singing for lung health programs transitioned to online delivery for wider reach. Limited evidence exists regarding the accessibility and effectiveness of these programs. "SINFONIA: A clinical trial examining the benefits of SingINg For breathing in COPD aNd ILD pAtients" adopted this novel online delivery approach in Australia.

AIM & METHODS: Longitudinal qualitative interviews were conducted to determine the attitudes and knowledge of people with chronic obstructive pulmonary disease or interstitial lung disease and their carers participating in the program. We sought to understand how their views may evolve, explored any barriers and enablers to participating online and analysed qualitative data for descriptive and analytical themes.

RESULTS: From 44 patients (12 women and 12 men, aged 50-89) and 6 carer interviews, five themes emerged: 1. anticipation and simultaneous reluctance to participate; 2 the personal power of music; 3. building a sense of mastery; 4. opportunities of group membership; and 5. delivery of SINFONIA. With technological support, even participants with limited digital literacy could transition from anxiety to mastery of their chronic condition by accessing the online program. Findings highlighted engagement complexities and reduced social isolation through group interactions.

CONCLUSION: Participants, including those facing technological challenges, received support to actively engage in the program, ultimately reducing their social isolation. Future work should involve patients and carers in program design and development to enhance intervention scalability and determine the most effective delivery mode for broader implementation.

212.

IS MECHANICAL POWER AN UNDER-RECOGNISED ENTITY WITHIN THE PRETERM LUNG?

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Background: Mechanical power is a major contributor to lung injury and mortality in adults receiving mechanical ventilation. Recent advances in our understanding ofmechanical power have allowed the different mechanical components to be isolated. The preterm lung shares many of the same similarities that would indicate mechanical power may be relevant in this group. To date, the role of mechanical power in neonatal lung injury is unknown. We hypothesise that mechanical power maybe useful in expanding our understanding of preterm lung disease. Specifically, that mechanical power measures may account for gaps in knowledge in how lung injury is initiated.

Hypothesis-generating data set: To provide a justification for our hypothesis, data in a repository at the Murdoch Children's Research Institute, Melbourne (Australia) were re-analysed. 16 preterm lambs 124–127d gestation (term 145d) who received 90 min of standardised positive pressure ventilation from birth via a cuffed endotracheal tube were chosen as each was exposed to three distinct and clinically relevant respiratory states with unique mechanics. These were (1) the respiratory transition to air-breathing from an entirely fluid-filled lung (rapid aeration and fall in resistance); (2) commencement of tidal ventilation in an acutely surfactant-deficient state (low compliance) and (3) exogenous surfactant therapy (improved aeration and compliance). Total, tidal, resistive and elastic-dynamic mechanical power were calculated from the flow, pressure and volume signals (200 Hz) for each inflation.

Results: All components of mechanical power behaved as expected for each state. Mechanical power increased during lung aeration from birth to 5 min, before again falling immediately after surfactant therapy. Before surfactant therapy tidal power contributed 70% of total mechanical power, and 53.7% after. The contribution of resistive power was greatest at birth, demonstrating the initial high respiratory system resistance at birth.

Conclusions: In our hypothesis-generating dataset, changes in mechanical power were evident during clinically important states for the preterm lung, specifically transition to air-breathing, changes in aeration and surfactant administration. Future preclinical studies using ventilation strategies designed to highlight different types of lung injury, including volu-, baro- and ergotrauma, are needed to test our hypothesis.

213.

SOCIAL DETERMINANTS OF HEALTH IN CLINICAL TRIALS EXAMINING LONG-TERM ORAL ANTIBIOTICS IN COPD: A SYSTEMATIC REVIEW

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INTRODUCTION: Social determinants of health (SDH) including age, gender, ethnicity, socioeconomic status, education, occupation, and rural status impact the development and prognosis of chronic obstructive pulmonary disease (COPD). It is currently unclear whether SDH are reported or considered in clinical trials examining the efficacy of long-term oral antibiotics (LTOA) in people with COPD.

AIM: To investigate the reporting and consideration of SDH in clinical trials of LTOA in people with COPD.

METHODS: A search of three clinical trial registries (clinicaltrials.gov, ANZCTR, ISRCTN) and Cochrane CENTRAL was conducted for trials involving LTOA prescribed to people with COPD registered between 1st Jan 2000 and 7th May 2023. Data were extracted regarding trial location, recruitment strategies, and eligibility criteria. Where available, reporting of SDH data and relevant subgroup analyses were extracted.

RESULTS: From 781 trials identified, 17 trials were included in this review. Most (94.1%) trials were conducted in high-income countries alone. 94.1% of trials described age and gender, and 12.5% described ethnicity within recruitment strategies or eligibility criteria. No other SDH were reported in recruitment or eligibility criteria. Of 7 completed trials with publicly available results (n=2888), all reported age and gender and 42.9% reported ethnicity, with no other SDH reported. Participants were predominantly male (33.7% female) and White (72.6% to 99.0%).

CONCLUSION: There was limited reporting of SDH in clinical trials investigating the efficacy of LTOA in people with COPD, and those that did report this information, demonstrated limited participant diversity. Consequently, the safety and effectiveness of LTOA in underrepresented patient populations remain unclear. Proactive recruitment of diverse populations and greater transparency in trials' reporting of participant demographics is needed.

214.

A PHASE II FEASIBILITY TRIAL OF DOMICILIARY NASAL HIGH FLOW THERAPY FOR BREATHLESSNESS IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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Introduction/Aim: Nasal high flow therapy (NHF) is an established treatment for acute respiratory failure, however data regarding benefits of domiciliary NHF in people with COPD are limited. This phase II trial aimed to determine feasibility and acceptability of NHF for people with COPD and severe breathlessness.

Methods: A single-arm, open label, mixed methods, phase II trial of an 8-day, air-only NHF intervention in adult patients with COPD and severe breathlessness not requiring domiciliary oxygen therapy.

Results: 15 participants were enrolled (mean age 73.6; 40% women; mean FEV_1 41% predicted; mean DLco 43% predicted; mean mMRC 3.7). 87% completed the trial with 54% keeping the device, 20% reported continued

use at 8 months post-trial. Adherence varied, with average daily usage higher amongst participants who kept the device compared to those who returned it (6.8±2.3h vs 3.4±3.7h). No significant changes in mean difference at day 8 relative to baseline were detected for worst breathlessness (0.7±1.2 (mean±SD), p=0.109), dyspnoea mastery (0.3±0.6, p=0.176) or fatigue (0.0±2.4, p=1.00). No significant adverse events were reported. Qualitative interviews demonstrated subjective improvements in breathlessness, dry mouth, and sputum production for some, whilst others found NHF uncomfortable. Fear of NHF dependence and concerns regarding long-term running costs were reported.

Conclusions: Domiciliary NHF was a feasible intervention, with varied adoption and acceptability. Trial implementation outcomes may have affected preliminary effectiveness outcomes. Further research is required to determine what role domiciliary NHF may have for people with COPD and severe breathlessness.

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