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Abstract Book

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ALLERGY AND IMMUNITY

1. FUNCTIONAL ASSESSMENT OF THE NOD2 SIGNALLING PATHWAY IN PATIENTS WITH PRIMARY IMMUNODEFICIENCY

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Despite advances in genomics, many primary immunodeficient (PID) patients remain genetically undiagnosed, limiting access to targeted therapeutics. In diagnosed antibody deficient patients, 70% of affected genes function in one of 5 critical immune signalling pathways. One is downstream of nucleotide-binding oligomerization domain-2 (NOD2), a receptor for muramyl dipeptide (MDP). We aimed to establish a robust assay to functionally assess 3 variants of unknown significance (VUS) within this pathway.

METHODS: Whole-exome-sequencing was performed on 3 PID patients. Patients' immune cells were evaluated by flow cytometry for L18-MDP-induced (NOD2-dependent) production of intracellular TNF-α. LPS-stimulated (NOD2-independent control) and unstimulated (negative control) samples were run concurrently.

RESULTS: In healthy donors, L18-MDP induced TNF-α production in 52% (range 27.9-95.9%) of monocytes. Three patients with X-linked lymphoproliferative disease due to an *XIAP* mutation had absent NOD2-dependent TNF-α production. In contrast, a patient with a heterozygous *TNFAIP3* (A20) VUS (p.Q150R) demonstrated high TNF-α production (82.8%) whilst another with a heterozygous *XIAP* VUS (p.Y139C; 32%) and one with a heterozygous *NOD2* VUS (c.2546+2dupT; 29%) exhibited low TNF-α production, but all within the healthy control range.

CONCLUSION: Here we show assessment of NOD2-dependent TNF-α production is able to identify patients with complete loss-of-function phenotypes. Due to the large spread in healthy controls, other read-outs are required for interpretation of subtler defects, such as L18-MDP-induced p38 and p65 phosphorylation. This *ex vivo* functional evaluation of immune pathways could provide rapid insights into pathogenicity of VUS, thereby expediting genetic diagnosis and treatment in PID patients.

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

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P-cresol sulfate is a microbial metabolite derived from L-tyrosine and was recently discovered to have immunoregulatory influences on allergic airway inflammation. Administering p-cresol sulfate 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 p-cresol sulfate as a molecular template to develop novel therapeutics against allergic asthma.

AIM: To determine the molecular mechanism of action of p-cresol sulfate and its molecular derivatives in alleviating allergic airway inflammation.

METHODS and RESULTS: 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 p-cresol sulfate. RNA sequencing of *ex vivo* mouse lung epithelial cells revealed that p-cresol sulfate 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 p-cresol sulfate 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 p-cresol sulfate and molecular derivative treated cells.

CONCLUSION: P-cresol sulfate acts on lung epithelial cells to reduce CCL20 production and consequently allergic airway inflammation. These results implicate EGFR and AHR in mediating the effects of p-cresol sulfate and its molecular derivatives. Overall, understanding the molecule's mechanism of action could lead to development of novel therapeutics against allergic asthma and other atopic diseases.

3. THIRD DOSE MRNA BOOSTER ENHANCES IGG4 ISOTYPE SWITCHING AND RECOGNITION OF OMICRON SUBVARIANTS BY MEMORY B CELLS AFTER MRNA, BUT NOT ADENOVIRUS PRIMING

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Global SARS-CoV-2 vaccination programs involved novel adenovirus and mRNA-based formulations, currently followed by mRNA boosters. While booster doses provide improved protection against severe disease from variants-of-concern (VoC), it remains unclear if this differs based on the primary vaccination type. We here addressed this by examining plasma IgG and memory B-cells (Bmem) directed against Wuhan-1 and Omicron subvariants following homologous (mRNA/mRNA) or heterologous (adenoviral/mRNA) boosters.

Healthy adults who received a primary BNT162b2 (Pfizer mRNA) (n=18) or ChAdOx1 (AstraZeneca vector) (n=25) vaccination were sampled 1 month and 6 months after their 2nd and 3rd dose (homologous or heterologous) vaccination. Recombinant nucleocapsid and spike receptor binding domain (RBD) from Wuhan, Omicron BA.2 and BA.5 variants were produced for ELISA-based serology, and tetramerized with fluorescent streptavidins for immunophenotyping of RBD-specific Bmem.

Dose 3 boosters transiently raised RBD-specific plasma IgG after 1 month and declined at 6-months. RBD-specific Bmem numbers were increased by ~2 fold at both 1- and 6-months post-dose 3, and these were predominantly IgG1+; up to 70-80%. mRNA double-dose vaccination elicited a population of IgG4+ Bmem, which expanded to 5-20% after dose 3. Heterologous vaccinated individuals did not form an IgG4+ Bmem population. Recognition of Omicron BA.2 and BA.5 by vaccine-elicited RBD-specific plasma IgG increased from 20% to 60% after the 3rd dose in both cohorts. Reactivity of RBD-specific Bmem to Omicron BA.2 and BA.5 only increased in homologous vaccinated individuals from 40% to 60%, whereas no significant changes were observed in the heterologous vaccine group.

A 3rd mRNA dose generates similarly robust serological and Bmem responses in homologous and heterologous vaccine groups and RBD-specific Bmem numbers remained stable between 1- and 6-months post-dose 3. mRNA primary vaccination was associated with expansions of IgG4+ Bmem, suggesting that the formulation or dosing schedule might differentially affect continual germinal centre activity and antibody maturation.

4. QUANTIFYING THE LIFESPAN OF IGE ANTIBODY-SECRETING CELLS IN MOUSE ALLERGIC AIRWAY DISEASE

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IgE antibodies cause allergies and are produced by IgE antibody-secreting cells (ASC). A school of thought proposes that all IgE ASC are short-lived, yet recent work using indirect measures reports a population of long-lived IgE ASC in mouse bone marrow, the site of long-lived ASC retention.

AIM: To resolve whether IgE ASC are short- or long-lived in house dust mite (HDM)-driven allergic airway disease.

METHODS: n=30 mice in which cre activity marks ASC with human CD4 (hCD4) were put through an allergy model. In the model, mice receive HDM intranasally three-times weekly for fifteen weeks. At the cessation of HDM exposures, cre was activated by tamoxifen gavage, marking ASC as hCD4+. Draining mediastinal lymph nodes, spleens and bone marrow of groups of n=6 mice were analysed for hCD4+ IgE ASC 2, 7, 21, 42 and 63 days later by flow cytometry. The IgE ASC half-life was calculated and compared to that of IgG1 ASC.

RESULTS: Two days after the final HDM exposure, mice possessed a geometric mean 2840 (range 864-9350) $hCD4^+$ IgE ASC and 77600 (range 33800-178000) $hCD4^+$ IgG1 ASC. hCD4+ IgE ASC declined with a half-life of ≈8 days while hCD4+ IgG1 ASC had an ≈17-day half-life. Approximately 10% of the starting IgG1 ASC were retained, with >80% of these residing in bone marrow at endpoint, whereas only 4% of IgE ASC remained at endpoint and these dispersed across multiple tissues, with <10% residing in bone marrow.

CONCLUSION: IgE ASC have a shorter half-life than contemporaneously generated IgG1 ASC and fail to populate bone marrow in meaningful numbers. The failure to accrue in bone marrow suggests that allergies are likely maintained by continuous IgE ASC production. Targeting IgE ASC formation rather than persistence may thus be a better means to control IgE-associated diseases such as allergy.

5. ALLERGEN IMMUNOTHERAPY MODIFIES ALLERGEN-SPECIFIC TYPE 2 MEMORY B CELLS IN PATIENTS WITH RYE GRASS POLLEN AND BEE VENOM ALLERGY

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Allergen immunotherapy (AIT) is the primary treatment for allergies, but its effectiveness varies. Understanding the reasons behind this variability and how AIT modifies the immune response is crucial for improving treatment outcomes. Recently, a type 2 memory B cell (Bmem) population expressing FCER2 (CD23) and IL4R was identified that was increased in allergic individuals. Here, we investigated type 2 Bmem in individuals allergic to bee venom (BVM) and rye grass pollen (RGP). While type 2 Bmem were present in these two allergic cohorts, significantly increased frequencies of type 2 Bmem with allergen-specificity (i.e. Lol p 1 for RGP, or Api m 1 for Lol p 1) were identified. This suggests that a large proportion of type 2 Bmem cells are specific to Lol p 1 in RGP allergy and Api m 1 in BVM allergy. We then examined the impact of AIT on type 2 Bmem cells. Increased expression of type 2 markers (FCER2 and IL4R) were found in Lol p 1-specific Bmem from RGP allergic subjects after AIT. AIT significantly expanded allergen-specific type 2 Bmem in both RGP and BVM cohorts upon AIT, while they did not change in subjects not receiving AIT. Additionally, AIT induced the expansion of CD29+ and IgG4+ type 2 Bmem in both allergic cohorts. These findings suggest that AIT promotes the expansion of allergen-specific type 2 Bmem cells and induces a modification of their phenotype. The discovery of type 2 Bmem cells and their association with AIT effectiveness provide insights into the potential role of these cells in allergen desensitization. Further research is aimed at understanding the function of type 2 Bmem cells in allergy and their contribution to allergen desensitization upon AIT.

ALLIED HEALTH

6. IMPACT OF TEST INSTRUCTIONS ON 6-MINUTE WALK DISTANCE IN ADULTS WITH CHRONIC RESPIRATORY DISEASE: A RANDOMISED CONTROLLED TRIAL

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INTRODUCTION: The 6-minute walk test (6MWT) is commonly used to assess functional exercise capacity in people with chronic respiratory disease in both clinical and research settings. However, two tests are required to achieve accurate results, due to a well-documented learning effect for 6-minute walk distance (6MWD). Whether it is possible to reduce or eliminate the learning effect by optimising 6MWT instructions is not known.

METHODS: People with chronic respiratory disease referred to pulmonary rehabilitation undertook two 6MWTs with random allocation to modified instructions (fast – walk as fast as possible) or usual instructions (far – walk as far as possible). The primary outcome was the learning effect, defined as the difference in 6MWD between test 1 and test 2. Subgroup analyses investigated whether effects varied in those who were naïve to 6MWT, or according to diagnosis (chronic obstructive pulmonary disease, interstitial lung disease, bronchiectasis).

RESULTS: A learning effect was present in both groups, with mean improvement in 6MWD on the second test of 14 metres in the fast (modified) group (95% CI 6 to 22) and 11 metres in the far (usual) group (95% CI 4 to 19). There was no statistically or clinically significant difference between groups in the magnitude of the learning effect (between group difference -3 metres, 95% CI -14 to 8). There was no significant effect of naivety to 6MWT or diagnosis.

CONCLUSION: Instructing patients to walk as fast as possible during the 6MWT did not affect the learning effect for 6MWD. The current recommended procedures for 6MWT, including standardised instructions and performance of two tests on each occasion, should be retained.

7. WALKING FOR TRANSPORT AND ALL-CAUSE MORTALITY: THE ASPREE LONGITUDINAL STUDY OF OLDER PERSONS

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BACKGROUND: Walking for transport may prolong survival in younger and middle-aged adults, however, evidence for older adults is scarce. We examined a prospective relationship between transport-related walking and all-cause mortality among adults aged 70 years and over.

METHODS: Community dwelling, apparently healthy older adults (n = 11,699; mean age 75.1 years, 53.2% females), participants of the ASPREE Longitudinal Study of Older Persons, reported their frequency of transport-related walking (never, rarely/once a week, more than once a week or every day). All-cause mortality was verified by two independent sources. Cox proportional-hazards models (hazard ratios [HR] and 95% CI) assessed the association between transport-related walking and all-cause mortality.

RESULTS: Of participants, 44.2% reported walking every day, 31.3% more than once a week, 21.7% rarely or once a week, and 2.8% never engaged in transport-related walking. During the median follow-up of 6.4 years (IQR: 5.4-7.8), 958 (8.2%) died. Compared to those who reported never walking for transport, the risk of all-cause mortality was lower for those walking rarely or once a week (HR 0.71 95%CI: 0.51-0.99); more than once a week, (HR 0.69 95%CI: 0.50-0.95); and every day (HR 0.64 95%CI: 0.46-0.89). Analyses were adjusted for age, sex, education, smoking, alcohol consumption, living status, rurality, household income, socio-economic status, chronic conditions, and BMI.

CONCLUSION: Engaging in any weekly transport-related walking helps older adults prolong survival. Public health campaigns and urban planning should promote and support transport-related walking to boost physical activity levels of older adults and support healthier aging.

8. DEVELOPMENT AND PRELIMINARY VALIDATION OF A NOVEL EATING DISORDER SCREENING TOOL FOR VEGETARIANS AND VEGANS

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INTRODUCTION: Eating disorders have one of the highest mortality of all mental illnesses but are associated with low rates of screening and early intervention. In addition, there remains considerable uncertainty regarding the use of current standardised screening tools in measuring eating pathology in minority groups such as vegetarians and vegans. With these groups presenting as potential at-risk groups for disordered eating development, the present study aimed to develop and preliminary validate a novel eating disorder screening tool, the Vegetarian Vegan Eating Disorder Screener (V-EDS).

METHODS: We utilised a mixed-methods approach, comprising four phases.

RESULTS: A conceptual framework was developed from 25 community, clinician, and lived experience interviews and used to derive a preliminary set of 163 items (Phase 1). Phase 2 piloted the items to establish face and content validity through cognitive debriefing interviews of 18 additional community, clinician, and lived experience participants, resulting in a reduced, revised questionnaire of 53 items. Phase 3 involved scale purification using Item Response Theory in analysis of 230 vegetarians and 230 vegans resulting in a further reduced 18-item questionnaire. Phase 4 validated the screening tool in a large community sample of 245 vegetarians and 405 vegans using traditional psychometric analysis, including factor analysis, construct validity, and test-retest reliability.

CONCLUSION: This study provided strong initial support for the psychometric validity and theoretical assumptions of the novel V-EDS screening tool. The V-EDS has the potential to increase early intervention rates for vegetarians and vegans experiencing eating disorder symptoms, further supporting advocacy and treatment approaches for these expanding dietary groups.

9. EFFECT OF EARLY PHYSICAL REHABILITATION ON FUNCTIONAL OUTCOMES AFTER TRAUMATIC INJURY: A SYSTEMATIC REVIEW

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BACKGROUND: After traumatic injury, adults report decreased mobility and physical function, reduced health-related quality of life (HRQOL), and mental health problems for several years. Early rehabilitation in the acute setting has been shown to enhance recovery from stroke, traumatic injury and hip fracture. A multidisciplinary approach is required to address the complexities of traumatic injuries.

AIM: To determine if early rehabilitation delivered by PT and occupational therapy (OT) resulted in improved physical function following traumatic injury.

METHODS: Three electronic databases (Ovid MEDLINE, Embase, and CINAHL) were searched from inception to December 2023. Studies that delivered either unidisciplinary or multidisciplinary early rehabilitation following major trauma were identified. We included studies that reported outcomes related to physical function and/or differences in HRQOL, physical impairments, mortality, adverse events, length of stay, and discharge destination. Two researchers independently extracted data and evaluated study quality using the Cochrane Risk of Bias 2 tool.

RESULTS: Three randomised controlled trials were included with six outcome measures of physical function, five outcome measures of HRQOL, and two outcome measures assessing physical impairments. Only two studies reported on length of stay and discharge destination. Meta-analysis of data was not feasible due to the varied outcome measures between the included studies. One study reported improved physical function on acute hospital discharge after early PT interventions. Post acute admission, early physical rehabilitation may favour home as a discharge destination although this effect was not significant. The dosage of early rehabilitation after traumatic injury remains unclear as this has not been investigated.

CONCLUSION: There is limited evidence on the outcomes and components of early rehabilitation after traumatic injury. Further studies developing core outcome measures in major trauma are needed to enable meta-analyses, and subsequently determine the effect on physical function and dosage of PT/OT interventions.

10. TRACHEOSTOMY EDUCATION FOR INTENSIVE CARE NURSING STAFF: AN INTERPROFESSIONAL EDUCATION APPROACH BY PHYSIOTHERAPISTS AND SPEECH PATHOLOGISTS

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BACKGROUND: The care of patients with a tracheostomy in intensive care settings requires complex skillsets and knowledge. Upskilling staff through interprofessional education models may help to improve clinical care and patient outcomes. The aim of this project was to determine the impact of interprofessional bedside education on nurse confidence with tracheostomy management.

METHODS: This was a single site pre-post study conducted over four months in a large intensive care unit. The intervention was individualised bedside education for nursing staff on up to four identified tracheostomy topics lead by allied health: ventilation and humidification, suctioning, Passy Muir Valve, and cuff deflation. Confidence ratings for each topic were collected pre and post the session using a 7-point Likert scale. Data was also collected about the quality of education, and the use of an interprofessional mode of education delivery.

RESULTS: 69 education sessions were delivered. The pre-test to post-test confidence ratings improved by a median of 2 points (95%CI 1.5-2.5, $p<0.001$). All nursing staff agreed the education session contributed to supporting their knowledge and skills for managing tracheostomy patients. Nursing staff also reported an increased understanding of the roles of allied health and an increased ability to work collaboratively in an interprofessional team.

CONCLUSION: Interprofessional education can successfully increase nursing staff confidence and skill building in the area of tracheostomy management. The use of interprofessional education also improves knowledge about allied health professionals and improves collaborative practice. Interprofessional education could be further utilised to provide education on other topics and in other settings.

ACKNOWLEDGEMENT: This study was conducted by staff in Allied Health Clinical Educator positions which were funded by the Victorian Department of Health.

11. INCIDENCE AND MANAGEMENT OF PERIPHERALLY INSERTED CENTRAL CATHETER-ASSOCIATED VENOUS THROMBOSIS IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCY

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Peripherally inserted central catheters (PICCs) are associated with complications including PICC-associated venous thrombosis (PAVT). The reported incidence of PAVT varies and primary thromboprophylaxis is not currently recommended. Additionally, anticoagulation strategies for managing PAVT vary.

AIM: To evaluate the incidence and management of PAVT in haematology patients at a quaternary referral centre.

METHOD: Retrospective cohort study of patients with haematological malignancy with PICC inserted between January 2020-December 2021, identified by radiology. Data were collected from electronic medical records; follow-up was one-month post PICC removal or up to 12-months following PICC insertion. The primary outcome was the incidence of objectively confirmed PAVT. Secondary outcomes included the management of PAVT and proportion of patients with subsequent venous thromboembolism (VTE) . Data was analysed descriptively, and chi-squared test was used to compare subgroups, with $p<0.05$ considered statistically significant.

RESULTS: There were 445 PICC insertions identified among 293 patients (average 1.5, range 1-6). The majority of participants were male (58%), median age was 66.2 years (IQR: 55.9,73.3). 270 (92.1%) patients had active cancer and 43 (14.7%) had a history of thrombosis. Median PICC dwell time was 30.5 days (13.3,71.8). There were 30 PAVT events (6.7%, 95% CI:4.6-9.5%) with median onset at 11 days (7,22), Two of these patients (6.7%) developed VTE (PE=1, proximal DVT=1). There were no significant differences in baseline demographics between patients with PAVT and those without. PAVT management included therapeutic anticoagulation (n=11, 36.7%), variable clinician-led anticoagulant dosing according to platelet count (7, 23.3%) and intermediate/prophylactic dose (2, 6.6%). Ten (33.3%) PAVT events were not prescribed anticoagulation. PICC removal following PAVT occurred in 16 (53.3%) patients.

CONCLUSION: The incidence of PAVT was 6.7% in this high-risk group, consistent with reported literature; subsequent VTE was infrequent. Significant heterogeneity exists in the management of PAVT, warranting standardisation of practice.

12. WHICH DIETARY ASSESSMENT METHODS ARE USED TO QUANTIFY INTAKE IN ACUTE CARE? A SCOPING REVIEW.

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Quantification of oral intake within the hospital setting is required to guide nutrition care. Multiple dietary assessment methods are available, yet details about their application in acute care settings are scarce.
AIM: To map and describe the dietary assessment methods reported in the literature for the measurement of oral intake in the acute or critical care setting.

METHODS: A review was completed according to a pre-registered protocol across four databases. Primary research studies conducted in the acute or critical care setting including adult patients consuming an oral diet and reporting on the application of a dietary assessment method to quantify dietary intake were eligible for inclusion. Data on study characteristics, assessment methods, completion and validation processes were charted and summarized according to JBI methodology and reported based on PRISMA recommendations.

RESULTS: 6161 articles were retrieved with 155 articles included from acute (n=153, 99%), critical care (n=1, <1%) and both settings (n=1, <1%). Studies were mainly single-centre (n=138, 88%) and of observational design (n=135, 87%). Estimated plate waste (n=51, 33%), food records (n=42, 27%) and 24-hour recalls (n=23, 15%) were the most frequent assessment methods with energy and protein the main nutrients quantified (n=81, 52%). Validation was completed in 23 (15%) studies, with the majority of these using a reference method reliant on estimation (n=17, 74%). A quarter of studies (n=39) quantified completion and four of these studies (2.5%) explored factors influencing completion.

CONCLUSION: A lack of high-quality evidence exists to guide selection and application of existing dietary assessment methods to quantify oral intake within acute care with a particular absence of evidence in the critical care setting. Further validation of existing tools, and definition and identification of factors influencing completion is required to inform oral intake quantification in both the research and clinical contexts.

13. DELIVERING THE MESSAGE: OPTIMISED PRODUCTION OF SAFE AND EFFICIENT NANOLIPOSOMES FOR ANTI-INFLAMMATORY mRNA GENE THERAPY

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Gene therapy is a promising new approach for the treatment of chronic inflammatory diseases. Cationic nanoliposomes (NLps) have demonstrated safe uptake of genetic material, however its current production is tedious and inconsistent. New methods to optimise NLps production will allow for efficient mRNA delivery. The objective is to design and develop NLps for in vitro and in vivo delivery of genetic material. The novel microfluidiser method for generation of NLps resulted in 150x more efficiency and reproducibility as compared to the conventional extruder method. Similarly high transfection efficiency of eGFP mRNA in Chinese Hamster Ovary (CHO) cells was demonstrated using microscopy and flow cytometry, regardless of production method, as measured by the fluorescence intensity (807.7 ± 444.3 vs. 1206.0 ± 575.5, AU, p=ns). Biodistribution analysis showed that the NLps remained present in the plasma one week post injection, with some accumulation in the kidney and liver for up to two weeks ($p<0.05$). Importantly, no significant adverse effects were observed. Using the traditional atherosclerosis murine model (ApoE−/− mice on 12 weeks high fat diet), fortnightly intravenous administration of anti-inflammatory CD39 mRNA loaded NLps (CD39-NLps) did not result in less plaque build-up in vivo, as compared to the controls using eGFP-NLps, CD39-only, and PBS. En face analysis of the aorta and histological analysis of the aortic sinus demonstrated no significant difference in the plaque sizes in either treatment or controls (p=ns). The lack of differences was attributed to the fact that our atherosclerosis animal model remained healthy and did not develop plaque. The microfluidiser method enables large scale, monodisperse and reproducible generation of NLps. These NLps preserve their high transfection efficiencies and safety profiles. Our in vivo experiments were inconclusive because the atherosclerotic murine model did not develop plaque; therefore we have started a new cohort of mice to determine our success.

14. THE ALFRED WELLNESS SCORE (AWESCORE©): MEASUREMENTS OF QUALITY OF LIFE BEFORE AND AFTER THE INTRODUCTION OF ELEXACAFTOR-TEZACAFTOR-IVACAFTOR (ETI) IN ADULTS WITH CYSTIC FIBROSIS

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The CFTR modulator, Elexacaftor-tezacaftor-ivacaftor (ETI), has recently been introduced in Australia for eligible patients with CF. The AWESCORE© is a recently developed valid, reliable, sensitive, easy, quick-to-score wellness measure.

AIM: To measure the effects of ETI on the five domains of quality of life using the AWESCORE© before and at least one month after commencement; to establish its usefulness in the outpatient clinic and online.

METHODS: Patients were asked to complete the AWESCORE© in the outpatient clinic or online (Telehealth) before starting ETI and at a subsequent clinic visit after at least one month on ETI during stable state lung function

RESULTS: A total of 123 (female 46) adults with CF across the range of lung function, body mass and age participated. The median (IQR) FEV1 was 64 (43.5, 84.5)%; BMI 23.5 (21.5, 24.9) kg/m²; age 36 (29, 44) years).Twenty-seven of the 123 patients were naive to CFTR modulators.

TABLE: AWESCORE© pre- and post-ETI

AWESCORE© elements	Pre-ETI - Median (IQR)	Post-ETI - Median (IQR)	p-value
Total Score	68 (60, 74)	86 (81, 90)	p<0.0001
Cough	6 (5, 7)	9 (9. 10)	p<0.0001
Sputum	6 (5, 8)	9 (9, 10)	p<0.0001
Energy	6 (5, 7)	8 (8, 9)	p<0.0001
Exercise participation	6 (5, 7)	8 (7, 9)	p<0.0001
Appetite	8 (7, 10)	10 (8, 10)	p<0.0001
Target weight	8 (7, 10)	9 (8, 10)	p<0.0005
Mood	7 (6, 8)	8 (8, 9)	p<0.0001
Anxiety	7 (5.5, 9)	8 (7, 9.5)	p<0.0001
Sleep quality and quantity	6 (5, 8)	8 (7, 9)	p<0.0001
General health	7 (6, 8)	9 (8, 9)	p<0.0001

CONCLUSIONS: Treatment with ETI resulted in highly significant improvements in all elements and domains of wellness. The AWESCORE© was found to be a useful tool to measure quality of life with patients present in the clinic or online.

15. WHAT ARE THE EXPERIENCES OF ALLIED HEALTH WHO BECOME DIGITAL HEALTH CHAMPIONS?

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As digital healthcare evolves in Australian hospitals, allied health clinicians are being recruited to the novel role of a digital champion to assist in the implementation and adoption of digital technology. Yet, allied health professionals barely feature in the implementation literature, and little is known about how they are recruited, utilised, and embedded as change agents within health organisations.

AIM: This study was conducted to understand how an 'allied health digital champion' and 'superuser' can be best supported as enablers of digital health innovation within their organisation.

METHODS: This qualitative study interviewed Allied health professionals who self-identified as a digital champion or superuser (n=10), snowball sampling was employed within their professional networks. Shea's (2021) conceptual model of a champion provided a framework for thematic data analysis of participant experience of their roles in the adoption of digital health technologies.

RESULTS: Allied health digital champions identified Four major themes:(1) Lack of role clarity specific to their professional context, during and beyond the implementation effort; (2) Valuing improved patient outcomes and being of service to others, were motivating factors in seeking a champion role; (3) Allied health professionals looking for leadership opportunities and novel experiences are drawn to the digital champion role; (4) becoming digital champions and leaders in digital healthcare should be legitimatised as a career pathway.

CONCLUSION: This study demonstrated that there remains untapped potential to utilise allied health clinicians to support digital health adoption and capability amongst their peers which may ultimately progress the digital maturity of their organisation. Organisations can continue to develop the role of allied health to include digital health capability and leadership opportunities in this evolving field.

16. "MAKING A COMEBACK": THE EXPERIENCES OF PEOPLE FOLLOWING SEVERE ABI AS THEY ADAPT TO LIFE IN THE COMMUNITY AND ENGAGE IN ACTIVITIES OF INTEREST.

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BACKGROUND: Community integration and maintenance of social connections has been recognised as a complex issue for people following severe acquired brain injury (ABI). ABI is one of the most common causes of acquired disability in adults, having a significant impact on physical, communication, cognitive and psychosocial functioning. Community integration remains challenging for people, as they navigate the consequences of their ABI, therefore it is vital to explore these challenges.

AIM: To gather the lived experience of individuals with severe ABI to understand their perspectives of engaging in the community during inpatient rehabilitation and the transition to community living.
METHODS: Using grounded theory methodology, 13 adults with severe ABI (6 males, 7 Females, mean age 36) participated in in-depth interviews. Participants were on average 3.5 yrs post discharge from rehabilitation, with mean rehabilitation length of stay of 9 mths. Data analysis followed an iterative process of coding to develop themes, sub-themes and exploration of relations between these.

RESULTS: Analysis revealed several practice relevant insights. Themes are consistent with missed opportunities to engage in the community and connect with friends and family across the continuum; lack of focus on re-engaging in life in the community; much of the responsibility in leading community participation fell to family members and finally a perception that society judges and devalues them due to their disability.

CONCLUSION: This study provides invaluable insights into the experience of people with severe ABI as they return to community engagement. It is important for clinicians to consider these experiences to support community integration and gain positive transition to community living.

17. EFFECTS OF THE MONASH POUCH DIET ON VOLATILE ORGANIC COMPOUNDS (VOC) IN THE POUCH LUMEN IN PATIENTS WITH AN ILEOANAL POUCH

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BACKGROUND: The Monash Pouch diet is a multi-prong diet strategy that theoretically targets 'correction' of the microbial metabolic activities, namely excessive sulphide reduction and protein fermentation in the pouch. The diet has previously been shown to be a feasible, highly tolerated and acceptable diet to patients with an ileoanal pouch with signals for clinical improvements[1].

AIMS: To assess the effects of the 5-week dietary intervention on the pouch microenvironment via volatile organic metabolites in patients with an ileoanal pouch.

METHODS: In a pilot, open-label study, patients with an ileoanal pouch for ulcerative colitis received dietary advice on a Monash Pouch diet for 5 weeks. They were instructed to restrict osmotically active carbohydrates, total and animal protein, sulphate/sulphite preservatives and carrageenan while increasing oligosaccharide intake. Faecal samples were collected at baseline and at the end of the 5-week intervention and analysed for VOCs using gas-chromatography-mass spectrometry. Changes in VOC were compared particularly for bacterial fermentative metabolites. Results were analysed using Metaboanalyst (version 5.0) and metabolites of interest were defined by paired fold-change analysis.

RESULTS: Eleven patients (6 men, mean age 55 years) completed the dietary intervention and provided faecal samples. Average number of VOCs detected between baseline and post-diet intervention (53 (9) vs 55 (7); *p*=0.59; paired t-test) were not significantly different. At baseline, percentage occurrence of protein fermentation metabolite was the highest for phenols (9/11, 81%) whereas the branched-chain fatty acids, 2- and 3-methylbutanoic acid (isovalerate) (45% and 64% respectively) and 2-methylpropanoic acid (isobutyrate) (54%), were detected. No volatile sulphur compounds were detected. The dietary intervention saw no significant changes in ethanoate (acetate) (*p*=0.88), propanoate (propionate) (*p*=0.44), butanoic (butyrate) (*p*=0.57) or any of protein fermentation metabolites (p>0.15). Fold-change analysis identified six important features that were altered from pre- to post-intervention. Ethyl-2-methylbutanoate (fold change: 4.07; Log_2 2.03), 3-isothiocyanatoprop-1-ene (2.01; Log_2 1.01) increased whilst pentane-2,3-dione (0.48; Log_2 -1.07), propanal (0.49; Log_2 -1.02) and 7-methyl-3-methylideneocta-1,6-diene (0.49; Log_2-1.02) decreased. Of the known bacterial fermentation metabolites, there was a trend for changes in intake of animal protein to correlate with changes in 3-methylbutanoic acid (r=0.57; *p*=0.07) and a significant correlation between fibre intake and propanoic acid (r=-0.66; *p*=0.03).

CONCLUSIONS: VOC analysis of ileal effluent has provided signals that protein fermentation may not be prominent (low concentrations of metabolites associated with protein fermentation) and that the Monash Pouch diet paradoxically shifted pouch microbial fermentation towards increased proteolytic activities (increased ethyl-2-methylbutanoate), suggesting the dietary strategy may require modification. However, given the small sample size of this cohort, these results should be interpreted with caution and the fold-change data be regarded as clues to VOCs that may be significant in a larger cohort of ileoanal UC pouch patients.

[1] Ardalan ZS, Friedman AB, Con Det al. . Accuracy of gastrointestinal ultrasound and calprotectin in the assessment of inflammation and its location in patients with an ileoanal pouch *J Crohns Colitis*. 2021.

18. A COMBINED EXERCISE AND SEDENTARY BEHAVIOUR INTERVENTION PRESERVES VO2PEAK IN ADULTS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION FOR HEMATOLOGICAL MALIGNANCY: THE ALLO-ACTIVE TRIAL

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BACKGROUND: Allogeneic stem cell transplantation (allo-SCT) provides a potential cure for high-risk, recurrent, and refractory hematological cancers (HC). However, allo-SCT survivors experience significant treatment-induced exercise intolerance and associated cardiovascular mortality.

PURPOSE: We conducted a randomized controlled trial in HC patients scheduled for allo-SCT to determine if a 4-month multifaceted activity program could preserve peak oxygen uptake (V̇O2peak) and its determinants.

METHODS: Sixty-two HC patients scheduled for allo-SCT were randomized to usual care (UC; n=32, 55±15 y, 63% male) or the activity program (Activity; n=30, 50±16 y, 60% male). Patients assigned to Activity completed thrice weekly aerobic and resistance exercise for 4-months and concurrently aimed to reduce sedentary time by 30-minutes/day via replacement with short (3-min), frequent (hourly), light-intensity activity. Cardiopulmonary exercise testing (CPET) was conducted prior to allo-SCT admission, and 12-weeks following discharge to assess V̇O2peak, as well as peak power output (PPO), respiratory exchange ratio (RER), and heart rate (HR). Peak lactate was also assessed via finger capillary sample.

RESULTS: Fifty patients completed follow-up (23 Activity; 27 UC), 96% of whom satisfied peak CPET criteria (22 Activity; 26 UC). Compared to UC, there was a significant treatment benefit for Activity on V̇O2peak (net difference: 2.5 ml/kg/min [95% CI 0.3, 4.8], p=0.03) due to a 15% reduction in UC (-3.4 ml/kg/min [95% CI -4.9, -1.8], p<0.001) and no significant change in Activity (-0.9 ml/kg/min [95% CI -2.5, 0.8], p=0.31). Similarly, PPO declined less in Activity than UC (-11% vs. -24%; interaction, p=0.03), while peak HR and lactate reduced similarly in Activity and UC (-9 vs. -7 beats/min, p=0.75; -1.3 vs -2.2 mmol/L; p=0.22). Peak RER was unchanged in both groups.

CONCLUSION: A multifaceted activity program targeting exercise and sedentary behaviour attenuates allo-SCT-induced declines in V̇O2peak. Whether these benefits on VO2peak translate to reduced cardiovascular morbidity and greater longevity warrants investigation.

19. PADDED HEADGEAR IN JUNIOR AND YOUTH AUSTRALIAN FOOTBALL: PLAYER INSIGHTS FROM A NATIONAL SURVEY

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Debate exists regarding concussion prevention and the role of padded headgear as protection. Some junior and youth Australian football clubs mandate headgear use despite the lack of evidence that it reduces sports related concussion.

AIM: To investigate beliefs and factors associated with headgear use in junior (<13 years) and youth (≥13 years) Australian football.

METHODS: Online survey of Australian football players aged U8 to U18 with variables: demographics, headgear use, concussion history, beliefs about headgear effectiveness, and risk-taking propensity. Analysis explored rates of headgear use, and beliefs associated with use.

RESULTS: A total of 735 players (including 190, 25.9% female) representing 206 clubs across the nation participated. Headgear was worn by 315 players (42.9%; 95% CI: 39.3-46.4). Most (59.5%) users wore it for games only and wore it voluntarily (59.7%), as opposed to being mandated to do so. Junior players were more likely than youth players (≥13 years) to agree to feeling safer ($P < 0.001$) and being able to play harder while wearing headgear ($P < 0.001$). Median responses were "disagree" on preferring to risk an injury than wear headgear, and on experienced players not needing to wear headgear. Beliefs did not differ between males and females. Headgear use was associated with players belonging to a club where it was mandated for other age groups (OR 16.10; 95% CI: 7.71-33.62, $P < 0.001$), youth players (OR 2.79; 95% CI: 1.93-3.93, $P < 0.001$), and female players (OR 1.57; 95% CI: 1.07-2.30, $P = 0.019$).

CONCLUSIONS: Club headgear culture (mandated for some age groups), older age and being female were prominent variables associated with voluntary headgear use. Players reported believing that headgear offers protection. The rate of voluntary and mandated headgear use identified is at odds with current scientific evidence that does not support it as effective concussion prevention.

20. COMMUNITY OCCUPATIONAL THERAPISTS' PROFESSIONAL REASONING PROCESSES WHEN CONSIDERING POSITIVE RISK-TAKING WITH COMMUNITY-DWELLING ADULTS LIVING WITH TRAUMATIC BRAIN INJURY

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INTRODUCTION: Participation in meaningful occupations can be limited due to a range of risk and safety concerns following traumatic brain injury (TBI). Research has shown that positive risk-taking (PRT), an approach that embraces elements of risk whilst enabling choice and control, has led to positive client-centred outcomes. However, there is no literature available to support the clinical application of, or guide the professional reasoning processes for, PRT with occupational therapist working in community TBI practice.

OBJECTIVES: Explore community occupational therapists' profession reasoning processes when facilitating PRT with adults with TBI.

METHOD: A qualitative descriptive research design was utilised to gather in-depth reflections from eight experienced, Australian-based occupational therapists working in community TBI practice (experience ranging from 8 – 32 years). Semi-structured interviews centred around vignettes and self-reflections we completed, transcribed verbatim and analysed thematically.

RESULTS: The overall findings highlighted a combination of professional reasoning processes were utilised to foster positive risk-taking within 'reasonable and accepted' limits. Ethical dilemmas were continually highlighted when attempting to balance risk with choice and control, as well as facilitators and barriers when applying PRT in practice. Descriptions of practical strategies to enact PRT were detailed by occupational therapist participants, with direct quotations drawn from participants.

CONCLUSION: This research begins to inform understanding of occupational therapists' professional reasoning, and ethical and practical challenges surrounding PRT in practice. Future research designed to build evidence that can guide occupational therapists' professional reasoning when considering PRT in TBI community practice is required.

KEY WORDS: Occupational therapy, positive risk-taking, safety, traumatic brain injury, professional reasoning

21. LONGITUDINAL CHANGE IN SKELETAL MUSCLE AND ADIPOSE TISSUE IN OESOPHAGOGASTRIC CANCER SURGERY: A PROSPECTIVE TRIAL

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INTRODUCTION: Low muscle mass (myopenia) and excess adiposity negatively impact surgical outcomes and survival after oesophagogastric (OG) cancer surgery. There are limited data evaluating body composition changes during OG cancer treatment. We aimed to assess longitudinal change in body composition and correlations with muscle strength and dietary intake throughout the surgical treatment pathway.

METHODS: This prospective observational study included patients having OG cancer surgery at Alfred Health. Skeletal muscle and adipose tissue area (cm^2) were assessed using CT images at diagnosis, restaging (preoperatively) and 12 months postoperatively. Myopenia and visceral obesity were defined using published thresholds. Anthropometrics, dietary intake and handgrip strength (HGS) was measured pre- and postoperatively.

RESULTS: There were 50 patients, 62% male, mean age 64 years (±10.3). Mean weight declined significantly over time (84.6, 82.1, 72.1kg, $p<0.001$). During neoadjuvant chemoradiation, skeletal muscle significantly reduced (152.7 vs 142.4cm^2, $p<0.001$), but there was no difference in adipose tissue (382.4 vs 357.7 cm^2, $p=0.919$). Postoperatively, there was significant loss of adipose tissue (357.7 vs 224.5cm^2, $p<0.001$), but skeletal muscle loss was not statistically significant (142.4 vs 133.6cm^2, $p=0.064$). Myopenia prevalence increased during neoadjuvant treatment (diagnosis 33%, restaging 49%, $p=0.02$) but not postoperatively (12 months 54%, $p=0.21$). Visceral obesity was common and stable between diagnosis and restaging (58% vs 54%, $p=1.00$) with a marked reduction at 12 months (19%, $p<0.001$). Dietary intake correlates with body composition pre- and postoperatively. HGS and skeletal muscle correlate at every time point.

CONCLUSION: Weight loss during neoadjuvant treatment is attributable to skeletal muscle loss without significant change in adipose tissue, whereas postoperatively, loss of adipose tissue is predominant. The development of myopenia during neoadjuvant treatment indicates that endeavours to improve body composition should begin at diagnosis, specifically aiming to preserve skeletal muscle. The influence of dietary intake requires further investigation in a larger cohort.

22. LIPOXIN (LX) MEDIATES RESOLUTION OF DIABETES-ASSOCIATED ATHEROSCLEROSIS (DAA) IN APOE-/- DIABETIC MICE

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The development of atherosclerosis in diabetes is driven by chronic low-grade inflammation resulting from chronic hyperglycemia. The pathogenesis involves complex signalling pathways and potentially the perivascular adipose tissue (PVAT) via "outside-in" signalling.

AIM: To investigate the mechanism that specialised pro-resolving mediators (SPMs) such as Lipoxin A4 (LXA4) protect against atherosclerosis and if this protection involved effects on PVAT.

METHODS: Six-week-old ApoE$^{-/-}$ mice were rendered diabetic by streptozotocin (five daily IP injections, 55mg/kg). Controls received citrate buffer alone. There were two arms to the study, the 10wk prevention study where mice received LXA4 as a preventative treatment from the beginning of diabetes, and the 16wk intervention study where LXA4 treatment commenced after 10wks of diabetes for a further 6wks. In both studies, LXA4 was administered by IP, twice weekly (5µg/kg). Tissues and plasma were collected at the end for gene and protein analysis, cryosection, ELIZA and imaging (n=30/gp).

RESULTS: Notably, LXA4 treatment did not affect blood glucose, cholesterol, triglycerides, or blood pressure in control or diabetic mice. However, a significant reduction ($p<0.0001$) in atherosclerotic plaque area was observed in diabetic mice receiving LXA4, in both the prevention and intervention studies. Gene expression in PVAT revealed that LXA4 administration led to a significant downregulation ($p<0.001$) of inflammatory genes (*IL-6, IL1-β, MCP-1, TNF-α, NFκB, RANTES, ICAM, VCAM*), and restored the expression of genes ($p<0.005$) involved with metabolic regulation (eg. *INSR-1, GLUT4, AMPK, UCP-1, AdipoQ, leptin*). In addition, LXA4 reduced the expression of macrophage markers ($p<0.005$) (*CD11-b, CD163, CD64, CD204, iNOS, Arg-1*).

CONCLUSION: Our studies support early findings that LXA4 protects against atherosclerosis by protecting PVAT against inflammation and enhancing metabolism activity without suppressing the immune system. Further investigations, particularly in type 2 diabetic and obesity models, are warranted to provide valuable insights for future clinical trials aimed at combating this global health concern.

23. A PERSONALISED APPROACH TO NEUROCOGNITIVE RISK IN STEREO-EEG RADIOFREQUENCY THERMOCOAGULATION

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AIM: Radiofrequency thermocoagulation (RFTHC) has been posed as relatively safe from a cognitive perspective, however, this tends to be reported in the absence of neuropsychological assessments. The current study is the first prospective evaluation of neuropsychological outcomes associated with stereo-EEG RFTHC in patients with focal drug resistant epilepsy.

METHODS: Thirty-nine stereo-EEG candidates (M=37.08±9.67 years, range=17–56 years, 54% female) were prospectively recruited across two Melbourne hospitals. All patients underwent RFTHC with a mean of 11.87 (SD=6.82, range=2-29) coagulation sites per patient. A comprehensive neuropsychological assessment was administered before and 3-months after RFTHC (M=104.51days, SD=29.25). Outcomes across cognitive domains were assessed at a group level with repeated measures t-tests. Repeated measures ANOVAs compared memory and language outcomes according to whether dominant mesial temporal lobe (mTL) structures were coagulated. Reliable change indices were undertaken to explore changes at an individual level.

RESULTS: At a group level, RFTHC was not associated with a decline on any neuropsychological measures. Overall, reliable change analysis found 26% of patients experienced a decline in least one cognitive domain. Subgroup analysis revealed a decline in delayed verbal recall following RFTHC of dominant mTL structures, $F(1,37)=4.46$, $p=0.04$, $\eta^2_p=0.11$ medium to large effect, although it did not remain significant after correction for false discovery rate. No significant differences between groups in visual memory or language were observed ($p>0.05$). Reliable change indices revealed 30% of patients experienced a decline in verbal memory and 20% in visual memory following RFTHC within the dominant mTL. By contrast, 14% experienced a decline in verbal memory and 7% in visual memory following RFTHC elsewhere. No decline was observed for language function.

CONCLUSION: While these findings suggest RFTHC is cognitively benign for most functions, the results raise the question of verbal memory decline in dominant mTL coagulation. Individualised neuropsychological counselling is essential to avoid unanticipated deficits.

24. UNDERSTANDING AND EVALUATING THE UPTAKE OF DELIRIUM RECOMMENDATIONS IN AN ACUTE OCCUPATIONAL THERAPY SERVICE

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BACKGROUND: Hospital admissions can be heavily impacted by delirium; a state of confused thinking and reduced awareness of the environment. Delirium may significantly complete hospital stays and is associated with poorer patient outcomes and delayed discharge. Research and localised Alfred Health has suggested a role for occupational therapy in managing delirium, through clear assessment, use of daily routines, and early cognitive stimulation.

AIM: To increase Occupational Therapy staff adherence to guideline-informed hospital processes for the prevention and management of delirium.

METHOD: A pre-post implementation study was conducted with ethics approval. Using the Knowledge to Action (KTA) framework, a staff education and training package was developed targeting Occupational Therapy service gaps related to working with patients with or at risk of delirium. The rate of compliance with delirium clinical recommendations was evaluated through a documentation audit at baseline and one- month post implementation of the education package.

RESULTS: The baseline audit of patient files (n=18) identified poor occupational therapy compliance with delirium recommendations. Therefore, the staff education package included the implementation of a delirium clinical pathway, a staff education package based on guideline-informed hospital requirements, and clinical resources to support the implementation of daily reorientation and patient and family education. From baseline, results of the post-implementation audit (n=18) indicated improvements in time to intervention (50% to 90%), acknowledgement (3% to 89%) and documentation (3% to 95%) of delirium risk screen, and documentation of delirium recommendations (2% to 89%). Delirium education to patients/families and updating the electronic care plan showed limited improvements.

CONCLUSION: The KTA framework supported the development of targeted delirium education and resources which demonstrated improvements across four domains of Occupational Therapy intervention. Further development is indicated to increase consistency of the provision of delirium education and documentation of delirium management strategies discipline-wide to optimise patient safety and outcomes.

25. IMPROVING MILD TRAUMATIC BRAIN INJURY MANAGEMENT BY OCCUPATIONAL THERAPISTS: MULTICOMPONENT EDUCATION AND IMPLEMENTATION OF A CLINICAL PATHWAY

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BACKGROUND: Occupational therapists have the potential to improve outcomes for adults with mild Traumatic Brain Injury (mTBI) through the implementation of Clinical Practice Guideline (CPG) recommendations. However, organisational challenges in a large hospital where part-time, weekend and rotational staff are common, may create inconsistency in how occupational therapists apply mTBI guideline recommendations.

AIM: To increase occupational therapy staff knowledge and implementation of clinical guideline recommendations in the assessment and management of adults with mTBI.

METHOD: A multi-method, pre-post implementation study was conducted using the Knowledge to Action (KTA) framework to develop training targeting occupational therapy mTBI guideline recommendations. A clinical guidelines determinants survey, adapted for mTBI, was administered at baseline and again one-month post-implementation of the education package to evaluate change in clinician beliefs and behaviour.

RESULTS: The education package was designed to be self-directed to facilitate the participation of part-time staff and included: a mTBI clinician checklist, documentation recommendations and a self-directed webinar and questionnaire. The questionnaire was completed by n=21 at baseline and post- implementation n= 28. Overall results indicate that the number of staff who have read and used the guidelines increased following implementation. Factors which enabled the use of guidelines included accessibility, support from seniors, clinical pathways and application of guidelines, whilst time was identified as the primary barrier.

CONCLUSION: Occupational therapy staff understand that using guidelines optimises evidence-based care, however, time constraints may affect reading and applying guideline recommendations. Use of the KTA framework supported the development of a targeted self-directed training package to enable knowledge translation and consistency of guideline implementation across a large hospital and casual workforce.

26. ARE COGNITIVE ASSESSMENT OF MINNESOTA (CAM) RESULTS ASSOCIATED WITH INPATIENTS' FUNCTIONAL PERFORMANCE?

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Occupational therapists routinely assess the occupational performance and functional capacities of hospitalised adults with suspected cognitive impairment. While some cognitive screening tools present a detailed cognitive profile of impairment, the raw scores rarely define the impact of cognitive impairment on functional performance in meaningful daily tasks. Despite this, clinicians are often asked to informally link the raw scores obtained on cognitive screening assessments to a person's global functional performance to describe the impact of newly acquired cognitive impairments at the point of discharge.

AIM: To investigate the association between performance on the CAM and functional outcome in a mixed subacute inpatient cohort with cognitive dysfunction.

METHOD: Retrospective cohort analysis of routinely collected data from inpatients who received occupational therapy at Alfred Health and had an identified need for cognitive assessment. A standardised cognitive assessment (CAM) and functional performance measure (Functional Autonomy Measurement System (SMAF)) were administered by occupational therapists as part of usual care with the available data analysed. Spearman's rho correlations and linear regression analyses were conducted.

RESULTS: An occupational therapist identified a clinical reason for CAM assessment in 225 patients, of which SMAF data were available for n=166. Patients had a mean age of 62±19 years, with the majority male (n=93, 56%) and diagnosed with stroke or traumatic brain injury (n=118, 71%). Of the 29 CAM subtest items, 19 had a significant correlation with SMAF total impairment score, however the strength of the correlation was very low (<0.4) and not clinically important. Bivariate stepwise regression identified one CAM subtest item 'Foresight and Planning' as a predictor of the SMAF total impairment score.

CONCLUSION: CAM results are associated with inpatients' functional performance, but not at a level that is clinically meaningful. The tests may measure different things and therefore occupational therapists should administer both tests within a hospital-based setting.

27. ADAPTING AND OPERATIONALISING ADOLESCENT TRAUMATIC BRAIN INJURY GUIDELINES TO SUPPORT OCCUPATIONAL THERAPY PRACTICE IN AN ADULT HOSPITAL

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BACKGROUND: Adolescents aged 15-17 frequently present to adult hospitals following a traumatic brain injury (TBI), creating unique challenges for occupational therapists. Whilst clinical practice guidelines (CPGs) offer evidence-based practices for adolescent TBI care, adapting these guidelines for the adult hospital setting is vital for effective implementation.

AIM: This study aimed to translate CPGs into a local protocol and resources using the ADAPTE and CAN-IMPLEMENT processes.

METHODS: A file audit was completed to determine the number of adolescents receiving occupational therapy services. To adapt and operationalise an adolescent TBI guideline, we applied all phases of the ADAPTE Framework. To provide additional clarity to the selection of the recommendations, and the decision and sectional phase of adoption, we followed the CAN-IMPLEMENT process. We reviewed five CPGs, with two occupational therapists assessing guideline quality using the AGREE II tool. The team collectively screened CPG recommendations and determined which to include within a local occupational therapy protocol and patient education resources. Finally, internal and external stakeholders, including consumers, reviewed the local protocol and patient education handouts.

RESULTS: The file audit identified 50 adolescents with a TBI who received occupational therapy services over 12 months, supporting the need for a localised CPG. Of the five guidelines reviewed, two CPGs were included in the final protocol; (i)PREDICT and (ii)Royal Children's Hospital. These achieved AGREE II ratings of 92% and 25% respectively. Where stakeholders identified gaps in the recommendations, additional evidence and training were sought to meet these needs i.e., cognitive assessment recommendations and alcohol and drugs. The resulting protocol provides assessment and intervention recommendations for occupational therapists at Alfred Health, along with patient resources.

CONCLUSION: Using the ADAPTE framework and CAN-IMPLEMENT process as a formal structured approach to guideline adaptation supported the selection of high-quality recommendations for developing a localised adolescent TBI protocol and patient resources.

28. EXAMINING THE PATIENT EXPERIENCE OF MEDICATION MANAGEMENT AND COMMUNICATION WITH THE OUTPATIENT PHARMACY

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BACKGROUND: A major metropolitan health service implemented an online ordering tool to improve prescription ordering and simplify communication for patients during the COVID-19 pandemic.

AIM: To evaluate patient communication pathways with pharmacy, the impact of online ordering for medication management, and guide future improvements.

METHODS: An Online Survey and Focus Group (FG) were used to evaluate patients' experience. The survey included 25 multiple-choice questions and free-text responses. Survey responses informed FG development. Thematic analysis reflected the priorities of the *Australian Charter of Health Care Rights* (ACHCR).

RESULTS: A link to the online survey was circulated to 1,701 recent outpatients, with 582 valid responses received (34.2% response rate). The most common communication methods with pharmacy are the online form: used regularly by 293 patients (50.3%), telephone (n=184, 31.6%), in person (n=180, 30.9%) (ACHCR: 'Access'). Of the 336 patients (57.7%) that had ever used the online form; 301 (89.5%) form users reported it easy to use, 166 (49.4%) felt it supported medication management (ACHCR: 'Information', 'Partnership'). When medications are new or changed 440 patients (75.6%) stated that it was explained to them by a pharmacist or their medical team (ACHCR: 'Safety').
Six patients attended the FG, universally reporting that medication management was the most important aspect of healthcare. Expanding the online form functionality would alleviate health-related anxiety (ACHCR: 'Access').
Survey and FG participants identified service improvements: access to prescription lists, repeat information and ordering histories, incorporated within the online form or in the Patient Portal (ACHCR: 'Information', 'Partnership').

DISCUSSION: Online medication ordering streamlines patient access to the pharmacy and is used regularly by half of the respondents. Patient feedback will guide service improvements that include extended medication consultations to address patients' safe use of new or changed medications, and access to prescription histories and repeats to support medication management.

29. FEESABILITY OF SWALLOWING ASSESSMENTS IN ICU

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There is a high prevalence of dysphagia and silent aspiration (no airway response) in patients with critical illness, which contributes to increased rates of pneumonia, longer length of stay and poorer patient outcomes. Fiberoptic Endoscopic Evaluation of Swallowing (FEES) is a portable instrumental assessment used by specialist Speech Pathologists to diagnose swallowing disorders (dysphagia) via nasendoscopy and identify patients at risk of silent aspiration. Current literature supports FEES in the intensive care unit (ICU) to guide dysphagia management. An increase in funding for Speech Pathologists (1.0 EFT) at The Alfred ICU in October 2022 created an opportunity to align with best practice.

AIM: To compare the number of FEES completed pre- and post- additional Speech Pathology funding, and to describe outcomes and changes in dysphagia management in ICU following FEES.

METHOD: Retrospective review of the medical record was undertaken, identifying the number of patients who had a FEES in the period pre- (2019-2022) and post- (October 2022-September 2023) funding. FEES reports post-funding were reviewed to determine oral intake status and silent aspiration occurrence.

RESULTS: The average number of FEES performed in the pre-funding period was 4 per year (2019 n=5, 2020 n=3, 2021 n=8, 2022 n=1) compared with 33 in the (11-month) post-funding period (686% increase). Of the 33, there were 18 (55%) patients who were identified to silently aspirate. FEES supported dysphagia management with a decrease in patients nil orally (n=27 [82%] to n=12 [36%]), and an increase in patients on oral intake (n=6 [18%] to n=21 [64%]).

CONCLUSION: The use of FEES significantly increased in The Alfred ICU after additional Speech Pathology funding. FEES resulted in a large portion of patients returning to oral intake, and prevented unsafe introduction of oral intake for patients with silent aspiration unable to be identified via bedside assessment, potentially reducing aspiration-related consequences.

30. IS APHASIA BEING LEFT BEHIND?

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48.4% of left hemisphere stroke patients have aphasia. National Stroke Guidelines advise communication screening for all stroke survivors, to support early identification of communication deficits, and therefore early intervention and improved communication outcomes. At The Alfred, systematic screening is only conducted for swallowing, patients are referred for communication ad-hoc as identified by the multidisciplinary team (MDT).

AIM: To evaluate whether the implementation of language screening all left hemispheric stroke patients admitted to an acute stroke unit at a major tertiary hospital increases the early identification of aphasia.

METHOD: Pilot intervention with patient participants with a confirmed left hemispheric stroke admitted to the stroke ward during an 8-week period (June-July 2023). Patients were screened using the Frenchay Aphasia Screening Test (FAST) by trained Allied Health Assistants. Patients who failed the screen were referred to SP for communication assessment. Patients were not screened if already referred to SP, end-of-life pathway, new visual impairments or pre-existing communication deficits.

RESULTS: 23 patients were admitted with left hemispheric stroke, with 12 (52%) diagnosed with aphasia. 17 (76%) were already referred to SP. Of the remaining 6 patients (26%), 1 on end-of-life pathway, 3 were discharged from hospital prior to screening being completed and 2 had a FAST. Of the two screens completed, only 1 patient failed the FAST, prompting a referral to SP to confirm aphasia. Therefore, the FAST screening resulted in an increase of 8% (N=1/12) of early aphasia identification.

CONCLUSION: Language screening of left hemispheric strokes admitted to The Alfred may contribute to a small increase in identification of aphasia. Administration of the FAST was feasible, approx. 15 minutes per patient. Current practices may be sufficient to support identification of aphasia at The Alfred, with incidence estimates consistent with literature. Screening of other stroke-related communication deficits (such as cognitive-communication) should be considered.

31. MUSCULARITY OF OLDER TRAUMA PATIENTS AT INTENSIVE CARE UNIT ADMISSION, ASSOCAITION WITH FUNCTIONAL OUTCOMES AND RELATIONSHIP WITH FRAILTY: A RETROSPECTIVE OBSERVATIONAL STUDY.

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Older individuals are at increased risk of delayed recovery following a traumatic injury. Measurement of muscularity and frailty at hospital admission may aid with prognostication and risk stratification.

AIM: To describe muscularity at intensive care unit (ICU) admission in patients admitted following trauma and assess the relationship between muscularity and clinical, long-term functional outcomes and frailty at ICU admission.

METHODS: This retrospective study utilised data from a prospective observational study investigating frailty in patients aged ≥50 years, admitted to the ICU following trauma. Patients were eligible if they had a Computed Tomography (CT) scan including the third lumbar vertebra at admission. CT-derived skeletal muscle cross-sectional area (CSA) was quantified and patients were classified into normal or low muscularity using published sex-specific cut-points. Demographic data, frailty, clinical, and long-term functional outcomes (Glasgow Outcome Scale-Extended (GOSE) and EQ-5DL-5L Visual analogue scale and utility score) were extracted from the original study.

RESULTS: One hundred patients were screened; 71 patients had a CT scan on admission with 66 scans suitable for assessment. Patients with low muscularity (n = 25, 38%) were older and had a higher Acute Physiology and Chronic Health Evaluation II score and lower BMI than patients with normal muscularity. Low muscularity was associated with frailty at admission (32% vs 5%, p = 0.005) but not long-term functional outcomes. As a continuous variable, lower muscle CSA was associated with a poorer outcome on the GOSE at 6 months (mean [standard deviation]: 150 [43] and 180 [44], respectively; p = 0.014), no association was observed after adjustment for age p = 0.43).

CONCLUSION: In a population of older adults hospitalised following trauma low muscularity was prevalent and found to be associated with frailty but not long-term functional outcomes. Larger studies are warranted to further explore the relationship between muscularity and long-term functional outcomes.

32. EXPERT CONSENSUS ON A COGNITIVE REHABILITATION TRAINING PROGRAM FOR NOVICE OCCUPATIONAL THERAPISTS

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BACKGROUND: Novice occupational therapists often struggle to determine a cognitive rehabilitation plan for patients with a brain injury, as this requires complex skilled clinical reasoning. Consequently, patients may not receive the optimal rehabilitation at the optimal time. In contrast, experts appear to use their clinical reasoning seamlessly to develop these plans.

AIM: To establish expert consensus on content and delivery method for a self-directed learning package to support novice occupational therapists' clinical reasoning when planning cognitive rehabilitation for patients with brain injury.

METHOD: An online five-step online Nominal Group Technique (NGT) methodology was used to extrapolate data from expert occupational therapists across Australia. Snowball recruitment occurred via social media and through the researchers' established clinical and academic networks. Experts were asked to identify the content and training methods for a learning package for novice occupational therapists. Subsequently, experts rated the importance of each item using an online tool (www.menti.com). Thematic analysis of the ideas generated was completed following Braun and Clark's five-stage process with 10% of the data coded by two researchers to confirm reliability.

RESULTS: Twenty-one expert occupational therapists participated in three focus groups. Overarching themes of '*knowing what', 'knowing how',* '*formulating and doing cognitive rehabilitation'* were developed from the thematic analysis. Expert occupational therapists ranked: *'activity analysis', 'how to grade and modify rehabilitation', 'understanding cognition',* and *'evidence-based practice*' as the most important content to include in a learning package. Methods prioritised for delivery of the learning package included video demonstrations, case studies, online modules, and practical assignments.

CONCLUSION: An online NGT method enabled rapid expert consensus to establish essential content and teaching methods for a cognitive rehabilitation learning package to enhance novice occupational therapists clinical reasoning to develop cognitive rehabilitation plan for patients with a brain injury. Subsequent research will develop and evaluate this learning package.

33. PSYCHOLOGICAL FACTORS AND RETURN TO WORK AFTER STROKE: THE UNSEEN CHALLENGES OF AN UNMET NEED

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Many stroke survivors experience significant difficulty returning to work. Vocational rehabilitation programs are designed to enable stroke survivors to re-engage in meaningful work. Existing programs appear to place emphasis on physical and environmental factors associated with vocational re-engagement, whereas psychological and psychosocial characteristics receive less attention.

AIM: To characterise the psychological and psychosocial factors in a cohort of stroke survivors, prior to their engagement in a vocational intervention program.

METHODS: Stroke survivors who were within four months post-stroke and identified an unmet need relating to work were recruited into a pilot randomised controlled trial (the Work Trial). Participants were recruited from acute, rehabilitation and community programs at Alfred Health. At baseline, psychological and psychosocial factors were evaluated, including anxiety and depressive symptoms – measured using the Hospital Anxiety and Depression Scale (HADS), and self-estimated work and social functioning – assessed using the Work and Social Adjustment Scale (WSAS). Univariate analyses were conducted to explore the data collected at recruitment into the trial.

RESULTS: Thirty-four stroke survivors (male: n=20; age: mean=49.7, SD=12.7, median=52.5, IQR=19, range: 21 to 69 years) were recruited. At trial commencement, almost half of the participants (14 of 32, 44%) experienced depressive symptoms and one-third (11 of 32, 34%) demonstrated anxiety, as indicated by a score ≥ 8 on the HADS-D and HADS-A respectively. More than half of the participants (21 of 34, 62%) recorded a greater difficultly when returning, or attempting to return, to previous occupations, activities and roles post-stroke, as indicated by a score≥16 on the WSAS.

CONCLUSION: In the Work Trial, stroke survivors commonly reported depressive symptoms, anxiety and increased difficultly in work and social functioning, prior to their engagement in a vocational rehabilitation program. Psychological and psychosocial factors should be considered alongside physical and environmental factors within vocational rehabilitation programs for stroke survivors.

34. LESSONS FROM EXCLUSIVE ENTERAL NUTRITION IN HEALTHY ADULTS

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BACKGROUND: Exclusive enteral nutrition (EEN) induces clinical remission in Crohn's disease, although its mechanism of action is poorly understood.

AIM: To examine the effect of EEN on intestinal physiology and microenvironment in healthy subjects (a confounder free model).

METHODS: In as single-centre pilot study, 10 healthy adults were evaluated on their habitual diet and after 3 weeks of EEN. Assessments comprised: gastrointestinal symptoms; intestinal barrier function and its response to stress, via 100 mg IV of corticotrophin-releasing hormone (CRH), using a 2-h lactulose:rhamnose ratio (LRR); inflammation via faecal calprotectin (FC) and serum highly-sensitive C-reactive protein (CRP); and regional gut transit times and intestinal H_2 concentration profiles via the Atmo gas-sensing capsule. Results were compared by paired t test (parametric data) or Wilcoxon signed rank test (non-parametric data).

RESULTS: New symptoms included halitosis (7/10) and headaches (6/10). EEN was associated with increased nausea ($p<0.04$). The variable effects of CRH-induced stress on LRR during the habitual diet were abolished by EEN (see ***Figure***). FC increased from 10.5 (0.0-43.55) to 40.6 (2.1-246.6) μg/g ($p=0.006$) with EEN but CRP did not change. During EEN colonic transit time was prolonged (35.7 [5.1-68.6] vs 16.1 [5.8-24.0] h, $p=0.04$). In the colon, H_2 concentrations were lower (area-under-the-curve EEN 36.9 [0-43.7] %.h vs habitual diet 52.7 [18.3-98.2] %.h, $p=0.45$) with a decreasing proximal-distal gradient on EEN compared with an increasing gradient on habitual diet.

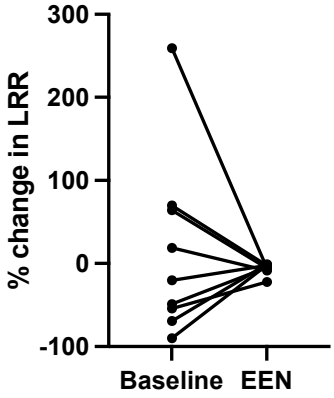

Fig. Change in LRR induced by acute exposure to CRH

CONCLUSION: Headaches, halitosis and nausea are EEN associated symptoms. EEN had favorable effects on small intestine with stabilisation of its permeability during acute CRH-induced stress, which may reflect the potential stabilising action of EEN on inflammatory mechanisms in Crohn's disease. However, less favorable effects were seen in the colon (prolonged colonic transit, reduced fermentation particularly in the distal colon, raised FC) which warrant further investigation.

35. PREFERENCES AND PERSPECTIVES REGARDING TELEHEALTH EXERCISE INTERVENTIONS FOR ADULTS WITH CYSTIC FIBROSIS: A QUALITATIVE STUDY

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OBJECTIVE: Physical activity and exercise are key components in the management of cystic fibrosis (CF). Completing exercise programs online may minimise the risk of cross infection and increase access for people with CF. This study aimed to understand the perspectives of people with CF regarding intervention content for a telehealth exercise program.

METHODS: Individual semi-structured qualitative interviews were conducted in adults with CF purposefully sampled for age, disease severity and social demographics. Interviews were recorded, transcribed verbatim and analysed thematically by two researchers independently.

RESULTS: Participants were 23 adults with CF (14 females,) aged from 21 to 60 years. Three major themes (sub-themes) were generated: "Personalising components to an exercise program" (customising an exercise program to the individual person and their unique health and exercise needs, enjoyment and variety of exercise activities, accessibility and exercise fitting around competing demands or commitments), "The importance of maintaining connections" (challenges regarding face-to-face interactions for people with CF, accountability of scheduled exercise sessions with others, shared experiences between people with CF and specialist support from the CF care team), and "Monitoring health and exercise" (perception of health status and monitoring and recording exercise participation and health).

CONCLUSION: This study provides important information regarding the preferences of adults with CF for telehealth exercise interventions. Interventions should be tailored to the individual person with CF, include an opportunity to maintain connections with peers and the CF multidisciplinary team, and provide a method to monitor progress over time.

36. DISCHARGING PATIENTS IN TAIL-END POST TRAUMATIC AMNESIA (PTA) FROM AN ACUTE TRAUMA CENTRE: QUALITY IMPROVEMENT PROJECT

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BACKGROUND: INCOG guidelines advocate that patients remain in hospital while in PTA but this is not always feasible due to hospital pressures. Evidence suggests that adults who are medically stable, well supported, and grossly oriented may discharge while in tail-end PTA without any adverse events.

AIM: The purpose of this implementation project was two-fold; i) to develop resources, staff development and education to guide occupational therapists with a new discharge process, and ii) to evaluate the impact of discharging patients in tail-end PTA from a large, metropolitan acute trauma centre.

METHOD: Participatory action research was used to first develop clinician-specific resources (to support clinical reasoning and discharge planning processes) and carer-specific resources (to support education and preparedness for safe discharge to the community). The Plan-Do-Study-Act (PDSA) quality improvement cycles were then used to trial and study those ideas in practice. Mixed methods were used to explore changes in occupational therapy service delivery and clinical reasoning.

RESULTS: The developed resources were implemented, with ongoing refinement and measurement of their effectiveness. Clinicians identified 25 potentially eligible patients, with only one discharged home in tail-end PTA. Results across six PDSA cycles suggest challenges include community-service acceptance of referrals of patients in PTA and clinician knowledge of how to assess PTA emergence without sole reliance on WPTAS scores. There were no adverse events.

CONCLUSION: Patients may be discharged before emergence from PTA. Findings highlight that an implementation package can support occupational therapy clinical reasoning.

37. INCREASING ADHERANCE TO THE ACUTE STROKE GUIDELINES: A QUALITY IMPROVEMENT INITITIVE FOR OCCUPATIONAL THERAPISTS BASED ON THE KNOWLEDGE-TO-ACTION FRAMEWORK

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BACKGROUND: Despite Alfred Health's participation in the biennial Stroke Foundation data audits and the Australian Stroke Clinical Registry (AuSCR) gaps remain in translating research evidence within everyday occupational therapy practice.

AIM: The aim of this study was to improve adherence to acute stroke clinical practice guidelines by occupational therapists through the development of a multifaceted tailored implementation program.

METHOD: An implementation science design was used from April 2022 to April 2023 to apply the Knowledge-to-Action Framework (KTA) to first review the clinical practice guidelines and select those applicable to occupational therapists. File audits collected outcomes at baseline (pre) and at 12-months (post) using a pre-determined audit tool. A working group was formed to support the translation of the Australian and New Zealand Clinical Guidelines for Stroke Management on a hyperacute stroke unit. Priority areas for change in practice were taken from existing research literature, the 2021 Stroke Foundation data and local baseline audits. A multifaceted quality improvement intervention was developed including evidence-based work instructions, a clinical pathway, alongside routine data collection for team feedback and performance monitoring.

RESULTS: Six clinicians participated in this quality improvement project. Clinical pathway data was collected from 470 patients seen by occupational therapy on the hyperacute Stroke Unit. Audit data from 40 patients (20 pre and 20 post) suggest percentage change improvements in the areas of: home environment screening (+7%), cognitive screening (+20%), return to work education (+100%), and completion of functional assessment (self-care +29% and hot drink preparation +38%).

CONCLUSION: It was feasible to implement a multi-faceted quality improvement intervention developed based on the Knowledge-to-Action Framework leading to improved occupational.

38. IMPLEMENTATION OF AN EVIDENCE-BASED TELEHEALTH FRAMEWORK FOR OCCUPATIONAL THERAPY PRACTICE: KNOWLEDGE-TO-ACTION FRAMEWORK

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BACKGROUND: Hospital-based occupational therapists need to deliver occupational therapy to inpatients without being in-person during the COVID-19 pandemic. Our Melbourne tertiary hospital had minimal prior telehealth experience despite a long history of using telehealth in the profession within Australia.

AIM: To implement and evaluate an evidence-based telehealth protocol for hospital occupational therapy services using the knowledge-to-action (KTA) framework.

METHOD: Implementation research was conducted across Melbourne based metropolitan hospital networks (three hospitals, >105,000 episodes of inpatient care, 80 occupational therapists). Three phases of the KTA framework (select, tailor and implement interventions; monitor knowledge use; and evaluate outcomes) guided the development and use of occupational therapy telehealth clinical protocols across mixed patient caseload.

RESULTS: Staff reported awareness of telehealth (n=32/40, 76%), however, few reported having the required resources to deliver programs using telehealth (n=12/40, 30%). Our clinical protocol outlined the range of telehealth modalities (store-and-forward, telephone, videoconferencing) and tele-encounters (support, monitoring, assessment, education, therapy and coaching), as well as the evidence underpinning their use in occupational therapy. Resources were developed across our service to support the delivery of effective occupational therapy using telehealth, including work instructions for assessments (e.g., PTA screening with COVID-positive inpatients), groups (e.g., hand-and-arm group), outpatient therapy (e.g., hand therapy), and student supervision.

CONCLUSION: Tailored resources and mentoring were key to support knowledge translation in telehealth within our hospital network and to support clinician needs. Judicious translation of evidence in the space of telehealth delivery is recommended, with further occupational therapy research required.

39. THE EFFECTIVENESS OF TELEHEALTH APPOINTMENTS IN OUTPATIENT, ADVANCED MUSCULOSKELETAL PHYSIOTHERAPY CLINICS AT THE ALFRED.

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BACKGROUND: The use of Telehealth (TH) is increasing, particularly since the COVID-19 pandemic. It can aid in the healthcare disparity in more geographically challenging areas and improve access to healthcare with cost reductions. Contrarily, TH has highlight disparities that arise with uptake, access and utilisation.

AIM: To identify factors associated with the attendance of TH consultation in advanced practice physiotherapy clinics.

METHODS: Data was obtained at the Alfred Hospital Outpatient, Advanced Musculoskeletal Practice (AMP) clinics between January 2021 to November 2021. Multi-variable regression analysis was performed to determine factors associated with unsuccessful TH appointments. Variables included age, gender, geographical location (rural/remote >100km vs. Metro <100km from the Alfred Hospital), Socio-economic Indexes for Areas (SEIFA), non-English speaking background (NESB) and clinic type (Orthopaedic or Neurosurgery). An unsuccessful TH appointment was defined as a video (or phone) call that did not proceed.

RESULTS: A total of 368 patients were included in this study, aged 21 to 91 with a median (IQR) age of 61 (50-71) years. Age was the only factor associated with failing to attend TH consultation when accounting for confounders. Patients aged 60-69 years were 3.69 times more likely to not attend a TH consultation (p=0.001). There was no association between type of clinic, SEIFA, NESB, gender, and location on TH success rate.

CONCLUSION: Patient age should be considered when referring patients >60 years old to AMP clinics via TH, irrespective of clinic type, SEIFA, NESB and geographical location. Future studies should consider looking at what contributing factors or trends there are associated with increased age and target support to those >60 years old to improve TH success. This will allow for developmental strategies and further comparison analysis.

40. VALIDITY OF THE ACTIVPAL AND ACTIGRAPH FOR MEASURING SITTING TIME AND STEPS IN HOSPITALISED ORTHOPAEDIC PATIENTS WITH ALTERED WEIGHT BEARING

Kirk, A., Kimmel, LA., Behm, K., Peiris CL. and Ekegren CL

PURPOSE: To determine the criterion validity of the activPAL and ActiGraph for measuring steps and sitting/sedentary time, compared to observation, in people hospitalised following orthopaedic lower limb injury who were weight bearing (WB) (i.e. walking) or non-weight bearing 1(NWB) (i.e. hopping).

MATERIALS AND METHODS: Participants wore an activPAL and ActiGraph on the hip/thigh/unaffected (UA)/affected ankle (AA) while completing bouts of walking and sitting. Lins Concordance Correlation Coefficient, Bland-Altman methods and ratio of agreement were used to compare device-measured to observed (videoed) step count, sitting/sedentary time.

RESULTS: In 42 participants, the ActiGraph demonstrated excellent concordance with the observed step count when worn on the ankle (LCC 0.91-0.92) compared to the hip (LCC 0.56) in participants that were WB. The ActiGraph AA achieved the highest concordance (LCC 0.71) with observed steps in participants NWB. The activPAL had poor concordance with observed steps, particularly at slow gait speeds, in participants that were WB (LCC 0.38-0.46), however was less influenced by gait speed and had good concordance in NWB participants (LCC 0.52-0.69). The activPAL (LCC 0.79-0.88) and ActiGraph UA (LCC 0.94) showed excellent concordance with observed sitting and sedentary time, respectively.

CONCLUSIONS: The ActiGraph worn at the ankle provided the most valid measure of steps in people who are WB and NWB following orthopaedic injury, while the activPAL was best for measuring sitting time.

DIABETES RESEARCH

41. LIPOXIN MODULATES GLOMERULAR MACROPHAGES AND PROTECTS PODOCYTE DEPLETION IN DIABETIC KIDNEY

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Kidney macrophages are a heterogeneous population of cells that contribute to the chronic unresolved inflammation that underlies diabetic kidney disease (DKD). The macrophage subpopulations initiating and promoting inflammation in DKD, particularly in the glomerulus, have not been characterized. There has also been growing interest in specialised pro-resolving mediators (SPMs) such as Lipoxin A4 (LXA4) as potential reno-protective agents.

AIM: To investigate the effect of LXA4 on kidney macrophages in a model of DKD.

METHODS: Six-week-old male ApoE KO mice were rendered diabetic by five daily IP injections of streptozotocin (55mg/kg). Controls received citrate buffer alone. After 10wks of diabetes, mice were randomly selected and were administered either vehicle (0.02% ethanol) or LXA4 (5µg/kg) via IP (n=30/gp) twice weekly for a further 6 weeks. At endpoint, mice were culled, and kidneys collected for gene expression analysis and single cell RNA sequencing (scRNA-Seq) of glomerular cells.

RESULTS: Diabetic mice had elevated blood glucose, glycated haemoglobin and albuminuria, increased expression of fibrotic (fibronectin, Col 4a3), inflammatory markers (IL1β, TNFα, MCP1, VCAM-1, ICAM-1) compared to control. Interestingly, LXA4 reduced albuminuria, inflammatory and fibrotic markers (IL1β, MCP1, ICAM1 and VCAM1) independent of any changes in metabolic parameters. scRNA-Seq of the glomerular cell populations demonstrated an increase in macrophages in kidneys of diabetic mice. These changes were associated with renal injury, including the increased expression of apoptotic markers and depletion of podocytes. LXA4 reduced macrophage numbers and prevented podocyte loss in the diabetic kidney.

CONCLUSION: LXA4 protects against DKD by reducing fibrotic and inflammatory signalling, macrophage numbers, preventing podocyte loss and improving kidney function. These data highlight the use of SPMs as typified by LXA4 as a novel treatment for DKD by targeting macrophages in the kidney.

42. HEPATIC RETINOL DEHYDROGENASE 11 DAMPENS CELLULAR STRESS ASSOCIATED WITH CHOLESTEROL HOMEOSTASIS

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Dysregulation of hepatic cholesterol metabolism can contribute to elevated circulating cholesterol levels, known as hypercholesterolemia, which is a significant risk factor for cardiovascular disease. Cholesterol homeostasis in mammals is a tightly regulated process, integrating a network of transcriptional and post-transcriptional signalling pathways. Whilst studies over the past few decades have identified many of the central regulators of these pathways, the extended supporting networks remain to be fully elucidated. Here, we leveraged an integrated discovery platform, combining multi-omics data from 107 strains of mice to investigate these supporting networks. We identified retinol dehydrogenase 11 (RDH11) as a novel protein associated with known regulators of cholesterol metabolism. Prior studies have suggested that RDH11 may be regulated by alterations in cellular cholesterol status, but experimentally this has been largely unexplored. Initially, we found that hepatic Rdh11 expression was regulated in mice when they were fed a high cholesterol diet or given statin-treatment (cholesterol synthesis inhibitor). Moreover, studies in human and mouse hepatocytes demonstrated that RDH11 expression was regulated by altered cellular cholesterol conditions, in a manner like that of putative sterol-response element binding protein 2 (SREBP2) target genes, HMGCR and LDLR. RDH11 loss- and gain-of-function studies in Hep3B cells demonstrated modulation of pathways associated with cholesterol metabolism, inflammation, and oxidative stress. Silencing of hepatic RDH11 in mice resulted in an increased abundance of hepatic free cholesterol, with a concomitant upregulation of mRNA expression of a marker of endoplasmic reticulum stress, Ddit3, and reduced expression of the cholesterol esterification marker Acat2. Finally, RDH11 silencing was associated with both a reduction in hepatic tetralinoleoyl cardiolipins and proteins of the electron transport chain CII/CIV which are indicative of perturbed mitochondrial function. Taken together, these findings support a role of RDH11 in the regulation of hepatic cholesterol metabolism and the impact on oxidative stress and mitochondrial pathways.

43. INVESTIGATING CELLULAR SUBSTRATES AND AGENTS TO MODEL HEPATIC LIPID METABOLISM IN THE CONTEXT OF FATTY LIVER DISEASE

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Diabetes predisposes individuals to the development of numerous metabolic complications including non-alcoholic fatty liver disease (NAFLD). NAFLD is characterised by the onset of, steatosis progressing to an inflammatory and fibrotic disease state known as non-alcoholic steatohepatitis (NASH) which is a significant risk factor for liver cirrhosis and hepatocellular carcinoma. Presently there exists no targeted pharmacological intervention for the treatment of fatty liver disease which highlights a significant unmet clinical need.
Our research aims to improve the understanding of the disease through four in vitro models. Specifically, our models serve as a comprehensive investigation into effects of metabolic substrates and agents which enable us to characterise key molecular pathologies associated with NAFLD.
Briefly, the human liver cell line, Hep3B, and the mouse liver cell line, Hepa1-6, were used to assess how pathogenicity of different metabolic substrates can induce fatty liver. Cells were treated for 24 hours with palmitic (PA) or oleic (OA) acids, high and low glucose or fructose concentrations, or agents that stimulate glucose and lipid pathways; glucosamine, TNFa and insulin.
Most notably in the Hepa1-6 cell line, treatment with 0.5mM OA and 5mmol of fructose was associated with an eight-fold increase in mRNA expression of perilipin 2 (PLIN2), a marker of lipid droplet development. Furthermore, this mixture triggered a significant inflammatory response evidenced by a four-fold increase in DNA damage inducible transcript 3 (DDIT3; $p < 0.0001$). Lipidomic analysis revealed fructose with OA induced a two-fold increase in triglyceride and cholesterol synthesis.
Taken together, our models provide for an expanded understanding of the metabolic landscape seen in NAFLD, while supporting the use of exogenous fatty acids and sugar substrates to recapitulate the deleterious effects associated with fatty liver disease. Additionally, these models could facilitate a high throughput format to test potential novel therapeutics for the treatment of fatty liver disease.

44. ELUCIDATING THE EFFECT OF NOX5 INHIBITION IN DIABETIC KIDNEY DISEASE IN A HUMAN 3D KIDNEY ORGANOID MODEL

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BACKGROUND: Diabetes related chronic kidney disease (CKD) is the leading cause of end stage renal failure. Oxidative stress due to excessive production of reactive oxygen species (ROS) plays a central role in diabetic kidney disease (DKD). The pro-oxidant enzyme NADPH oxidase-NOX5 is considered as a major contributor of renal ROS mediated kidney damage in diabetes.

AIM: To identify the renoprotective effect of NOX5 inhibition in *in vitro* human renal cells and a novel human kidney organoid model exposed to diabetic milieu.

METHODS: We examined the effect of NOX5 inhibition using a small molecule NOX5-specific inhibitor on ROS formation as well as on the markers of fibrosis, inflammation and ROS-sensitive factors in human induced pluripotent stem cells (iPSCs) derived 3D kidney organoid model and renal cell lines (proximal tubular cells and glomerular podocytes) exposed to normal glucose (5 mM) and high glucose (25 mM).

RESULTS: In response to high glucose, we found upregulation of NOX5 and enhanced levels of ROS formation as well as increased expression of markers of fibrosis (collagen I and fibronectin), inflammation (MCP-1, TLR-4) and ROS-sensitive factors (PKC-α, EGR-1) in both kidney organoids and renal cell models. Interestingly, Inhibition of NOX5 attenuated the high glucose induced increased gene expression of markers of inflammation, fibrosis and ROS sensitive factors via reduction in ROS formation.

CONCLUSION: These novel findings support NOX5 as a potential therapeutic target in human diabetic kidney disease and warrant further evaluation in *in vivo* settings of diabetes driven renal complications, particularly in the rabbit model which express NOX5 endogenously like humans.

45. EXPLORING THE GUT-KIDNEY-AXIS IN A MOUSE MODEL OF DIABETIC KIDNEY DISEASE

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BACKGROUND: Emerging research has unveiled the concept of the gut-kidney axis, revealing a potential link between intestinal barrier integrity and kidney function. A previous study from our group has shown evidence of an impaired intestinal barrier in a mouse model of diabetic kidney disease (DKD), the Leprdb/db mice. However, whether the gut and kidney have a causal relationship in the DKD context remains unknown. Larazotide is a drug currently used in clinical trials for improving intestinal permeability in coeliac disease, but it has not been investigated in DKD.

AIM: This study aimed to demonstrate whether larazotide can improve DKD in a mouse model of type 2 diabetes.

METHODS: Leprdb/db mice were treated with 20mg/kg/day larazotide in drinking water for 10 weeks. FITC-dextran assay was performed to assess intestinal permeability. Kidney function was evaluated by urinary albumin, and structural damage was assessed by periodic acid Schiff's staining and glomerulosclerotic index scoring.

RESULTS: Diabetic Leprdb/db mice displayed greater intestinal permeability compared to the non-diabetic controls, as shown by the FITC-dextran assay (4.322±1.081µg/ml vs 1.597±1.126µg/ml, $p<0.05$) which was not improved by larazotide treatment. Interestingly, larazotide appears to exacerbate albuminuria in diabetic mice at the endpoint (869.0±269.2µg/24hr vs 472.6±124.3µg/24hr, $p<0.05$). This finding corresponds to the increased kidney weight in the diabetic mice treated with larazotide (0.01420±0.002 vs 0.01322±0.001), suggesting the treatment increased kidney hypertrophy. No changes in glomerulosclerosis were observed with larazotide treatment.

CONCLUSION: Preliminary results have confirmed that Leprdb/db mice with DKD exhibited increased intestinal permeability compared to non-diabetic controls. However, larazotide treatment did not improve intestinal permeability. Notably, kidney injury markers were exacerbated in Leprdb/db mice treated with larazotide. This finding has raised an intriguing question of whether larazotide is nephrotoxic in diabetes. Further investigations are required to unravel the underlying mechanisms of this observation.

46. AMPK ACTIVATION PREVENTS CLONAL HAEMATOPOIESIS OUTGROWTH IN DIABETES

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The leading cause of death in patients with diabetes mellitus (DM) is cardiovascular disease (CVD). Individuals with CVD and DM are strong candidates for acquiring haematological dysfunction arising from somatic mutations in haematopoietic stem cells (HSCs), a condition called clonal haematopoiesis of indeterminate potential (CHIP). The most commonly mutated gene in CHIP carries is in *DNMT3A* (*Dnmt3a*$^{+/R878H}$). Interestingly, the progression of CHIP, characterised by rate of clonal outgrowth appears to be enhanced in people with diabetes. Notably, AMPK directly phosphorylates and stabilises TET2. Thus, in diabetes, AMPK and subsequently TET2 activity and DNA hydroxymethylation is reduced. Pre-clinical studies have revealed that co-deletion of *Dnmt3a* and *Tet2* display a myeloproliferative disorder.

AIM: We hypothesized that diabetes would accelerate *Dnmt3a*-CHIP expansion due to dysregulated AMPK-TET2.
Methods: To mimic human-CHIP, we performed a BM transplant where WT mice received 90% WT and 10% of Dnmt3a$^{+/R878H}$ (or control) cells. After BM reconstitution mice were made diabetic with STZ injections or left as controls. To test if AMPK activation could reverse Dnmt3a-CHIP, diabetic mice received chow diet with/without O-304.

RESULTS: High glucose settings *in vivo* and *in vitro* reduced AMPK and subsequently TET2 activity as measured by DNA hydroxymethylation in BM-HSPCs *in vivo* and *in vitro*. We found that diabetic *Dnmt3a*-CHIP mice displayed reduced TET2 function in BM HSPCs and increased clonal expansion of circulating myeloid cells. This was also true of the HSPCs in the BM, blood, and spleen. Notably, treatment with O-304 was able to reverse clonal expansion in all tissues through the restoration of TET2 activity in HSCs.

CONCLUSION: Diabetes directly induces TET2 dysfunction and accelerates *Dnmt3a*-CHIP. Mechanistically, diabetes accelerates *Dnmt3a*-CHIP through reduced AMPK-TET2 axis. Importantly, this can be reversed using a novel AMPK activator currently in phase II clinical trials, which could be used to prevent clonal outgrowth in CHIP-carriers.

47. HbA1c VARIABILITY AND DEMENTIA RISK IN A DIVERSE COHORT OF OLDER ADULTS WITH TYPE 2 DIABETES

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Type 2 diabetes is associated with a two-fold increase in dementia risk. Although HbA1c variability is becoming increasingly recognised as contributing to end-organ damage, less is known about its contribution to dementia risk.

AIM: To study the association between HbA1c variability and dementia risk in a large, diverse sample of people in Northern California.

METHODS: Over 209,000 members of a health care system with type 2 diabetes aged ≥ 50 years were followed from 1996 to 2018 to obtain repeated measures of HbA1c, dementia diagnoses, and comorbidities. Variability was measured using standard deviation (SD) and coefficient of variation. Cox proportional hazards models estimated the association between HbA1c variability in the first 3 years of cohort entry and incident dementia at least 2 years after the end of the exposure period adjusting for age and baseline comorbidities.

RESULTS: There were a total of 209,703 people in the cohort (mean study entry age 61.0 years (SD=9.2), 47.5% women). Approximately 49.6% of the sample were White. The mean number of HbA1c values available for each participant was 5.8 (SD=2.3). The mean HbA1c for each participant in the first 3 years was 7.4% (SD=1.33). Greater HbA1c variability was associated with greater hazard of dementia when measured using SD (aHR=1.12 [95%CI:1.10, 1.14]) or coefficient of variation (aHR=2.17 [95%CI:1.85, 2.55]). When stratified by mean HbA1c, we found that - relative to the lowest quintile of variation - increasing variability of SD of HbA1c was associated with greater hazard of dementia in HbA1c categories of <6% (p=0.0004) and 6-8% (p<0.0001) but not in those with a mean HbA1c ≥8% (p=0.42).

CONCLUSION: Greater HbA1c variability is associated with greater dementia hazard in those with good glycemic control. These results support current clinical recommendations to minimize glycemic variability and extend known benefits to include lowering of dementia risk.

BASIC / LAB

48. POST-DEVELOPMENTAL DISRUPTION OF MUSCLE POLG1 EXONUCLEASE ACTIVITY INDUCES MITOCHONDRIAL STRESS AND A CACHEXIA-LIKE PHENOTYPE

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Mitochondrial DNA (mtDNA) is replicated within the mitochondria by DNA polymerase gamma (PolG), which has three enzymatic actions: polymerase activity, exonuclease activity (proofreading), and base excision repair. As the sole polymerase found in mitochondria, PolG is essential for the replication and maintenance of mtDNA, and subsequently, mitochondrial health and function. 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, known as the PolG "mutator" mouse ($PolG^{D257A}$), is a global transgenic with 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 ($PolG^{fl/fl}$-mutator), generated by inserting LoxP sites flanking the proofreading/repair exonuclease domain of the PolG gene. We have subsequently crossed $PolG^{fl/fl}$-mutator with tamoxifen inducible-Cre mice (ACTA1-Cre-ERT2) to generate mature mice with muscle specific-PolG insufficiency. Muscle specific-$PolG^{fl/fl}$-mutator mice exhibited progressive weight loss approximately 15-weeks post-tamoxifen administration, characterised by reductions in both muscle mass and fat mass. The reductions in muscle and fat mass were accompanied by elevated muscle and plasma FGF21 and GDF15, but with no alterations in food intake, glucose or insulin tolerance. Proteomic and functional analysis demonstrated reductions in mitochondrial complexes CI, CIII and CIV abundance and activity. Combined with transcriptomics, our data indicates initiation of the integrated mitochondrial stress and unfolded protein response including alterations to ribosomal and translational machinery, consequently leading to mitochondrial dysfunction in muscle and systemic reductions in fat mass. Thus, our tissue specific PolG mutator model both recapitulates aspects of the traditional mutator mouse whilst displaying unique characteristics, highlighting the advantages of investigating mtDNA mutation-driven pathology in a tissue specific manner.

49. NOVEL POLYGENIC MODEL OF COMPLEX I DEFICIENCY DISPLAYS A SEVERE ATAXIA AND NEURODEGENERATIVE PHENOTYPE

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Mitochondria are small cellular organelles involved in many of our bodies' essential processes, including the critical role of energy production for physiological processes. Mitochondrial disease is caused by genetic mutations impacting the mitochondria's ability to correctly produce much needed energy, mainly manifesting in high-energy-demand tissues such as the brain, heart and muscle. Unfortunately, there is currently no cure for mitochondrial disease, and therapies are mostly limited to treating symptoms and improving quality of life. This limitation is linked to the lack of a suitable research model available in the field. To overcome this limitation our lab has used a panel of 100+ genetically diverse inbred mouse strains to identify suitable genetic models of mitochondrial disease. We identified a mouse model with a polygenic deficiency in mitochondrial complex I across multiple tissues and have subsequently aged this model to 12 months and completed neurobehavioral and molecular phenotyping.
Through behavioural analysis, our lab observed this mouse model to have a severe ataxia phenotype characterised by poor motor coordination and strength as they age. These mice have a distinct hind limb clasp indicating a disconnect between their motor and sensory systems, often observed in conditions such as MND. Through western blotting and proteomic techniques, we have demonstrated this model has a severe deficiency in mitochondrial complex I proteins within the brain, including core proteins NDUFS1 and NDUFS4. With the combined severe ataxia and mitochondrial complex, I deficiency findings this model demonstrates, suggests this model can be used for further research in mitochondria diseases.

50. PROXIMAL GASTRIC ANATOMY VARIANT POST SLEEVE GASTRECTOMY: A PHYSIOLOGICAL APPROACH TO SYMPTOMS

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INTRODUCTION Proximal gastric anatomical variations following sleeve gastrectomy can be associated with severe adverse symptoms or none; suggesting substantial variability in the functional significance of these variations. Current investigations lack validations and definite diagnostic criteria to facilitate objective diagnosis. We hypothesised that these variations will be significant if it resulted in physiological abnormalities identified on readily available investigations: high resolution manometry (HRM) and nuclear scintigraphy (NS) with some adaptations.

METHODS We undertook a prospective trial (ACTRN12616001089426) evaluating all patients with anatomical variations noted on surveillance endoscopy. All subjects were categorised based on the presence of symptoms and underwent endoscopy, liquid contrast swallow, HRM, 24-hour pH analysis (pH) and protocolised NS utilising tailored diagnostic criteria developed by a Delphi process. The findings were validated against asymptomatic controls with normal sleeve anatomy.

RESULTS A total of 40 patients (22 symptomatic vs 18 asymptomatic) were included and validated against 66 asymptomatic controls. Endoscopy and liquid contrast swallow findings were similar in all groups. HRM in symptomatic patients showed an elevated peak oesophageal (9.7 $\pm$ 5.4mmHg vs 5.1 $\pm$ 1.5mmHg, p=0.04) and proximal intragastric isobaric pressure (32.1 $\pm$ 19.2mmHg vs 20.9 $\pm$ 4.7mmHg, p=0.03). pH analysis showed higher total reflux events (124.9 $\pm$ 87.6 vs 55.1 $\pm$ 55.6, p<0.001). When validated against the control group, these data correlated with NS; showing elevated reflux events in the symptomatic group 95.4 $\pm$ 42.4 vs asymptomatic: 86 $\pm$ 48.8 vs control 4.8 $\pm$ 2.7 (p-value<0.05), prolonged gastric emptying half-time (37.1 $\pm$ 19.5 vs 29.4 $\pm$ 11.7 vs 18.8 $\pm$ 3 minutes, p=0.001) and higher percentage of retained meal in the proximal stomach 10.5 $\pm$ 8.5% vs 4.3 $\pm$ 3% vs 3.3 $\pm$ 4.6%, p=0.008.

CONCLUSION Symptomatic patients with proximal gastric anatomical variations can be stratified into 2 main groups: bolus obstruction characterised by elevated isobaric oesophageal and proximal gastric pressures; and stasis characterised by radionucleotide retention in the proximal stomach with repeated macro reflux events. These configurations were readily distinguished on HRM and NS using tailored diagnostic criteria.

51. TIME TO PERFORM COMPUTED TOMOGRAPHY BRAIN IMAGING IN CRITICALLY ILL PATIENTS: COMPARISON OF FIXED VERSUS MOBILE SCANNING.

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INTRODUCTION: Transporting critically ill patients to radiology for Computed Tomography (CT) brain imaging occurs frequently in trauma and neurocritical care. This procedure is labor-intensive, time-consuming and has a risk of adverse events. To improve efficiency and safety, we introduced a mobile CT scanner into our ICU, the first in this environment in Australia. This study aimed to quantify the time taken to prepare for and perform a CT brain using a conventional fixed CT scanner, as compared with a mobile CT scanner brought to the patient's cubicle.

METHODS: A prospective, observational, before-and-after study was performed between October 2022 and July 2023. A convenience sample of 40 ICU patients having non-urgent, non-contrast CT brain imaging was included (n=20 fixed, n=20 mobile). Demographic and diagnostic data were collected, as well as times for preparation, transport and performance of scans. Patient-related and technical complications were recorded.

RESULTS: Diagnostic category (trauma: 55% static, 55% mobile), gender (male: 75% static, 85% mobile) and intubation rate (100% static; 95% mobile) were similar between the groups. The mean time to prepare for CT imaging was similar between the groups (25mins vs 22mins; p=0.46). The mean time for transport and performing the scan was significantly shorter in the mobile CT group (14.5mins vs 32.5mins; p=0.<0001). Fixed CT imaging was associated with episodes of raised intracranial pressure and increased intravenous sedation boluses. There were no complications related to mobile CT scanning.

CONCLUSION: Mobile CT scanning is time-efficient, with less adverse events than conventional CT transports, in ICU patients.

52. EXPLORING THE DIAGNOSTIC AND PROGNOSTIC POTENTIAL OF PLASMA BRAIN-DERIVED NEUROTROPHIC FACTOR IN MILD TRAUMATIC BRAIN INJURY

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INTRODUCTION: Comprehension of the intricate pathophysiological cascade following mild traumatic brain injury (mTBI) has been steadily improving in recent years. Although heterogeneous, mechanisms like inflammation and apoptosis may be key determinants of outcome after TBI. As such, it has been hypothesised that brain-derived neurotrophic factor (BDNF) may serve as a reliable biomarker of mTBI due to the key role that it plays in many of these processes.

AIMS: To investigate the diagnostic and prognostic utility of BDNF as a biomarker of mTBI.

METHODS: 190 adults (135 mTBI, 55 healthy controls) aged 18-50 were recruited from either The Alfred Emergency & Trauma Centre or the Victorian Amateur Football Association. Participants underwent symptom evaluation using the Rivermead Post-Concussion Questionnaire, and CogState cognitive testing at <48hrs, 1-week, and 1-month post-injury. Blood was collected at <48hrs and 1-week for plasma biomarker quantification of BDNF using a Simoa HD-X Analyser.

RESULTS: mTBI participants had significantly elevated plasma BDNF levels at <48hrs compared to healthy controls (p=0.005), but no differences were found at 1-week. However, plasma BDNF had a relatively poor ability to distinguish mTBIs from controls at <48hrs (AUROC=0.63; 95%CI=0.54-0.72). Plasma BDNF levels at <48hrs (p=0.026) and 1-week (p=0.045) were elevated in participants with high symptom severity compared to those with low severity or no symptoms at 1-week post-injury (48h: AUROC=0.63; 95%CI=0.52-0.73); 1w: (AUROC=0.62; 95%CI=0.51-0.73). Decreased BDNF levels at 1-week were associated with deficits in psychomotor speed at both 1-week (p=0.050; AUROC=0.68; 95%CI=0.51-0.84) and 1-month (p=0.030; AUROC=0.67; 95%CI=0.55-0.7).

CONCLUSIONS: Although plasma BDNF levels were significantly elevated in mTBI compared to controls at <48hrs, diagnostic utility was relatively poor. Conversely, reduced BDNF levels were associated with worsened symptom recovery and cognitive deficits, indicating that it may have utility as a prognostic biomarker of mTBI outcomes. As such, further research is necessary to investigate these nuances.

53. TRANSFORMING SURVIVORSHIP CARE: PATIENT INFORMED FOLLOW UP CARE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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AIM: To examine the patient experience of attending a Long Term Follow Up (LTFU) clinic for individuals after allogeneic stem cell transplantation (alloSCT) and identify opportunities for consumer informed quality improvement.

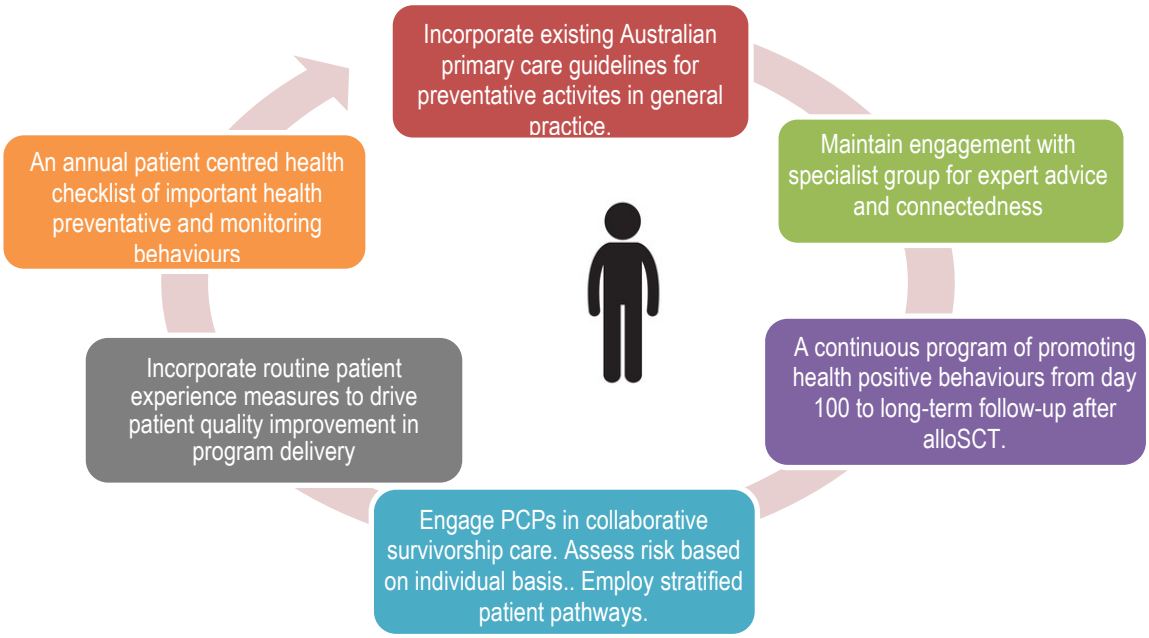
METHOD: Consecutive individuals attending the LTFU clinic surviving at least 2 years after alloSCT were enrolled in an interview based qualitative study. Interview questions are provided in Box 1 and were conducted by three experienced long-term follow up practitioners. Following each clinic, interviewers met and analysed responses, agreed on themes and informative patient responses were identified.

BOX 1: Interview questions

1. Tell me about your experience of the late effects clinic, care plan and pre-clinic investigations.
2. How does your attendance at the LTFU clinic relate to the care you receive from your primary care physician (PCP)?
3. Do you have any recommendations for optimal focus of the LTFU clinic?

RESULTS: Eighty-eight interviews were conducted (43% females) with median age at interview 54 years and acute leukaemia accounting for 63% of participants. Fifty-two (59%) of participants had a diagnosis of chronic graft versus host disease (cGvHD). The majority of patients 81 (92%) reported a positive response to attending the LTFU clinic, maintaining engagement with the specialist team was a recurring theme. A high number of participants 69 (78.4%) reported extensive pre clinic investigations were a burden and often replicated across health care visits including with PCP. Most participants 75 (88%) had a PCP and described confidence in their PCP providing non-specialist care. The most common response for the optimal focus of the clinic was an accessible optimal health checklist, replacing the detailed survivorship care plan following transplant. Figure 1 summarises the consumer informed proposed changes to the delivery of supportive care after transplantation.

FIGURE 1: **Key recommendations to post transplant supportive model of care**



CONCLUSION: We describe the value of incorporating consumer feedback to achieve patient-centred, safe and clinically relevant survivorship care following alloSCT. Based on our findings, we propose personalising survivorship care through empowerment of patients and enabling them to control their own survivorship care plans through a health checklist. Given the potential complexity following alloSCT, engagement with specialist groups for expert advice and connectedness will still remain core for optimal post alloSCT care.

54. TRANSFER OF MATERNALLY ADMINISTERED VALPROATE INTO THE FETAL BRAIN IN A RAT MODEL OF EPILEPSY FOLLOWING DIFFERENT CHRONIC TREATMENT REGIMENS

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Babies *in utero* may be exposed to maternally ingested antiepileptic drug valproate, a known teratogen. In some patients, valproate is the only effective drug and chronic treatment is often required. Its deleterious effects on the developing brain are not well understood.

AIMS: This study utilised a rat model of absence epilepsy, Genetic Absence Epilepsy Rat from Strasbourg (GAERS) to investigate transfer of valproate across placenta, and entry into cerebrospinal fluid (CSF) and brain of fetuses at embryonic day (E) 19 following different maternal chronic treatment regimens.

METHODS: GAERS females consumed low- or high-dose valproate diet (7 or 20 g/kg chow) from 2 weeks prior to mating until E19. Some females on high-dose diet switched back to normal diet at E12. Controls had normal chow. All dams at E19 received intravenous injection of valproate (30 mg/kg) with its [3H] tracer. Thirty minutes later fetal blood, CSF and brain were collected along maternal samples. Radioactivity was measured and transfer expressed as ratios of radioactivity in fetal over maternal plasma (placental barrier) or in CSF or cortex over fetal plasma (fetal brain barriers).

RESULTS:

- Placental valproate transfer was similar in control and in all chronic treatment groups (~50-65%).
- Compared to controls, entry of valproate into fetal brain in pups of dams on high-dose diet was higher irrespective of treatment length (~60% to ~100%).
- Fetal CSF entry of valproate increased by ~30% only in dams on high-dose diet until E19.

CONCLUSION: Placenta provided significant protection as only ~50% of maternal plasma valproate transferred to fetuses regardless of treatment regimens. Entry of valproate into the fetal brain and CSF increased only following high-dose treatment, suggesting a potential benefit of reducing drug doses during pregnancy. Withholding valproate exposure from late gestation, a sensitive period in brain development, appears to reduce its entry into fetal CSF.

55. REVISED UK-NEQAS CSF-XANTHOCHROMIA METHOD IS FIT-FOR-PURPOSE TO INVESTIGATE SUSPECTED SAH CASES: A SINGLE CENTRE RETROSPECTIVE STUDY

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Subarachnoid haemorrhage (SAH) requires prompt diagnosis and treatment due to its high morbidity and mortality. In patients with negative findings on CT-brain and delayed presentation, cerebrospinal fluid (CSF)-xanthochromia testing is the recommended second line investigation if performed after 12-hours.

AIMS: To identify the accuracy and usefulness of CSF-xanthochromia testing
To identify the mortality outcome for patients with delayed presentation
To clarify the interpretation of equivocal CSF-xanthochromia reports

METHOD: A retrospective audit of all CSF-xanthochromia tests at our health service over 8 years (1.06.2014 – 1.06.2022) was performed. The service follows the revised United Kingdom National External Quality Assessment Service (UK-NEQAS) method.

RESULTS: 545 cases (F=301, median age 44yrs) were reviewed after applying inclusion and exclusion criteria. 19 (3.5%) had SAH confirmed by imaging studies and neurosurgical opinion. Overall, CSF-xanthochromia testing was found to have a sensitivity of 100%, specificity of 98.1%, positive predictive value (PPV) of 65.5% and negative predictive value (NPV) of 100%. In 282 cases (F=155, median age 43yrs) where LP was performed more than 24-hours from the onset of headache (median time to LP=72hr, range 24.1- 672hr), the sensitivity and specificity of the CSF-xanthochromia was 100% and 97.4% respectively (PPV 100%, NPV 68.2%). In this group, 197 cases (69.9%) had 12-month follow up following their CSF-xanthochromia test and all survived.
Interpretation of CSF-xanthochromia testing depends on the Net-Bilirubin-Absorbance (NBA) and Net-Oxyhaemoglobin-Absorbance (NOA) values. In cases where the NBA is <=0.007 and NOA is >0.02 but <0.1 the UK-NEQAS reporting guidelines changed from “equivocal” (2003) to “negative” (2008). We encountered 48 such instances and none had SAH, supporting the revised UK-NEQAS guideline as safe and effective.

CONCLUSION: Our study confirmed that CSF-xanthochromia testing using revised UK-NEQAS method is fit-for-purpose in the investigation of suspected SAH in patients with negative CT-brain including delayed presentation over 24-hours from headache onset.

56. FUNCTIONAL ASSESSMENT OF THE PI3K PATHWAY CAN STRATIFY PATIENTS FOR TARGETED TREATMENT WITH PI3K INHIBITORS

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BACKGROUND: Activated PI3-kinase-delta syndrome (APDS) is treated with pharmacological inhibitors targeting enhanced Akt-PI3K-mTOR-S6 signalling pathway function. APDS classically presents in childhood with combined immunodeficiency and comorbidities including lymphoproliferation and autoimmunity. APDS-1 is caused by heterozygous gain-of-function *PIK3CD* variants, and APDS-2 by heterozygous loss-of-function *PIK3R1* variants. It remains unclear whether other immunodeficient patients have enhanced PI3K signalling and could benefit from targeted treatment.

METHODS: We applied an optimised flowcytometric assay for evaluation of phosphorylated-S6 in blood B- and T-cells to detect enhanced PI3K function.

RESULTS: Patient 1 is a 25-year-old female with a clinical phenotype consistent with APDS-2 carrying a novel heterozygous *PIK3R1* variant (c.716C>T;p.T239M). Patient 2 is a 43-year-old female presenting with hypogammaglobulinemia and harbouring a novel heterozygous *SYK* variant (c.1769G>A;p.R590Q). Both B- and T-cells of patient 1 displayed increased tonic and ligand-induced phosphorylated-S6 levels. Patient 2 demonstrated increased SYK autophosphorylation, and increased tonic and ligand-induced phosphorylated-S6 levels in B- but not T-cells.

DISCUSSION: We describe the first case of APDS-2 with a *PIK3R1* variant residing outside of exon 11.In patient 2, this is the first demonstration that increased SYK autophosphorylation in B-cells leads to activated PI3K signalling.
Both patients expand the spectrum of genetic variants causing activated PI3K, as evaluated by phosphorylated-S6 detection. Importantly, this illustrates that patients other than those with classical APDS could benefit from PI3K inhibitors treatment. We argue that clinical studies should use functional signalling definition including PI3K as a rationale for treatment with PI3K inhibitors, and to stratify patients for treatment with novel biologicals.

57. INTERLEUKIN-21, ACTING BEYOND THE IMMUNOLOGICAL SYNAPSE, INDEPENDENTLY CONTROLS T FOLLICULAR HELPER AND GERMINAL CENTER B CELLS

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The generation of protective antibodies in response to vaccination or infection relies on the coordinated behaviour of T and B cells in transient structures called germinal centres (GCs). IL-21, a pleiotropic T cell-derived cytokine, is a central modulator of GC size, maintenance and output and studying how it exerts its actions provides an opportunity to understand the fundamental principles underlying antibody based immunity. Following this theorem, we genetically restricted IL-21 production and receipt in vivo to show how its independent actions on T and B cells combine to regulate the GC. IL-21 established the magnitude of the B cell response by promoting $CD4^+$ T cell expansion and T follicular helper cell differentiation in a dose-dependent manner and with paracrine activity. Simultaneously, by activating AKT and S6, IL-21 accelerated cell cycle progression and the rate of cycle entry of B cells, increasing their contribution to the ensuing GC. Within GC, IL-21 specifically promoted B cell centroblast identity and, when bioavailability was high, plasma cell differentiation. Critically, these actions occurred irrespective of cognate T-B interactions, making IL-21 a general promoter of growth as distinct to a mediator of affinity-driven selection via synaptic delivery. This promiscuous activity explains the consequences of IL-21 deficiency on antibody-based immunity. These findings have important implications for understanding how the immune system balances maintaining a diverse repertoire of reactivities with selecting cells for high affinity antibody output, thereby achieving optimal protective immunity.

58. ENLARGED PERIVASCULAR SPACES DENSITY INVERSELY CORRELATED WITH QUANTITATIVE STEREO-ELECTROENCEPHALOGRAPHY EPILEPTOGENICITY MARKERS

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OBJECTIVE: Enlarged perivascular spaces (ePVS) are parts of the glymphatic system which has been demonstrated to be involved in many neurological conditions including epilepsy and can be quantitated on high-resolution MRI. This study aims to determine the correlation between MRI ePVS density with quantitative stereo-electroencephalography (SEEG) epileptogenicity markers.

METHODS: We conducted a cross-sectional observational study in a cohort of patients implanted with SEEG for drug-resistant focal epilepsy. Spikes, high-frequency oscillations (HFO), and fast ripple (FR) rates were quantified using the Delphos toolbox based on 20-minute N3 sleep recordings. SEEG contacts were classified into thermocoagulated contacts, top 10% spikes x HFO contacts, top 10% spikes x FR contacts, and top 10% spikes contacts. Contact coordinates were calculated using an in-house MATLAB program. ePVS from pre-implantation T1-weighted MRI scans were identified using an automated U-Net model. ePVS density was calculated within a spherical 10 mm radius for each voxel. Contact coordinates and ePVS density map were co-registered using SPM12 in each patient's native space. Statistical analysis involved Mann-Whitney and binary logistic regression tests.

RESULT: 4,067 SEEG contacts (3,902 for thermocoagulation) from 33 patients with drug-resistant epilepsy who underwent SEEG implantation (66.7% female, mean age 35.84±10.02 years) were included for this analysis. Mean ePVS count and volume were 156.36±100.33 and 989.31±745.18 ml respectively. Increased ePVS density inversely correlated with thermocoagulated contacts ($p<0.001$),top 10% spikes x HFOs ($p<0.001$), top 10% spikes x FR ($p<0.001$), and top 10% spikes contacts ($p=0.036$).

CONCLUSION: Reduced ePVS density around epileptogenic contacts may indicate impaired glymphatic clearance or early ePVS shrinkage in the epileptogenic zone. Longitudinal studies are necessary to determine the correlation between thermocoagulation or epileptogenic zone resection with ePVS density.

59. DIFFERENCES IN CELLULAR LIPID COMPOSITION AFFECTS IMMUNE CELL SENSITIVITY TO FERROPTOSIS

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Our laboratory has recently characterised the cellular lipidome of the human and mouse immune systems. One of the most striking effects we observed was a marked variance in the levels of poly-unsaturated fatty acids containing phospholipids (PUFA-PLs) between different immunes cell types. Given the importance of these distinct phospholipids in ferroptosis and our lipidomic data, we explored the susceptibility of immune cells to ferroptosis. Immune cells isolated from murine bone marrow were incubated with varying doses of ML210, a GPX4 inhibitor. Cell viability analysis revealed that T and B cells, cells with the highest abundance of PUFA-PLs, were the most susceptible to ferroptosis. Importantly, ML210-induced cell death in T and B cells was prevented by treatment with inhibitors of ferroptosis. In contrast, neutrophils and monocytes, cells with the lowest abundance of PUFA-PLs, were protected from ferroptosis. Importantly, supplementation with exogenous fatty acids to re-model the immune cell lipidome altered immune cell susceptibility to ferroptosis, indicating that differences in immune cell lipid composition govern susceptibility to ferroptosis. Collectively, our work identifies the basis for previously described differences in immune cell susceptibility to ferroptosis and raises exciting questions about the potential physiological reasons myeloid cells may wish to avoid ferroptosis.

60. ASYMMETRIC PERIVASCULAR SPACE DISTRIBUTION IN POST-STROKE EPILEPSY

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INTRODUCTION: Around 10% of stroke patients develop post-stroke epilepsy (PSE), leading to long-term impairments and higher mortality rates. Various risk factors for PSE have been reported, including stroke-severity, cortical-involvement, and carotid circulation territory involvement.
The glymphatic system is thought to be the brain's primary "waste" clearance system, eliminating soluble metabolites and proteins within the neuropil. It consists of cerebrospinal fluid, interstitial fluid, and a conduit between the two, perivascular spaces (PVS), which are channels formed by astroglial cells surrounding the blood vessels. PVS can be observed on high-resolution T1-weighted MRI images. This study investigates PVS as a novel imaging biomarker for PSE.

METHODS: 25 patients with PSE following an acute ischemic stroke (AIS) were studied. They were matched with 31 patients who had had AIS but without PSE, and 27 healthy controls. All participants were recruited from the Hospital das Clinicas, Campinas, Brazil. They were scanned with T1-weighted MRI on a 3T Phillips MRI scanner, resolution 1.0x1.0x1.0mm. A deep-learning algorithm, U-Net, was trained and applied to segment PVS. The number of PVS and asymmetry in PVS were extracted and used as predictors of PSE in a logistic regression with hypertension, cardiopathy, dyslipidemia, NIHSS, vascular-territory, and cortical-involvement included as nuisance covariates.

$$Absolute\ Asymmetry\ Index\ (AAI)\ =\ \left|\frac{\#PVS(lesion-side)\ -\ \#PVS(nonlesion-side)}{\#PVS(lesion-side)\ +\ \#PVS(nonlesion-side)}\right|$$

RESULTS: AAI was an independent predictor of PSE (beta(se)= -18.19(8.77), z=-2.074, p=0.038), but number of PVS was not (beta(se)=-0.001(0.004), z=-0.206, p=0.837).
Conclusion: These findings suggest that asymmetry in PVS is an independent predictor of PSE after an AIS (after accounting for several clinical characteristics associated with PSE). If confirmed in larger studies, PVS could potentially serve as a biomarker to predict high-risk AIS patients, be used to monitor antiepileptogenic trials closely, and eventually assist the selection of more individualized treatment streams.

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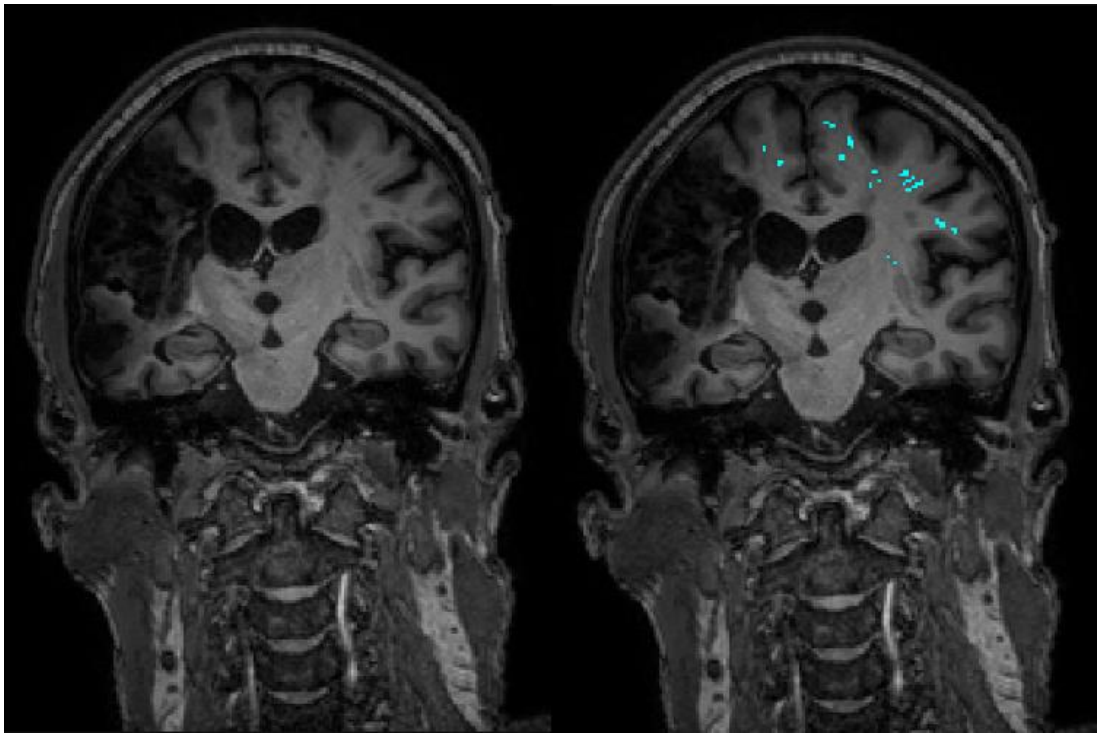

Figure 1: A PSE patient with high PVS asymmetry (right). U-Net segmentation of the perivascular spaces is in light blue (left).

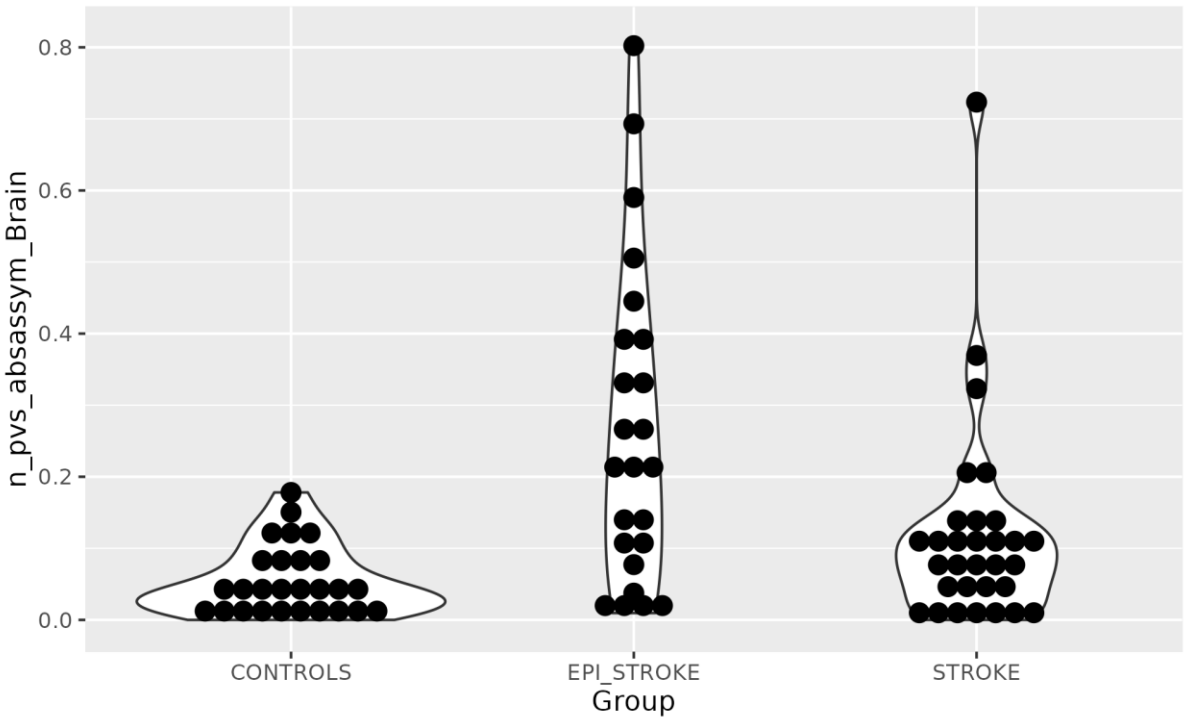

Figure 2: Violin plots of Number of PVS (top), and absolute symmetry index (bottom).

61. THE POTENTIAL ROLE OF MATRIX METALLOPROTEINASES IN THE DEVELOPMENT OF HAEMOPHILIC ARTHROPATHY

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In the sex-linked disease Haemophilia, deficiency in coagulation factors can lead to spontaneous bleeding episodes. Repeated joint bleeding induces arthritis that can lead to Haemophilic Arthropathy (HA) with devastating consequences. Matrix metalloproteinases (MMPs) are key players in inflammatory arthritis. Its role in HA is still unclear.

AIM: To study the involvement of MMPs and their associated pathways in HA development in a mouse model and explore MMP inhibition as adjuvant treatment for HA.

METHODS: We simulated HA in knee joints of haemophilic mice by inducing 2 knee injuries, assessing joint inflammation over 2 and 4 weeks. We performed IHC (Haematoxylin/ eosin-HE, Safranin O/ Fast Green- Saf-O, Perl stain) and IF for inflammation markers. MMP expression and activity were studied with gelatin zymography and western blotting. Plasminogen activity was measured with ELIZA. We investigated effects of MMP inhibition by subcutaneous injection of pan MMP inhibitor Ilomastat (GM6001; 50mg/kg/ 3 doses post injury). Synovial cell line (SW982) was used in in-vitro experiments to study behaviour of synovial fibroblasts in HA pathogenesis.

RESULTS: Knee inflammation was evident as by 1 week (knee diameter) persisting to 4 weeks. Inflammation and cartilage damage was confirmed with IHC (HE and Saf-O scoring) and IF. Significant activation of gelatinases MMP2 and MMP14 (MMP2 activator) were found in injured knees. uPA, a potential activator for MMP14, was significantly upregulated at 2 weeks in injured knees. The effect of uPA on MMP14 activation was confirmed in in-vitro experiments highlighting the role of synoviocytes on MMP activation. Administration of MMP inhibitor Ilomastat resulted in significant reduction of knee inflammation (knee diameter, IHC, IF) and thus cartilage damage.

CONCLUSION: The plasmin- MMP axis has a critical role in the development of HA. MMP blockade is a novel therapeutic approach that could complement current haemophilia management in mitigating joint damage.

INFECTIOUS DISEASE

62. CHANGES IN ANTIMICROBIAL RESISTANCE AND ANTIBIOTICS CONSUMPTIONS USING CEFTRIAXONE MONOTHERAPY VERSUS DUAL THERAPY WITH AZITHROMYCIN FOR TREATMENT OF GONORRHOEA IN MELBOURNE, AUSTRALIA

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Since the late 2020s, several countries have changed gonorrhoea treatment from ceftriaxone (0.5g IM)/azithromycin (1g po) dual therapy to ceftriaxone (1g IM) monotherapy as per the CDC guidelines. Dual therapy remains as the first-line treatment in Australia. In August-2021, the Melbourne Sexual Health Centre's in-house gonorrhoea treatment guidelines were changed from dual therapy to monotherapy.

AIM: To examine changes in antimicrobial susceptibility and antimicrobial consumption before and after the change of the treatment guidelines.

METHODS: We compared antimicrobial resistance (i.e. ceftriaxone, azithromycin, ciprofloxacin and tetracycline) and consumption between the dual therapy period (3-Aug-2020 to 08-Aug-2021) and monotherapy period (09-Aug-2021 to 26-Aug-2022) at MSHC.

RESULTS: 2,223 N. gonorrhoeae isolates (890 in dual therapy and 1333 in monotherapy period) were included. Cases were predominantly males (92.3%, n=2052). Monthly use of ceftriaxone increased (mean 24.1 vs 55.5 defined daily doses [DDD]/1000 presentations; p<0.0001) and azithromycin decreased (mean 83.5 vs 24.0 DDD/1000 presentations; p<0.0001) from the dual therapy to monotherapy period. After changing from dual therapy to monotherapy, there was a significant increase in azithromycin resistance (0.8% vs 5.2%; p<0.0001), ciprofloxacin resistance (49.6% vs 73.4%; p<0.0001) and tetracycline resistance (47.6% vs 62.1%; p<0.0001). However, there was a reduction in decreased susceptibility to ceftriaxone (1.1% vs 0%; p<0.0001). Multivariable analyses showed that while the switch to monotherapy was not significantly associated with azithromycin resistance (aOR=1.02; 95%CI: 0.21-4.97); the re-opening of Australia's international borders (i.e. 15-Dec-2021) was significantly associated with azithromycin resistance (aOR=8.21; 95%CI: 1.99- 33.80).

CONCLUSION: Following switching from dual therapy to ceftriaxone monotherapy, we saw a reduction in gonococcal strains with decreased susceptibility to ceftriaxone. While there was also a rise in azithromycin resistance, this was significantly associated with reopening of Australia's borders, possibly reflecting importation of antimicrobial resistance. Future genomic work should assess the lineages of N. gonorrhoeae currently circulating in our setting.

63. HUMORAL IMMUNITY TO ANCESTRAL AND VARIANT STRAINS OF SARS-COV-2 FOLLOWING COVID-19 VACCINES IN PEOPLE WITH HIV

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BACKGROUND: Humoral immune responses to several vaccines are reduced in people with HIV (PWHIV) compared to people without HIV. SARS-CoV-2 variants of concern (VoC) are characterised by an ability to evade immune responses to both infection and vaccination. We aimed to describe humoral immunity to ancestral SARS-CoV-2 and important VoC in PWHIV receiving up to 3-doses of ancestral COVID-19 vaccines.
Methods: We prospectively enrolled PWHIV receiving antiretroviral therapy, collecting blood for analysis before the first vaccine dose, then at 1- and 6-months post second dose, and 1-month post third dose. SARS-CoV-2 IgG antibody responses were quantified in microg/mL by enzyme-linked immunosorbent assay (ELISA) for receptor binding domain (RBD) and nucleocapsid (NCP). Titres of neutralising antibodies (nAb) were determined in a live-virus microneutralization assay, against ancestral, Delta, Omicron BA.2 and BA.5 SARS-CoV-2 variants.

RESULTS: Twenty-one PWHIV were recruited (95% male, median CD4 count 660 cells/microL [IQR 490-858], 81% on INSTI-based regimens). Twelve received mRNA vaccines for all 3 vaccine doses. The median concentration of RBD-specific IgG was 22.1 (IQR 4.4-39.1) microg/mL after two, and 61.2 (IQR 54.7-83.3) microg/mL after three doses of COVID-19 vaccine. Recipients of two mRNA vaccine doses had higher concentration of RBD-specific IgG (38.2 microg/mL, IQR 9.2-44.0) than those receiving a two doses of adenoviral vector vaccines (16.1 microg/mL, IQR 7.9-24.1). The ancestral COVID-19 vaccines generated high titre nAb responses to wild type and Delta variants, but titres to Omicron variants BA.2, and BA.5 were markedly reduced.

CONCLUSION: All PWHIV in this cohort developed SARS-CoV-2 RBD and neutralising antibody responses to ancestral strain COVID-19 vaccines, which increased after a third dose. However, most participants did not develop nAb to the most recent omicron variant tested (BA.5). More data are needed to understand the role of contemporary COVID-19 booster vaccines targeting Omicron variants to maximise SARS-CoV-2 immunity in PWHIV.

64. PROTECTING PLEASURE: SEXUAL HEALTH SERVICE USERS' ORAL STI PREVENTION STRATEGIES AND VIEWS ON STI PREVENTION MEASURES

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** Co-last authors*

Rising prevalence of bacterial STIs such as gonorrhoea, chlamydia and syphilis is a concern in the context of antimicrobial resistance, patient and healthcare burden, and reproductive outcomes.

AIM: This research sought to explore strategies used by attendees of a sexual health service to reduce oral transmission of STIs, and their views on measures currently under investigation (i.e., mouthwash, vaccination and antibiotic prophylaxis).

METHODS: A qualitative research design was used to explore strategies people used, or might be willing to use, to prevent being infected with or transmitting an oral STI. Purposive sampling and semi-structured interviews allowed for description and comparison of participants' perspectives from a range of ages, sexual orientations, genders and nationalities.

RESULTS: Twenty-one participants with and without a history of an oral STI were interviewed. Participants enjoyed a range of practices that increased their risk of an oral STI (e.g. oral sex, spit play, etc) but generally had not been engaged in conversations about these by health care professionals. Whilst individuals varied in the STI prevention strategies they used, and would consider, generally they were unwilling to engage in STI prevention measures that impacted the pleasure and intimacy of sex. As such, use of barrier methods like condoms and dental dams for oral sex were considered unacceptable to many participants and their partners. Conversely, STI testing, treatment and partner notification were preferred to protect themselves and others from STIs. Additional factors influencing the acceptability of novel prevention measures (e.g., mouthwash, vaccination, antibiotic prophylaxis) included accessibility, practicality, effectiveness and safety, with concerns about antimicrobial resistance featuring prominently in relation to antibiotic prophylaxis.

CONCLUSION: This research highlights the central role pleasure plays in decision-making about STI prevention strategies, underscoring the salience of sex positive approaches in clinical practice, research priorities and sexual health education.

65. VENOUS THROMBOEMBOLISM IN HOSPITALISED PATIENTS AT A QUATERNARY REFERRAL AND MAJOR TRAUMA CENTRE: ASSESSING PREVENTABILITY

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Hospital-acquired venous thromboembolism (HA-VTE) is associated with significant morbidity and is the leading cause of preventable inpatient death. Our quaternary referral and major trauma centre is a critical outlier for HA-VTE, with high-acuity casemix and proactive DVT surveillance. Appropriate thromboprophylaxis reduces HA-VTE incidence, however many cases are not preventable.

AIM: To determine the proportion of potentially preventable HA-VTE events.

METHODS: Retrospective cross-sectional study of patients with VTE, identified from ICD10-AM codes, from Jan-2019 to Dec-2022. Episodes coded incorrectly (e.g. absence of VTE; arterial thrombosis) or VTE prior to hospitalisation were excluded. Data collected included demographics, VTE risk factors and thromboprophylaxis prescribed. HA-VTE was deemed preventable if there was suboptimal VTE prophylaxis (including delayed commencement (>24hours) or under-dosing) in the absence of contraindications. Data were analysed descriptively. Chi-squared test of association was utilised for group comparisons, $p<0.05$ was considered statistically significant.

RESULTS: There were 576 patients screened; 495 were confirmed to have HA-VTE. Mean age was 58 years, 66.1% were male and length of stay was 23.7 days. The largest represented unit was Trauma (n=215). Majority of patients (n=479, 96.8%) were high-risk for VTE, with an average 2.6 risk factors. Pharmacological prophylaxis (predominantly enoxaparin) was prescribed to 407 patients (82.2%) and mechanical prophylaxis provided to 146 (29.5%). Overall, 26.9% (n=133) of HA-VTE events were assessed as preventable; the primary reason was delayed initiation (n=68). Almost half (48.4%) of the high-risk patients had one or more contraindications to thromboprophylaxis, with a significantly lower rate of preventable VTE (19.3%) compared to those without contraindications (35.2%) (OR 0.45,95% CI 0.30-0.69; p=0.0002).

CONCLUSION: Most HA-VTE episodes among a complex, high-risk group are not preventable. Increased clinician vigilance is required for patients with contraindications to thromboprophylaxis. Hospitals and healthcare authorities should measure and report HA-VTE where prophylaxis was suboptimal to improve modifiable aspects of patient care.

66. TITLE EFFICACY OF SITAFLOXACIN FOR M. GENITALIUM IN AN ERA OF INCREASING ANTIMICROBIAL RESISTANCE

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BACKGROUND Macrolide resistance in M. genitalium exceeds 50% in many regions, and fluoroquinolone resistance is rising. In Australia, resistance-guided therapy based on macrolide-resistance profile is used to direct treatment. Macrolide-resistant M. genitalium is treated with doxycycline followed by moxifloxacin, and patients who fail moxifloxacin are then treated with either pristinamycin, minocycline or a sitafloxacin-based regimen. We evaluated the efficacy of sitafloxacin-based regimens for macrolide-resistant M. genitalium at Melbourne Sexual Health Centre over 5 years.

METHODS Patients with macrolide-resistant M. genitalium who received a sitafloxacin-regimen between January 2017-February 2022 were included. Before June 2017, patients received doxycycline followed by sitafloxacin; subsequently, patients received doxycycline followed by combined doxycycline+sitafloxacin. Microbial cure was defined as a negative test-of-cure within 14-90 days after completing sitafloxacin. Proportions and 95% confidence intervals (CI) were calculated. Logistic regression with generalised estimating equations were used to explore factors associated with sitafloxacin failure.

RESULTS Of 229 patients treated with a sitafloxacin-regimen, 80.6% (95% CI: 74.9-85.5) experienced microbial cure. In adjusted analyses, prior failure of moxifloxacin was the only factor associated with sitafloxacin failure (Adjusted-Odds-Ratio=7.56, 95% CI 2.38-24.04, p<0.001). Due to correlated variables, we stratified cure based on prior moxifloxacin failure to evaluate the efficacy of the two sitafloxacin regimens. There was no difference in cure between the regimens when patients were stratified by past failure of moxifloxacin (p>0.05), however small numbers limited comparisons.

CONCLUSION Microbial cure following sitafloxacin was 80.6% for macrolide-resistant M. genitalium over the past 5 years, with past failure of moxifloxacin associated with an 8-fold increased odds of failing sitafloxacin, reflecting the likely presence of key fluoroquinolone resistance mutations (i.e. S831). These data provide contemporary information about sitafloxacin efficacy for M. genitalium in an era of rising antimicrobial resistance, and highlight the benefit of incorporating markers of fluoroquinolone resistance into diagnostic assays to assist clinical decision-making.

67. ORAL CIPROFLOXACIN ACTIVITY AGAINST PSEUDOMONAS AERUGINOSA IN A NOVEL CATHETER-ASSOCIATED URINARY TRACT INFECTION PHARMACODYNAMIC BIOFILM MODEL

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BACKGROUND: Catheter-associated urinary-tract-infections (CAUTIs) account for 30% of healthcare-associated infections, leading to increased costs, antibiotic usage, prolonged hospital stays, patient morbidity. Pseudomonas aeruginosa commonly causes CAUTIs within biofilm formation.

AIM: To design a pharmacokinetic(PK)/pharmacodynamic(PD) CAUTI in-vitro model to quantify uropathogen biofilm formation and antibiotic-induced disruption.

METHODS: Multicompartment in-vitro model with 16-bladder compartments with urinary-catheters was designed. Urodynamics simulated with synthetic-human-urine, inflow into bladders (25 mL/h; volume 50mL), with matching outflow through urinary-catheters. P. aeruginosa ATCC-27853 (ciprofloxacin [CIP] MIC 0.25mg/L) and 15 clinical P. aeruginosa uropathogens (CIP MIC 0.125-64mg/L) were selected. Planktonic bacterial density in the bladder (cfu/mL) and catheter biofilm mass (cfu/cm2, in triplicate) were quantified over 72h drug-free incubation and after 3-days of CIP therapy, targeting urinary concentrations following 750mg oral 12-hourly. PK/PD target for relative change in biofilm mass (%) was determined by Emax nonlinear regression.

RESULTS: The average biofilm mass was 7.0±1.0 log10cfu/cm2. Reduced biofilms were observed in 3-isolates (92669, 61963, 01643) with non-confluent coverage (triplicate range: 4.6-6.7, 3.9-7.4, 3.0-7.4 log10cfu/cm2, respectively). Biofilms extended along the entire length of catheter, quantified from segments dissected every 5cm. Following CIP exposure, ten isolates with MIC ≤4mg/L all had biofilm eradication (n=4) or disruption (n=6), and all had >3 log10 planktonic bacterial kill. All isolates with MIC >4mg/L (n=6) had biofilm resistance and failed to reduce the planktonic bacterial density. Post-exposure rise in CIP MIC (≥2 two-fold-dilutions) from regrowth was more common from planktonic bacteria (12/13 isolates) compared with the biofilm (5/12 isolates). AUC0-24/MIC IC50 target for relative change in biofilm mass (%) was 1430 (R2 0.9133).

CONCLUSIONS: A novel dynamic in-vitro model was able to simulate the treatment of CAUTIs. Following CIP exposure, P. aeruginosa isolates with MIC ≤4mg/L had biofilm disruption and bacterial kill in the bladder. However, emergence of CIP resistance was promoted.

68. PERFORMANCE OF NORFLOXACIN DISC DIFFUSION COMPARED WITH BROTH MICRODILUTION: IMPLICATIONS FOR CLINICAL BREAKPOINTS

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Accurate reporting of fluoroquinolone susceptibility is paramount in informing treatment options for multidrug-resistant uropathogens. Despite this, discrepancies in susceptibility interpretations between EUCAST and CLSI guidelines exist.

AIM: To report the accuracy of EUCAST and CLSI fluoroquinolone disc diffusion breakpoints at distinguishing resistant and susceptible isolates, in a collection of ceftriaxone-resistant clinical urinary isolates.

METHODS: One hundred and thirteen ceftriaxone-resistant clinical uropathogens (E. coli 97, K. pneumoniae 16) were selected from a surveillance collection. Selected isolates underwent norfloxacin and ciprofloxacin reference broth microdilution (BMD) MIC testing. Results were compared to susceptibility category as determined by disc diffusion, applying 2022 and 2023 EUCAST breakpoints, and 2023 CLSI breakpoints. A pefloxacin disc screen for fluoroquinolone resistance was also performed.

RESULTS: Norfloxacin BMD susceptibility was 18.6% (for EUCAST 2022/23) and 39.8% (for CLSI). Ciprofloxacin susceptibility was 31.9% (for both EUCAST 2022/23 and CLSI). EUCAST 2022 norfloxacin disc diffusion breakpoints (S≥22mm, R<22mm) demonstrated a very major error (VME; false susceptible) rate of 19.6% (18 isolates) compared to BMD MIC. EUCAST 2023 norfloxacin disc diffusion breakpoints (S≥24mm, R<24mm) demonstrated a VME rate of 8.0% (7 isolates) and a major error (ME; false resistant) rate of 14.3% (3 isolates). CLSI norfloxacin breakpoints (S≥17mm, R≤12mm) yielded no VMEs or MEs. Ciprofloxacin disc diffusion breakpoints for EUCAST 2022/23 (S≥25mm, R<22mm) and CLSI (S≥26mm, R≤21mm) performed similarly, with no VMEs or MEs. Pefloxacin disc screens were able to accurately predict fluoroquinolone resistance, displaying 100% sensitivity for both norfloxacin and ciprofloxacin, utilising both EUCAST and CLSI breakpoints.

CONCLUSION: The EUCAST 2023 norfloxacin disc diffusion breakpoints fail to predict susceptibility in ceftriaxone-resistant Enterobacterales, albeit improved from the 2022 breakpoints. In contrast, EUCAST ciprofloxacin breakpoints performed well. CLSI breakpoints performed well for both agents, although the clinical correlation with these breakpoints is uncertain. Pefloxacin disc diffusion accurately predicted fluoroquinolone resistance.

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

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BACKGROUND: Primary immunodeficiencies (PIDs) are rare genetic diseases causing immune dysfunction. The majority of patients have an antibody deficiency, resulting in recurrent infections and poor vaccination responses, posing them at greater risk of developing severe COVID-19 disease. In healthy individuals, COVID-19 vaccination effectively elicits neutralising SARS-CoV-2-specific antibodies and durable memory B cells (Bmem) that recognise circulating SARS-CoV-2 variants. It remains incompletely understood if the heterogeneous PID population mount antibody and Bmem responses that recognise SARS-CoV-2 variants.

AIM: To evaluate the capacity of PID patients to mount IgG and Bmem responses to ancestral and omicron sub-lineages BA.2, BA.5, BQ.1.1 and XBB.1.5 after two and three COVID-19 vaccine doses.

METHODS: 31 PID patients and 43 controls were sampled one-month after doses two and three. Recombinant spike receptor-binding domains (RBD) of ancestral and omicron sub-lineages were utilised for ELISA-based quantification of IgG responses. RBDs were biotinylated and tetramerised with fluorochrome-conjugated streptavidin's for enumeration of absolute numbers and immunophenotypes of variant RBD-specific Bmem using flowcytometry.

PRELIMINARY RESULTS AND EXPECTED OUTCOMES: The median concentration of ancestral-specific IgG was boosted from 11 µg/ml following dose two to 23 µg/ml following dose three in PID patients. In contrast, the controls were boosted from 34 µg/ml to 160 µg/ml respectively. Moreover, levels of IgG specific for all omicron variants was significantly increased following dose three in both cohorts. Reactivity of ancestral IgG to all omicron variants was below 40% for PID patients compared to ≥55% in the controls. Flowcytometric assessment of the magnitude and capacity of Bmem cells to recognise omicron variants in PID patients is ongoing. Preliminary results suggest that additional vaccinations in this cohort are necessary for inducing variant-specific Bmem levels comparable to controls. Measuring Bmem potentially provide a better marker of immune competence, as antibody measurement is confounded by antibody replacement therapy in this cohort.

70. CAUSATIVE ORGANISMS AND ANTIBIOTIC SUSCEPTIBILITY AND USE FOR URINARY TRACT INFECTIONS IN ADULT FEMALES ATTENDING THE MELBOURNE SEXUAL HEALTH CENTRE

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BACKGROUND: Urinary tract infections (UTIs) are one of the most common infections. Management of UTIs often involves empirical antibiotics which can contribute to antibiotic overuse in an era when addressing antimicrobial resistance is a global priority.

AIM: To investigate the causative organisms, prevalence of antimicrobial resistance and empirical prescribing practices to improve antibiotic use for UTIs.

METHODS: We conducted a retrospective audit of UTIs in non-pregnant, premenopausal adults with vaginas attending the Melbourne Sexual Health Centre from 2/1/2018–24/1/2023. We calculated the proportion of culture samples with a pathogen isolated, and their antimicrobial resistance profiles with 95% confidence intervals (CI). We compared empirical antibiotic prescriptions with antibiotic resistance profiles of isolated organisms, and assessed adherence to first-line Australian Therapeutic guideline recommendations for acute uncomplicated lower UTIs (trimethoprim, nitrofurantoin and cephalexin).

RESULTS: We included 1694 acute UTI episodes (n=1582 participants). Midstream urine culture was performed in 1517 episodes, with 921 (60.7%, 95%CI:58.2-63.2) samples classified as laboratory-defined probable or possible UTIs. Most common isolates were *Escherichia coli* (n=609/921; 66%, 95%CI:62.9-69.1) and *Staphylococcus saprophyticus* (n=171/921; 19%, 95%CI:16.5-21.7). One-third of *E. coli* isolates were resistant to trimethoprim. Empirical antibiotics were prescribed for 1547 (91.3%, 95%CI:89.8-92.6) episodes; trimethoprim accounted for 842 (54.4%, 95%CI:51.9-56.9) prescriptions. Most prescriptions (1465/1547; 94.7%, 95%CI:93.5-95.8) adhered to first-line recommendations. For patients prescribed an empiric antibiotic, 128 of 730 (17.5%, 95%CI:14.8-20.5) isolates were resistant to the prescribed antibiotic. The potential number of patients requiring an alternative antibiotic was highest for those prescribed trimethoprim empirically, with 86 of 329 (25.8%, 95%CI:21.2-30.9) isolates in those prescribed trimethoprim demonstrating resistance.

CONCLUSION: *E. coli* was the leading uropathogen, with 1/3 demonstrating trimethoprim resistance. Empirical antibiotics were almost always prescribed and trimethoprim accounted for >50% of prescriptions. We found trimethoprim was not indicated in 1/4 cases where it was prescribed, suggesting changes to antibiotic recommendations are needed.

71. THE OMICRON BA.1 BIVALENT COVID-19 BOOSTER VACCINE ENHANCES THE CAPACITY OF SARS-COV-2-SPECIFIC MEMORY B CELLS TO RECOGNISE OMICRON BA.5 AND BQ.1.1.

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To overcome limited recognition of SARS-CoV-2 Omicron subvariants by the vaccine-elicited antibody response, bivalent COVID-19 mRNA vaccines comprising ancestral Wuhan-Hu-1 (WH1) and Omicron BA.1 or BA.5 have been administered globally. Here, we compared monovalent and BA.1 bivalent 4th dose boosters in their capacity to enhance neutralising antibody (NAb) and memory B-cell (Bmem) recognition of the Spike receptor binding domains (RBD) of Omicron BA.1, BA.5, and BQ.1.1.

AIMS: 1) Quantify and phenotype the RBD-specific Bmem compartment elicited by the monovalent and BA.1 bivalent 4th dose booster; and 2) determine their capacity to bind BA.5 and BQ.1.1 RBDs.

METHODS: Peripheral blood was sampled before and 1 month after a 4th dose from healthy adult recipients of a monovalent (n=18) or BA.1 bivalent mRNA vaccine (n=34). Plasma NAb against WH1, Omicron BA.1, and BA.5 were quantified with a plaque reduction neutralisation test. Fluorescent tetramers of in-house recombinant RBDs of the WH1, BA.1, BA.5, and BQ.1.1 variants were incorporated in a spectral flow cytometry panel to quantify the absolute numbers and immunophenotype of RBD-specific Bmem.

RESULTS: The monovalent and bivalent vaccines similarly boosted NAb against WH1 and BA.5, whereas the response to BA.1 was significantly higher following the BA.1 bivalent booster. Only the BA.1 bivalent vaccine significantly boosted the numbers of Bmem recognising WH1 and BA.1, and moreover it enhanced the frequencies of WH1-specific Bmem that recognised BA.1, BA.5, and BQ.1.1. Additionally, BA.1-specific Bmem elicited by either vaccine had increased capacity to also bind BA.5 and BQ.1.1 RBDs compared to WH1-specific Bmem.

CONCLUSION: The BA.1 bivalent booster can significantly boost NAb and Bmem specific for BA.1, and may be able to improve recognition of descendent subvariants beyond that of a conventional vaccine. This provides new insights into the capacity of a bivalent Omicron-based booster to improve variant-specific immune memory to protect against severe COVID-19.

72. PERSISTENCE OF MONKEYPOX VIRUS AT ORAL AND RECTAL SITES FOLLOWING CLINICAL CLEARANCE OF CUTANEOUS LESIONS.

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The 2022 global mpox outbreak predominantly affected gay, bisexual, and other men who have sex with men (GBM).

AIM: To ascertain the infectiousness of mpox from oral and anal sites, relative to the resolution of mucocutaneous mpox lesions.

METHODS: This prospective cohort study recruited GBM with suspected mpox, at Melbourne Sexual Health Centre, from June to October 2022. Men self-collected oral and anal swabs, and urine for mpox PCR and viral culture at first presentation (Day 0), with repeat testing weekly, when reviewed for clinical clearance, until lesion resolution.

RESULTS: 14/19 (74%) GBM had initial oral PCR detection with 6/14 (42%) still positive by oral PCR and culture (median 14.5, IQR: 10.5-17 days) at or after resolution of mpox lesions at other sites. Of the 14, one had oral mpox lesions at the initial visit. 16/19 (84%) men had initial anal PCR detection with 9/16 (64%) still positive by anal PCR (median 11, IQR: 9-16 days) and 6/16 (43%) by anal culture (median 10.5, IQR: 9-15.5 days) at or after resolution of mpox lesions elsewhere. Of the 16, nine had anal mpox lesions. Among 16 men who underwent serology, 8 (50%) had mpox antibodies detected, including four with positive serology while culture positive, and two negative on day 15.

CONCLUSION: Australia had relatively few mpox cases, limiting our sample size. Detection of mpox by culture suggests virus viability and potential infectiousness. Our data indicate a proportion of men who had resolution of mpox lesions and who would be cleared by public health authorities, and advised their mpox infection is no longer contagious, may still be infectious from oral and anal sites and should be advised to abstain from physical and sexual contact involving these sites for a longer period. Further longitudinal studies using culture are needed to define this period.

73. RESPIRATORY SYMPTOMS AFTER COALMINE FIRE AND PANDEMIC: A LONGITUDINAL ANALYSIS OF THE HAZELWOOD HEALTH STUDY ADULT COHORT

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BACKGROUND: Extreme but discrete fine particle <2.5µm (PM2.5) exposure from events fire events is associated with higher prevalence of respiratory symptoms. It is unknown whether these effects abate, persist, or worsen over time, nor whether COVID-19 exacerbates PM2.5 effects. Using survey data from a cohort exposed to smoke during the 2014 Hazelwood coalmine fire in regional Victoria, we examine the longitudinal effects of smoke-related PM2.5 on respiratory symptoms and whether they are exacerbated by COVID-19.

METHODS: We analysed data from a 2016/2017 survey (n=4,056) and 2022 follow-up (n=612) of people residing in Morwell, which is adjacent to the coalmine, as well as nearby but unaffected Sale during the fire. Items included questions about 7 respiratory symptoms, history of COVID-19, and time-location diaries that were combined with modelled geospatial data of fire-related PM2.5. Associations were examined using logistic and mixed-effects logistic regressions. We accounted for missing data with multiple imputations and loss-to-follow-up with inverse probability weighting.

RESULTS: PM2.5 exposure predicted higher prevalence of chronic cough and current wheeze 2-3 years post-fire. At the 2022 follow-up, PM2.5 exposure was associated with worsening prevalence of chronic cough and possibly current wheeze. While were no detectable interaction effects between PM2.5 and COVID-19, PM2.5 was only associated with other respiratory symptoms – including nocturnal shortness of breath, chronic phlegm, and possibly chest tightness – among those with a history of COVID-19.

CONCLUSION: Short-term but extreme PM2.5 may increase the long-term prevalence of chronic cough, while COVID-19 may exacerbate the effect on other respiratory symptoms. As climate change increases the frequency, intensity, duration, and spread of fires, smoke exposure will grow as a global public health problem, and, along with habitat destruction and the wild animal trade, may be exacerbated by the spread zoonotic disease.

CANCER

74. 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 biomarkers available to predict these events. We here performed in-depth evaluation of the blood T-cell compartment to identify reliable predictive biomarkers to rationalise ICB use.

METHODS. Peripheral blood samples were collected from 30 patients with stage III-IV melanoma at baseline and after one cycle of combination PD-1/CTLA-4 blockade, and 21 age-matched healthy controls. Patients were classified as responders or non-responders by best overall response to treatment, as well as grouped on the occurrence of severe toxicity. Absolute immune cell counts were obtained at the time of sampling, and PBMCs were cryopreserved prior to spectral flow-cytometric analysis of the T-cell compartment.

RESULTS. At 6 months post ICB commencement, 14 patients (47%) failed to respond to treatment and 15 (50%) experienced severe toxicity. At baseline, non-responders had fewer circulating T cells than controls (median, 804 vs. 1297 cells/μL), mainly due to lower $CD4^+$ (p=0.0047) and $CD8^+$ (p=0.0031) naive T cells, as well as higher proportions of $CD8^+$ (p<0.0001) and $CD4^+$ (p=0.0003) T cells expressing Ki67, and increased highly-suppressive T-regulatory cells compared to responders. One cycle of ICB selectively expanded existing T-cell memory in all patients, and responders showed significantly greater upregulation of Ki67 expression in $CD4^+$ central memory (p=0.0043) and regulatory (p=0.0065) cells than non-responders. Severe toxicity associated with small but significant changes to $CD8^+$ T effector memory phenotype.

DISCUSSION. Response to ICB was associated with distinct T-cell profiles before and after one cycle of ICB, but toxicity was linked to only minor differences. Hence, pre- and early on-treatment immunophenotype are a promising source of response biomarkers, but further work is required to identify drivers of toxicity.

75. ESTABLISHING THE UPPER GASTROINTESTINAL CANCER REGISTRY LIVER CANCER MODULE: EXPANSION OF A MULTI-MODULAR CLINICAL QUALITY REGISTRY

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AIM: To establish a prospective hepatocellular carcinoma (HCC) registry by leveraging the Upper Gastrointestinal Cancer Registry (UGICR) and improve the quality of care provided to people diagnosed with HCC in Australia.

METHODS: A national primary liver cancer module was established to be embedded in the multi-modular upper gastrointestinal cancer clinical quality registry. The UGICR currently has two other active modules – pancreas and oesophagus.

Quality indicators were developed using a modified Delphi process and a minimum dataset was determined. The database was developed in the secure web platform, Research Electronic Data Capture (REDCap). Data for the HCC module is clinician-entered. Patient recruitment for the HCC module commenced on March 28, 2023 with 10 sites and 241 patients currently participating in the module.

RESULTS: The UGICR's multi-modular registry design, and single protocol has been beneficial in the development of the Primary Liver Cancer module. Allowing for streamlined module activities, leveraging off an existing framework and resources and promoting the sharing of knowledge and design. This presentation will outline the strengths and challenges of a multi-modular registry expansion. The development of the HCC module has highlighted challenges in utilising a multi-modular registry. A liver cancer patient care and treatment journey is different from the other UGICR modules, which required different approaches with clinician engagement. Clinician-entered data rather than centrally employed data collectors present different data collection, database and management challenges. The HCC Module is leading the registry's goal of national expansion across in South Australia, Queensland, Western Australia and Northern Territory. However, expanding the registry nationally presents its own challenges despite more streamlined ethics review under the National Mutual Acceptance scheme.

CONCLUSION: A multi-modular registry design requires careful consideration and planning. However, streamlining project activities and resources has substantial benefits in the short and long term.

76. CAN A NEW STANDARD OF RADIOLOGY REPORTING HELP IN THE DIAGNOSIS OF PANCREATIC CANCER?

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BACKGROUND: Pancreas Ductal Adenocarcinoma (PDAC) is predicted to become the second commonest cause of cancer death by the end of this decade. With no screening test for early detection currently available for PDAC, surgery with or without chemotherapy remains the mainstay of treatment for early stage disease.
Failure to accurately classify a PDAC as resectable may lead to patients missing an opportunity for potentially curative treatment.

AIM: The SCANPatient clinical trial aims to improve and standardise the way doctors classify patients as resectable or non-resectable by introducing a structured synoptic report for pancreas CT scans.
We hypothesise that the introduction of the synoptic report will alter the rate of diagnosis of resectable PDAC compared to standard reporting approaches because of attention to detail of the requisite vascular fields.

METHOD: SCANPatient is a multi-centric batched stepped-wedge, comparative effectiveness, cluster randomised trial. The trial will be based at 34 Australian hospitals (including Northern Health). The study started on the 1st of July 2023 with the first batch of 12 hospitals and the whole study will last for 3 years. The synoptic reporting arm will start in randomised sites from January 2024.

RESULTS: Since the 1st of July, 2023, we have recruited 95 patients with PDAC from the first group of 12 hospitals (SCANPatient study sites) located in Victoria (9 hospitals), Queensland (1 hospital) and South Australia (2 hospitals). Of the 95 patients and based on standard radiology reports, 4.4% of them were classified as clearly resectable; 14.1% as borderline resectable; whilst in 44.6% of the patients, their resectability status was "not stated".

CONCLUSIONS: Our preliminary data shows that the resectability status of a considerable proportion of patients from enrolled hospitals was not clear. More detailed information is needed to accurately classify resectability for patients with PDAC to ensure outcomes are optimised.

77. TRIALHUB: ALLOWING PATIENTS TO PARTICIPATE IN CANCER CLINICAL TRIALS CLOSER TO HOME

Anne Woollett, Director, TrialHub, Rebecca McLean, Communications Manager, TrialHub, Kylie Shackleton, Senior Program Manager, TrialHub, Will Evans, Teletrial Manager, TrialHub, Marylou Rainsford, Project Officer, TrialHub, Thobe Mthethwa-Pitt, Education Manager, TrialHub

OVERVIEW: TrialHub was established in 2020 and is an Australian-first pilot partnership program that supports regional, rural and outer metro hospitals to establish, or expand, their own clinical trial unit. Specifically, we have been focused on cancer clinical trials to improve the access to potentially life-saving treatment for patients in these areas. Leveraging the clinical trial expertise at The Alfred, we have been supporting six Victorian hospitals; Latrobe Regional Health, Bendigo Health, Mildura Base Public Hospital, Peninsula Health (Rosebud), Bass Coast Health, and Northern Health.

AIMS

To reduce the mental and travel burden for these patients, especially when they're very unwell
To increase regional workforce opportunities in cancer research and support the retainment of staff
To improve awareness of clinical trials, and their benefits, in communities
Maximise a new concept called a teletrial to increase clinical trial activity outside of Melbourne

RESULTS

- We have enabled cancer clinical trials to open for the first time in regional/rural Victoria
- Nine unique teletrials have opened
- Supported the increase in the overall multi-disciplinary clinical trial workforce
- Founded a Victorian Rare Cancer Alliance to build rare cancer clinical trial capacity and availability in regional and rural Victoria.
- Implemented clinical trial participant ambassador program across into communities
- Produced a patient-led and patient-written lay brochure about teletrials
- Total participants recruited onto trials have increased since 2020.
- Pharmacists received formal clinical trial pharmacy training (developed by Alfred Health pharmacists)
- We published an Australian-first Trial Capability Framework, now used by Queensland, Northern Territory and Victorian health services.
- Increased employment opportunities in research and clinical trials for regional/rural workforce
- Latrobe Regional Hospital opened its first ever international melanoma clinical trial in June

CONCLUSIONS: Three years into the pilot program, TrialHub is delivering on its goal of improving access to clinical trials closer to home.

78. TRENDS OVER TIME IN PATIENT CHARACTERISTICS, TREATMENT, AND OUTCOMES FOR OLIGOMETASTATIC COLORECTAL CANCER IN AN AUSTRALIAN SETTING.

Authors: Helen Pham, Peter Gibbs, Marty Smith.

INTRODUCTION: The treatment of metastatic colorectal cancer (mCRC) has evolved over the last two decades, with curative intent resection possible in some patients with oligometastatic disease. We aimed to examine trends in the incidence, patient and tumour characteristics, treatment and outcomes of Australian patients presenting with liver or lung only disease.

METHODS: Prospectively maintained data from the multi-site TRACC (Treatment of Recurrent and Advanced Colorectal Cancer) were reviewed over three consecutive periods; 2009-2013, 2014-2018, and 2019-2023. The impact of key clinical, pathology and metastatic site variables on resection rates was explored. Survival outcomes were determined by Kaplan-Meier method.

RESULTS: Of 4613 patients with mCRC, 2713 (58.8%) were male, median age was 66 years (interquartile range 56-76) and 3769 (81.7%) had an ECOG performance status of 0-1. At diagnosis, 2356 (51%) patients had a single metastatic site. Compared to the earlier periods, patients diagnosed in 2019-2023, were younger, had better ECOG scores and were more likely to have three or more metastatic sites. The proportion of patients with liver-only metastases decreased over the three consecutive periods from 32.0% (n=462), to 27.0% (n=498) to 25.9% (n=33), $p<0.001$, however the proportion of liver-only metastases patients undergoing resection increased to 25.2% in 2019-2023 period, $p<0.001$. Neoadjuvant chemotherapy was increasingly used in over the years in liver-only metastasis, however this was not statistically significant.
The incidence and resection rate of lung-only metastases were unchanged. Median overall survival following liver and lung resection was improved in the more recent years in 2019-2023 at 34.2 months (95% CI 29.9-38.5), $p<0.001$.

CONCLUSION: The increasing number of metastatic sites and reduced number of patients with liver only metastases is potentially explained by the increased use of FDG PET imaging at baseline, finding additional disease not seen on CT alone. The increased proportion of liver only disease undergoing resection may be explained by an evolving definition of resectable disease and increasing use of neoadjuvant chemotherapy in an attempt to convert initially inoperable patients.

79. DEDICATED ENDOCRINE SERVICE IMPROVES SURGICAL SELECTION AND POSTOPERATIVE OUTCOMES IN PATIENTS WITH CONN'S SYNDROME

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INTRODUCTION: Primary aldosteronism (PA) is the most common surgically curable cause of endocrine hypertension. It is unclear if the management of patients with the unilateral subtype of PA through a dedicated Endocrine Hypertension Service (EHS) confers better outcomes, compared to standard management offered by independent clinicians.

METHODS: In this retrospective cohort study, patients from the Monash University Endocrine Surgery Database were divided into the EHS group, where patients were managed by a dedicated multidisciplinary team; or the Standard group, where patients were managed by individual physicians. The comparisons included patient selection for unilateral adrenalectomy, perioperative blood pressure, surgical cure rate, and the adequacy of postoperative follow-up.

RESULTS: Despite similar perioperative blood pressure control, patients in the EHS group (n=41) were on fewer antihypertensive medications (1 vs 2, p=0.011) compared to the Standard group (n=55). A larger proportion of EHS patients had either bilateral adrenal nodules or no adrenal lesions on CT (41% vs 18%, p=0.013). Patients in the Standard group had larger adrenal lesions on CT (median 15mm vs 10mm, p=0.032). Postoperatively, biochemical cure rate was higher in the EHS group at 6-12 months (97% vs 76%, p=0.021). More EHS patients were followed up with endocrine markers for detecting residual disease and recurrence.

CONCLUSION: Patients managed by the dedicated endocrine hypertension service were more likely to be diagnosed with surgically curable PA without a unilateral adrenal adenoma on imaging, required fewer medications for perioperative blood pressure control and experienced higher rate of postoperative biochemical cure. We recommend that patients with confirmed PA who are surgical candidates should seek investigations and management from the multidisciplinary team.

80. THE RELATIONSHIP BETWEEN ADVERSE GASTROINTESTINAL QUALITY OF LIFE AND ADVERSE GASTRO-INTESTINAL SYMPTOMS IN POST OESOPHAGECTOMY PATIENTS: A PROSPECTIVE CLINICAL TRIAL

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INTRODUCTION AND AIM: Post oesophagectomy, many patients have increased rates of dysphagia, reflux, and dumping. Despite this, multiple studies have demonstrated their overall quality of life as similar or better than preoperative/population scores. We aim to compare our patient's quality of life with age matched controls and investigate the relationship between adverse gastrointestinal symptoms and quality of life.

METHODS: Post oesophagectomy patients with mature gastric conduits were prospectively recruited. Demographic details and Allen's scores, Dakkak Dysphagia Scores, and RAND-SF-36 health survey scores were calculated.

RESULTS: 40 patients, of which 75% were male, with a mean (SD) age of 64 (10), completed combined questionnaires at mean of 31.2 (24.2) months post oesophagectomy. When compared with age matched Australian population values, patients 2 years post oesophagectomy demonstrated similar QOL in domains relating to physical functioning, role limitations due to physical or emotional health, emotional wellbeing, pain and general health. They had significantly decreased quality of life in the energy domain (mean score 44.1 vs 64.1 p<0.001) and social function domain (71.25 vs 83.3 p=0.013) post-surgery. Linear regression analysis identified dysphagia as a key predictor of general health outcomes in post-surgical patients – for every single point increase in the dysphagia score (max 12) there was a corresponding decrease of 4.55 in overall health (max 100) p=0.025, r2=0.148.

CONCLUSION: Patients post oesophagectomy have a quality of life close to population norms in most domains. A subgroup of patients with dysphagia experience significantly reduced quality of life, emphasising the need to investigate for treatable causes of dysphagia and treat aggressively. Causes of dysphagia are broad and not well understood and consequently remains a good target for ongoing research.

81. MALIGNANCY RISK AND MORTALITY AFTER LUNG TRANSPLANTATION: A SINGLE INSTITUTION EXPERIENCE OVER 31 YEARS

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BACKGROUND: Malignancy is a long-term complication of lung transplantation (LTx), however, contemporary Australian data and detailed evaluation of non-reportable cancers are lacking.

AIM: To quantify the burden and identify clinical associations of malignancies in LTx survivors.

METHODS: Retrospective review of LTx recipients' medical records and registry data linkage were performed to identify histologically proven malignancies, and baseline clinico-demographic variables were collected.

RESULTS: There were 1,715 LTx in 1,631 patients between 1989-2021, with a follow-up of 9,696 person-years. 893 (54.8%) patients were male, and the median age at first LTx was 54.7 years. There were 886 deaths, and median overall survival was 7.5 years (95% CI 6.8-8.3 years). 1,774 separate invasive cancer events occurred across 407 patients, of which, 1,588 (89.5%) were non-melanoma skin cancers (NMSCs), translating to a 9-fold increased incidence of NMSCs and a 4-fold increased incidence of other cancers compared with the general population. Cancer mortality reached parity with chronic lung allograft dysfunction as the leading cause of death ten years post-first transplant (n=37, 30.3% of 122 deaths), and was independently associated with age (HR per year increase in age 1.02 [95% CI 1.01-1.03], p=0.001), EBV primary mismatch (HR 3.24 [95% CI 1.68-6.25], versus non-mismatch, p=0.0004) and cancer count (HR per cancer event 1.19 [95% CI 1.13-1.24], p<0.0001).

CONCLUSIONS: This 31-year single-centre data is approximately double the size of comparable analyses, and demonstrates the significant mortality burden of malignancies in LTx survivors, dominated by NMSCs that are poorly reported in cancer datasets. This has led to the protocolisation of multi-disciplinary cancer screening at our institution. Our LTx program volume and survival has markedly increased over the last decade, and with increasing proportions of older recipients, we expect that malignancy will be an increasing concern as transplant survival outpaces parallel improvements in cancer prevention and treatment in this cohort.

82. IMPACT OF THYROIDECTOMY EXTENT ON QOL: AN AUSTRALIAN PERSPECTIVE

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INTRODUCTION: Despite a rapid increase in incidence, thyroid cancer is associated with low mortality and excellent prognosis overall. Recent literature has debated the role of less extensive hemithyroidectomy as definitive treatment for patients with low-risk thyroid malignancy. We sought to compare quality of life (QOL) after different extents of thyroidectomy in this relatively young surgical cohort.

METHODOLOGY: A prospective observational study was conducted to investigate the differences in QOL between hemithyroidectomy and total thyroidectomy patients. Responses to the European Organisation for Research and Treatment of Cancer (EORTC) Thyroid Cancer QOL Module were collected at 3, 6 and 12 months postoperatively. Analysis was conducted using the Wilcoxon Rank Sum Test and multiple linear regression modelling.

RESULTS: Of 291 total thyroidectomy and 246 hemithyroidectomy patients included, the proportion of malignant cases was 95.3%. Hemithyroidectomy patients reported significantly better scores in 4 of 32 QOL domains at 3 months, with higher scores for role function (p=0.006) and less issues with pain (p=0.001), discomfort (p=0.012) and worry about others (p=0.024). For the 6 month cohort decreased pain (p=0.009) was again observed in the hemithyroidectomy group, in addition to a lower incidence of voice concerns (0.037). Social support scores were higher for total thyroidectomy patients at 6 months (p=0.004). No statistically significant score differences were detected at 12 months.

CONCLUSION: The extent of thyroidectomy performed is a significant predictor of QOL within the first postoperative year, after which it becomes negligible. These results can help guide the extent of surgery performed for suspicious lesions, and they allow surgeons to reassure patients that resulting QOL differences are likely to be temporary.

83. TESTOSTERONE RECOVERY FOLLOWING ANDROGEN SUPPRESSION AND PROSTATE RADIOTHERAPY (TRANSPORT) – INDIVIDUAL PATIENT-DATA META-ANALYSIS FROM THE MARCAP (META-ANALYSIS OF RANDOMIZED TRIALS IN CANCER OF THE PROSTATE) CONSORTIUM

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The time-to-testosterone recovery (TR) following androgen deprivation therapy (ADT) and prostate radiotherapy varies following cessation of ADT. This may impact on the quality of life in men with prostate cancer.

AIM: To quantify the association between time-to-TR and duration of ADT and age.

METHODS: We identified prospective randomized trials of prostate radiotherapy and ADT in the MARCAP consortium for which prospectively collected serial testosterone data is available. The time-to-full TR (FTR) (>10.nmol/L) were estimated from the end date of prescribed ADT using the Kaplan Meier method. Cox regression was used to evaluate the differences in time-to-FTR for men aged <65 years and ≥65 years for each duration of ADT. Interaction effects between ADT duration and age on TR were evaluated.

RESULTS: 2392 men from 5 international trials (TROG9601, TROG0304, PCSIII, PCSIV, and OTT0101) met the inclusion criteria for analysis. Of these, 1485, 731, and 176 men had 6-, 18-, and 36-months of ADT respectively. The median (range) time-to-FTR were 16.7 (0.3-95), and 26.0 (0.2-90) for men who had 6- and 18-months of ADT, respectively, while the median time-to-FTR was not reached in men who had 36-months of ADT. In men who had 6-months of ADT, men aged ≥65 years were 35% (95%CI=26-43%) less likely to have FTR compared to men aged <65 years, while for those who had 18-months of ADT, men aged ≥ 65 years were 52% (95%CI=41-60%) less likely to have FTR compared to men aged <65 years. There was no statistically significant interaction between the effect of ADT duration and age on the time-to-FTR (interaction P=0.07 for the entire cohort).

CONCLUSION: This is the largest individual patient-data meta-analyses of prospectively collected serial testosterone from randomized trials, indicating substantial delay in FTR in men receiving longer durations of ADT, with approximately 1-in-3 men did not achieve FTR.

CARDIOVASCULAR

84. A NOVEL ANTI-INFLAMMATORY AND ANTI-FIBROTIC AGENT, EBP979, TREATMENT AMELIORATES ANGIOTENSIN II-INDUCED VENTRICULAR REMODELLING AND VASCULAR DYSFUNCTION

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BACKGROUND: Heart failure with preserved ejection fraction (HFpEF) is still a major health burden globally with a lack of effective treatment due to complex pathophysiology and multiple comorbidities. Several major risk factors, namely advancing age, female sex, and obesity aggregates the pro-inflammatory and pro-fibrotic phenotype. We aim to investigate the therapeutic potential of a novel anti-inflammatory and anti-fibrotic compound, EBP979, in young and old, female, and male mice with angiotensin II (AngII)-infusion. This study also aims to evaluate gender and age differences in AngII and EBP979 responses.

METHOD: Both male and female C57BL/6J mice, young (12 weeks old) and aged (99 weeks old) were used. HFpEF was induced through AngII-infusion at 0.25mg/kg/day via a minipump for four weeks. Animals were randomised to Control (Sham+Veh), AngII+Vehicle, EBP979 (50mg/kg/day in drinking water) treatment either start at week 2 (AngII+EBP979) or at week 0 (AngII+EBP979 PRE) to study its therapeutic and preventative potential. Echocardiography, EchoMRI, and metabolic cage analysis were performed at baseline, weeks 2 and 4. Tissues were collected at the end of the study for vascular function, histology, and gene expression analysis.

RESULTS: AngII-infusion was associated with blood pressure increase and cardiac remodelling. EBP979 treatment and pre-treatment were associated with improvements in cardiac remodelling. Pre-treatment was also associated with improvements in endothelial-mediated vasodilation amongst aged mice. Furthermore, male sex and ageing were associated with an increased response to AngII and EBP979 treatments.

CONCLUSIONS: AngII-infusion led to increased blood pressure, cardiac remodelling and cardiovascular dysfunction. Treatment with EBP979 improves vascular function and attenuates cardiac remodelling. Our results suggest that EBP979 may be a potential therapy for HFpEF.

85. METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE IS ASSOCIATED WITH ATRIAL FIBRILLATION BUT NOT ALL-CAUSE MORTALITY IN OLDER ADULTS

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While the burden of metabolic dysfunction-associated steatotic liver disease (MASLD) is increasing globally, uncertainty exists as to the impact of MASLD on cardiovascular health and mortality among older adults.

AIM: To identify whether MASLD increases the risk of Major Adverse Cardiovascular Events (MACE), Atrial Fibrillation (AF), or all-cause mortality in older adults, and whether primary prevention with aspirin attenuates this.

METHODS: A non-specified post-hoc analysis of the ASPREE (ASPirin in Reducing Events in the Elderly) randomized trial and ASPREE-XT cohort study was performed, which had enrolled community dwelling relatively healthy older adults aged ≥70 years without a history of clinically evident pre-existing cardiovascular disease. The well-validated Fatty Liver Index (FLI) was used to identify the presence of MASLD. Cox proportional hazards models (adjusted and unadjusted) were used to evaluate the impact of MASLD on all-cause mortality, MACE, and AF.

RESULTS: 9,097 randomised participants were stratified into groups according to FLI. On unadjusted analysis, there was an association of MASLD with MACE (HR 1.48 [95% CI 1.17 – 1.87]) and AF (HR 1.40 [95% CI 1.08 – 1.81] but not risk of death (HR 1.09 [95% CI 0.91 – 1.30]) in the MASLD vs no-MASLD group (Figure 1). While the association with MACE was lost when adjusting for all known cardiovascular risks in ASPREE subjects (HR 1.10 [95% CI 0.83 – 1.47]), the association remained between MASLD and AF (HR 1.47 [95% CI 1.07 – 2.01]). Aspirin did not ameliorate the risk of MACE (HR 1.11 [95% CI 0.77 – 1.61]) or death (HR 1.31 [95% CI 0.92 – 1.87]) in the MASLD sub-group.

CONCLUSION: MASLD is associated with an increased hazard of MACE and incident AF but not all-cause mortality in community-dwelling older adults in ASPREE, though the association with MACE is lost when adjusting for known predictors. Primary prevention with aspirin does not ameliorate these risks.

86. CAUSAL INFERENCES BETWEEN SLEEP DISRUPTIONS AND BLOOD PRESSURE USING GENOME-WIDE SNP DATA

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Observational studies have identified associations between sleep disruptions and many cardiovascular diseases, including diastolic and systolic blood pressure (DBP and SBP, respectively). However, many of these associations are due to confounding effects and the causal directions of these associations are poorly understood. Mendelian Randomisation (MR) leveraging instrumental variables such as Single Nucleotide Polymorphisms (SNPs) overcomes confounding factors for association analyses and provides additional insights into potential causal effects of exposures.

AIM: To identify causal associations between sleep disruptions and BP using MR.

METHODS: Systematic MR analyses were conducted between 8 self-report sleep phenotypes (exposure) and BPs (outcome), using SNP summary data from genome-wide association studies (GWAS) performed on ~1 million people ($p_{GWAS} < 5 \times 10^{-8}$). These data were analysed using 3 linear MR methods: 1) generalised summary-data-based Mendelian randomisation (GSMR) accounting for pleiotropy, 2) MR-egger and 3) MR-weighted median. Non-linear causal associations were also analysed by using two methods PolyMR and SUMnlmr using raw data from the UK Biobank (N>350,000).

RESULTS: Based on the agreement between the 3 linear MR methods, we found that longer sleep, shorter sleep, more daytime sleepiness (corrected for BMI), day nap and morning chronotype are significantly ($8.6 \times 10^{-25} <$ multi-test adjusted $p_{MR} < 0.024$) and causally associated with increased DBP and/or SBP. Further MR analyses identified significant non-linear causal effects of sleep duration on BPs, where causal associations between sleep duration and SBP were stronger than causal associations between sleep duration and DBP.

CONCLUSION: Our analyses suggested potentially causal roles of sleep disruptions in increasing BPs and the existence of optimal relationships between sleep durations and blood pressure. Our study provides novel insights linking sleep behaviour with cardiovascular health.

87. CD14 BLOCKADE REPROGRAMS THE MACROPHAGE RESPONSE AND PRESERVES LEFT VENTRICULAR SYSTOLIC FUNCTION, VOLUMES, AND HEMODYNAMICS FOLLOWING ST-ELEVATION MYOCARDIAL INFARCTION (STEMI)

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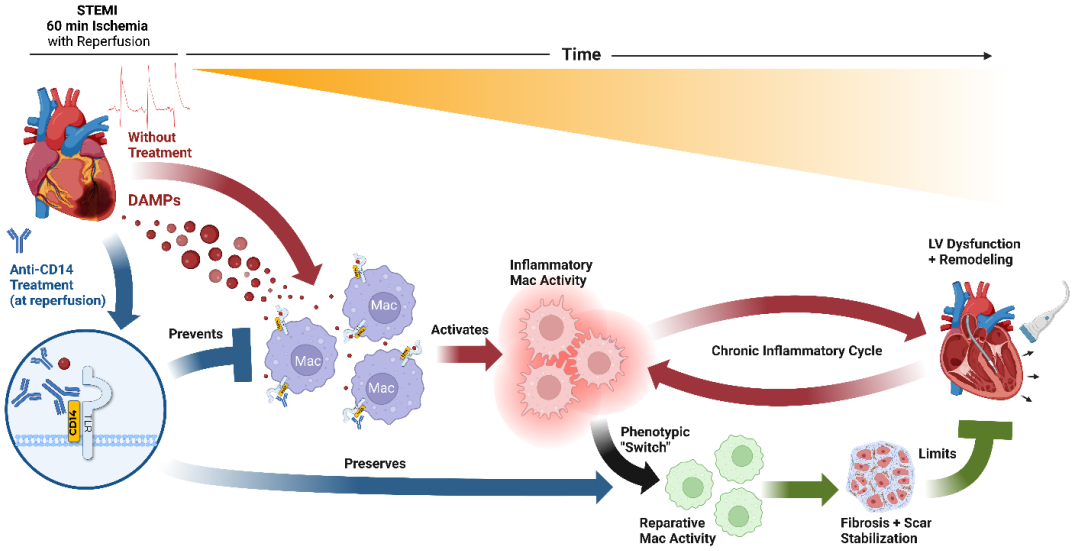
CD14 mediates the monocyte and macrophage response to damage-associated molecular patterns (DAMPs) released from injured cells following acute myocardial ischemia.

AIM: To determine the efficacy of CD14 blockade in a murine model of large anterior ST-elevation myocardial infarction (STEMI) and associated left ventricular (LV) dysfunction and dilatation.

METHODS: A total of 218 C57BL6 mice had surgically induced left anterior descending (LAD) occlusion followed by reperfusion at 60 min, and were randomized to receive blinded anti-CD14 antibody, IgG2a isotype control or phosphate-buffered saline following reperfusion. ST segment elevation on electrocardiogram was the pre-defined inclusion criteria across all studies. Outcome measures included blinded assessments of function by echocardiography (including global longitudinal strain; GLS), cardiac Magnetic Resonance (CMR) imaging, and invasive LV pressure-volume hemodynamics up to 28 days post-STEMI. Mechanism of action studies included measurements of infarct size, circulating high-sensitivity troponin, histological fibrosis, immunohistochemistry, flow cytometry, single cell RNA sequencing (scRNAseq) and quantitative proteomics of sorted cardiac macrophages.

RESULTS: Compared to untreated STEMI, anti-CD14 treatment preserved LV ejection fraction (30±1 vs 24±1 % EF, p<0.01), end-diastolic volume, GLS, and LV developed pressure (by echocardiography, cMR, and pressure-volume catheterization) up to 28 days post-STEMI. These changes were preceded by a substantial reprogramming of macrophages to downregulate inflammatory activity with anti-CD14 treatment (>600 transcripts) while preserving both their abundance in the myocardium and critical reparative functions (observed by scRNAseq and proteomics). Whole tissue proteomics of the infarcted myocardium revealed reduction of tissue hypertrophy markers and enrichment of the mitochondrial protein network. These changes were independent of acute infarct size and plasma troponin levels that were unaffected by anti-CD14 treatment.

CONCLUSIONS: These data support the hypothesis that CD14 is a key upstream target of the secondary pro-inflammatory response to STEMI and inform its candidacy for clinical trials of safety and efficacy in STEMI patients.



88. RESUSCITATION TO RECOVERY: EXPLORING SEX BASED DIFFERENCES IN NEUROLOGICAL FUNCTION AND PATIENT SURVIVAL AFTER CARDIAC ARREST.

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BACKGROUND/RATIONALE: Over 20,000 Australians die from Cardiac Arrest (CA) yearly with survivors left with mild-to-severe neurological impairment severely impinging on their quality of life. Despite advances in resuscitation methods and a century of research into CA, poor prognosis and a 10% patient survival rate have reflected the inefficacy of preclinical research with no pharmacologic treatment available. An increasingly apparent disparity is the *inequity of survival outcomes between men and women*. Female patients display worse neurological symptoms and poorer survival rates than males of the same age and health status. Yet no biological basis for this distinction has been investigated.

AIM & HYPOTHESIS: This project aims to investigate and compare the extent of neurological damage and dysfunction in male and female CA affected mice compared to their non-CA controls. It was hypothesised that female mice would display greater neurological damage and dysfunction compared to male mice subjected to CA.

METHODS: 8-12w C57BL6 mice allocated to sham and experimental CA groups underwent comprehensive neurological testing at 24h, 48h and 72h post-arrest. In vivo and ex vivo MRI to quantify neuronal damage was also performed and compared to H&E histology of brain sections in addition to immunohistochemistry and plasma serology.

RESULTS: Preliminary results suggest male mice develop worse post-arrest morbidity despite displaying equal likelihood of attaining ROSC compared to female mice. Neurological impairment was most noticeable 24h after CA induction in both sexes, and demonstrated no significant difference between female and male mice despite the latter's significantly decreased survival (M:51.5%,F:75.0%,p=0.0496). Markers of neurological damage are currently being assessed to investigate mechanistic drivers.

CONCLUSION: Whilst these findings support the well-known cardio-/neuro-protective effects of oestrogen, they deviate from clinical population data. As our model uses young mice, this may reflect that the loss of oestrogen in older female cohorts correlates with a loss of neuroprotection.

89. BEYOND BOUNDARIES: COMBINED ANTI-PLATELET/ANTI-COAGULANT STRATEGIES FOR LONG CIRCULATING THROMBOPROPHYLAXIS AND CARDIAC PROTECTION CARDIAC

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Thrombosis-related cardiovascular diseases are the leading cause of disability and morbidity worldwide. Existing antithrombotic drugs have limitations due to bleeding risks and short efficacy. To overcome these challenges, we developed a novel treatment called targeted long-circulating protein (Targ-LC-TAP). Targ-LC-TAP combines a platelet-targeting antibody, a human serum albumin for extended circulation, and a tick anticoagulation peptide (TAP) to inhibit clotting. A non-binding control of Targ-LC-TAP (Non-Targ-LC-TAP) was used as the control. Our experiments confirmed Targ-LC-TAP's ability to bind specifically to activated platelets and effectively prevented platelet aggregation and clot formation in vitro. In an acute thrombosis murine model, Targ-LC-TAP significantly improved blood flow in the carotid artery compared to the Non-Targ-LC-TAP treated mice (2340 vs 1104, AUC, P=0.0029), providing up to 16 hours of thromboprophylactic benefits. In a mouse model of myocardial ischemia-reperfusion injury (occlusion of the left anterior descending artery for 60 min to recapitulate the clinical scenario of patients with MI undergoing recanalization), we demonstrated that the administration of Targ-LC-TAP prior to injury preserved cardiac function, as evidenced by increased ejection fraction compared to the Non-Targ-LC-TAP group (53 vs 31, %, P<0.0001). Strain analysis showed a reduction in the deformation of the myocardium and the histology of the left ventricle further supported a reduced infarct size for those treated with Targ-LC-TAP, as compared to PBS control (23 vs 6, P=0.0001). Importantly, Targ-LC-TAP did not cause prolonged bleeding, as opposed to the currently used medication Clexane (268 vs 1800, sec, P<0.0001). This targeted approach enables the administration of lower doses, reducing the risk of bleeding complications associated with current therapies. Overall, Targ-LC-TAP shows great promise as a safe and effective long-lasting thromboprophylactic drug, offering a potential strategy to broaden the therapeutic window and improve patient outcomes in the prevention of blood clots.

90. QUADRICEPS MUSCLE SIZE IS ASSOCIATED WITH EXERCISE CAPACITY IN FIBROTIC INTERSTITIAL LUNG DISEASE

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Skeletal muscle dysfunction contributes to exertional intolerance in patients with fibrotic interstitial lung diseases (ILD). It is unclear if quadriceps muscle size is associated with aerobic exercise capacity in fibrotic ILD, and if this relationship is affected by disease severity and exertional circulatory oxygen delivery to the working muscle.

AIM: To investigate the relationship between quadriceps muscle size, exercise capacity, and disease severity in people with fibrotic ILD.

METHODS: Quadriceps muscle thickness (MT) was measured by B-mode ultrasonography. Pearson's correlations with subgroup analyses for exertional oxyhaemoglobin saturation (SpO_2 < 90%, n = 24; SpO_2 ≥ 90%, n = 21) assessed the relationship of MT with six-minute walk distance (6MWD), cardiopulmonary cycle test peak workload, endurance time in a constant work-rate test, forced vital capacity (FVC), transfer factor for carbon monoxide (TLCO), demographics and Dyspnoea-12 domain scores. Stepwise linear regression analyses investigated predictors of aerobic exercise capacity in fibrotic ILD.

RESULTS: 45 participants were recruited. Greater quadriceps MT was associated with higher 6MWD (r = 0.49) and higher cycle test peak workload (r = 0.60; p < 0.01). Relationships of MT with exercise capacity and disease severity were stronger in participants that experience exertional oxyhaemoglobin desaturation (MT and 6MWD r = 0.69, peak workload r = 0.75, FVC r = 0.57, TLCO r = 0.48; p < 0.05). In regression analyses, FVC and quadriceps MT were predictors for 6MWD and cycle test peak workload.

CONCLUSION: Greater quadriceps muscle size is associated with higher aerobic exercise capacity and reduced disease severity, particularly in individuals who experience exertional oxyhaemoglobin desaturation. Disease severity and muscle size are predictors of aerobic exercise capacity in fibrotic ILD. Impairment to muscle size may be a process by which aerobic exercise capacity is limited with progression of fibrotic ILD.

91. NEUTRON SCATTERING AS PROBE FOR INTERROGATING STRUCTURES OF BIOMEMBRANE-INTERFACED MICRO- AND NANOMATERIALS

Mark Louis P. Vidallon,[1,2,3,4,*] Ashley Williams,[3] Mitchell J. Moon,[5] Haikun Liu,[1,2] Boon Mian Teo,[3] Sylvain Trepout,[6] Alexis I. Bishop,[7] Rico F. Tabor,[3] Liliana de Campo,[8] Karlheinz Peter,[2,4,5,9] and Xiaowei Wang[1,2,4,9]

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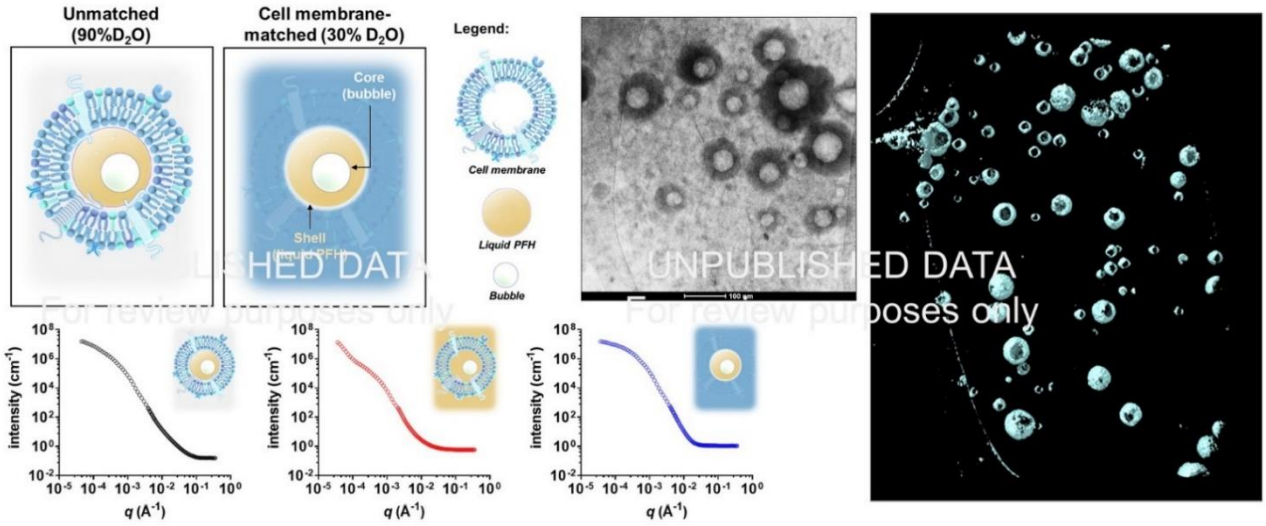
Coating nanomaterials with cell membranes, a process known as biointerfacing, holds immense promise for enhancing the biological properties and stability of nanosystems. Particularly, biointerfaced perfluorocarbon nanodroplets have emerged as game-changing tools for ultrasound imaging, oxygen delivery, and drug administration. Despite their potential, limited information exists regarding their structures and responsiveness, mainly due to the challenges in characterisation. Conventional techniques, such as optical and electron microscopy or dynamic light scattering have inherent limitations that hinder the comprehensive analysis of complex nanostructures and the monitoring of sample responsiveness under different conditions. To overcome these challenges, we use state-of-the-art small- and ultra-small-angle neutron scattering (SANS and USANS) techniques. We investigated the structure of perfluorohexane (PFH)-filled red blood cell and platelet membrane-shelled emulsions (RBC/PFH and PLT/PFH). Results confirmed that the lamella structure of the cell membranes are present in both samples and that PFC are indeed encapsulated and dispersed as nano- and mesoscale droplets: 400–500 nm and 600–800 diameter for RBC/PFH and PLT/PFH droplets, respectively. RBC/PFH were also found to be more stable to aggregation, compared to PLT/PFH, which can be attributed to the difference in the surface chemistry of these materials and the larger droplet size of PLT/PFH. Results of SANS and USANS, supported by cryogenic transmission electron microscopy, revealed a compound PFH bubble–droplet system, a multiphase colloidal material that has never been reported previously. The unique combination of components and phases make these materials suitable for cardiovascular theranostics—cell membrane coating for droplet stabilisation and targeting function and compound bubble–droplet payload as ultrasound-responsive switch for imaging and drug delivery.



92. UNDERSTANDING SEX DIFFERENCES IN CARDIAC PATHOPHYSIOLOGY FOLLOWING CARDIAC ARREST AND RESUSCITATION

Student Name: Ms Sherine Abraham, Supervisor Name: Dr Daniel Donner

BACKGROUND: More than 25,000 men and women in Australia suffer from Cardiac Arrest (CA) each year, and outcomes from asystolic CA remain poor. In this project, we aim to test the hypothesis that females suffer worse pathophysiology following CA than males and suffer worse cardiovascular function.

AIMS AND HYPOTHESIS:
A1: To assess cardiac damage caused by asystolic CA in male and female mice.
H1: Increased cardiac damage in female mice post-CA.
A2: To assess cardiac function following CA in male and female mice.
H2: Decreased cardiac function in female mice post-CA.

STUDY DESIGN: To achieve those aims, we plan to use a murine model of CA established by our lab. Briefly, male and female C57BL6 mice undergo CA for 8 minutes, followed by CPR and epinephrine (adrenaline) administration. Successfully resuscitated mice will undergo echocardiography and pressure-volume (PV) loop analysis to assess their Left Ventricular (LV) function. LV tissue samples are collected at endpoint to be analysed by immunohistochemistry, Masson's trichrome and whole blood is analysed to assess the damage sustained by the heart.

EXPECTED OUTCOME: Female mice are expected to have increased myocardial scarring deposits and impaired cardiac function compared to males. This study is the first of its kind designed to elucidate the role of biological sex in cardiac arrest pathophysiology.

93. ENDOTHELIAL-TARGETED CD39 AS A NOVEL TREATMENT FOR ACUTE LUNG INJURY (ALI) DUE TO INFECTION

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ALI is the leading cause of death in intensive care patients with bacterial sepsis or COVID-19 infection. Both conditions involve a cytokine storm with uncontrolled activation of innate immune cells and release of extracellular ATP (eATP). eATP promotes neutrophil migration and activation by binding endothelial activation surface molecules VCAM-1/ICAM-1 (vascular/ intercellular cell adhesion molecule-1), while inducing microvascular thrombosis and coagulopathy. CD39 is an endogenous enzyme that converts pro-inflammatory eATP to anti-inflammatory adenosine and has been shown to improve outcomes following thromboinflammation.

AIM: To develop a novel therapeutic 'Anti-VCAM-CD39' as a treatment for COVID-19 and sepsis. Anti-VCAM-CD39 localises the potent anti-inflammatory, vasodilatory and antithrombotic properties of CD39 to the inflamed microvasculature by binding to VCAM-1.

METHODS: C57BL/6 mice were challenged intranasally with human clinical isolate of SARS-CoV-2 VIC2089 (N501Y). Sepsis was induced in C57BL/6 mice with intraperitoneal injection of LPS (5mg/kg) and anti-VCAM-CD39 (0.8 mg/kg, intravenous) was administered 1h later.

RESULTS: Lungs from COVID-19 infected mice showed an increase in pro-inflammatory cytokines, and VCAM-1, and a reduction of CD39, supporting the rationale for anti-VCAM-CD39 therapy.LPS induced hypothermia 6 hours post injection (35.60C versus 37.8 0C in shams) and lung damage was confirmed on H&E sections with interstitial infiltration and oedema. Systemic adenosine halved (255 pmol from 505 pmol), with concomitant reduction in CD39 expression while VCAM-1 protein expression in lung increased by 2.2 fold. Anti-VCAM-CD39 treatment restored core temperature (n=5) and reduced histologic lung damage. qRT-PCR analysis of lung tissue showed that anti-VCAM-CD39 significantly decreased endothelial activation markers (ICAM p=0.003, e-selectin p=0.02) and pro-inflammatory cytokines IL6 (p=0.01), TNFα (p=0.035), IL18 (p=0.002), IL8 (p=0.01) and MCP1 (p=0.04). Furthermore, anti-VCAM-CD39 administration was able to recover plasma adenosine levels (p=0.03).

CONCLUSION: Treatment with anti-VCAM-CD39 mitigates lung damage after systemic infection and therefore could potentially ameliorate thromboinflammation in patients with sepsis and COVID-19.

94. EXPLORING PLASMALOGEN METABOLISM AND OBESITY IN LARGE COHORTS USING LIPID RATIOS AND GWAS

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Population studies have revealed reduced plasmalogens, a class of glycerophospholipids with reported health benefits, are implicated in obesity.

AIM: Use a systems genomic approach to investigate the relationship between plasmalogen metabolism and obesity.

METHODS: Integrated plasma lipidomics data from The Australian Diabetes, Obesity and Lifestyle Study and The Busselton Health Study (BHS), alongside genomics data from the BHS and liver RNA-sequencing data from The Hybrid-Mouse-Diversity Panel (HMDP). The HMDP dataset consisted of 107 inbred male mouse strains (2-3 mice per strain) on a high-fat-high-sugar (HFHS) diet (n=227) or chow diet (n=254) for 8 weeks. We performed linear regression analysis to assess the associations between 65 lipid ratios and markers of obesity. GWAS was performed on the lipid ratios using imputed genotype data (13.8 million single-nucleotide-polymorphisms (SNPs)).

RESULTS: BMI was inversely associated with total plasmalogen levels relative to total phospholipids. Ratios capturing plasmalogen synthesis, such as plasmanylethanolamine-desaturase-1 (PEDS1), had a positive association with BMI (p-value 2.37×10^{-25}). HMDP data supported the ratios, demonstrating an increase in PEDS1 expression in mice on a HFHS diet compared to a chow diet ($p<0.0001$, Mann-Whitney U test). Glycerol-3-phosphate dehydrogenase, responsible for converting glycerol-3-phosphate into dihydroxyacetone phosphate (DHAP), decreased in mice on the HFHS diet compared to chow fed mice ($p<0.001$, Mann-Whitney U test).

GWAS results further validated the ratios, revealing strong associations with loci linked to plasmalogen synthesis. Importantly, ratios capturing the synthesis of choline-plasmalogens had strong associations with SNPs in the transmembrane 229B (TMEM22B) gene region ($p<5x10^{-22}$).

CONCLUSION: The reduction in total plasmalogens relative to total phospholipids may stem from limited DHAP availability, rather than modulation of enzymes involved in plasmalogen synthesis directly. Additionally, this study identified TMEM229B as a novel gene involved in plasmalogen metabolism. Together, these results demonstrate the power of bioinformatic approaches to gain mechanistic insights in disease settings.

95. ACUTE KIDNEY INJURY FOLLOWING TRANSCATHETER AORTIC VALVE IMPLANTATION – A CONTEMPORARY PERSPECTIVE OF INCIDENCE, PREDICTORS AND OUTCOMES

Anant D Butala[1], Shane Nanayakkara[1,2,3], Rohan V Navani[1], Sonny Palmer[1,4], Samer Noaman[1], Kawa Haji[1], Nay M Htun[1,2], Antony S. Walton[1,3], Dion Stub[1, 2,5]

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BACKGROUND: Acute kidney injury (AKI) is a known complication following transcatheter aortic valve implantation (TAVI), associated with increased morbidity and mortality. Most of this data relates to higher risk patients with early generation TAVI valves. With TAVI now established as a safe and cost-effective procedure for low-risk patients, there is a distinct need for an updated analysis.

AIMS: We aimed to assess the incidence, predictors and outcomes of AKI in a contemporary cohort of TAVI patients across the clinical risk spectrum.

METHODS: 2564 patients undergoing TAVI from 2008–2023 included in the Alfred-Cabrini-Epworth TAVI Registry were analysed. Patients were divided into AKI and no AKI groups. Outcomes were reported according to the Valve Academic Research Consortium-3 criteria.

RESULTS: Of 2564 patients, median age 83 (78-87) years, 57.4% men and median STS score of 3.6 (2.4-5.5), 163 (6.4%) patients developed AKI. On multivariable analysis, independent predictors of AKI were male sex (adjusted OR [aOR] 1.89, p=0.005), congestive cardiac failure (aOR 1.52, p=0.048), eGFR 30-59 (aOR: 2.79, p<0.001), eGFR<30 (aOR 8.65, p<0.001), non-femoral access (aOR 5.35, p<0.001), contrast volume (aOR 1.01, p<0.001), self-expanding valve (aOR 1.60, p=0.045), and bleeding (aOR 2.88, p=0.005). AKI was an independent predictor of 30-day (aOR: 6.07, p<0.001) and 12-month (aOR: 3.01, p=0.002) mortality.

96. A Prospective Audit of Inpatient Cardiology Consultations at The Alfred Hospital

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Consultation services are designed to enhance patients' care by accessing specialised expertise.

AIM: It is well-established that the Cardiology General (CAGE) unit operates at a high capacity, often accommodating up to fifty inpatients. This significant workload occasionally results in limited availability of the CAGE consultant to the cardiology consultation registrar. Our objective was to assess the impact of substituting the Cardiothoracic Surgical Support (CASS) consultant in place of the CAGE consultant.

METHODS: We prospectively recorded consultation requests received from inpatient units from August 1 to August 31, 2021. A re-audit was conducted between April 1 and April 30, 2023 where the CASS consultant was now responsible for consultations.

RESULTS: In August 2021, the CAGE consultant's opinion was sought for 25% of medical referrals compared to 16% of surgical referrals. The re-audit in April 2023 demonstrated that the CASS consultant's opinion was sought for 26% of medical referrals compared to 16% of surgical referrals.

For the referrals from medical specialities, consultants were involved for rhythm advice, procedural requests such as coronary angiography or right heart catheterisation and pericardial effusions. For the referrals from surgical specialities, there was no clear pattern of which referral request warranted consultant opinion; referrals included troponinemia, pericardial effusion, valvular issue, rhythm advice and procedural request.

CONCLUSION: The transition from the CAGE to CASS consultant did not lead to a significant difference in the number of patients discussed. Despite the availability of the CASS consultant, they were only involved for one in every five patients referred. This may suggest that most referrals made are for routine cases that can be effectively handled by registrars. Many referrals relate to conditions with existing guidelines. Establishing local guidelines for ease of access and/or delivering targeted education sessions may help empower referring teams to institute early management prior to cardiology review.

97. ENHANCED MRNA TRANSFECTION USING ULTRASOUND-ACTIVATED PHASE-CHANGE NANODROPLETS

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Since the emergence of the COVID-19 pandemic, mRNA therapeutics have captured global attention, accelerating research and development in this field. However, the progress of mRNA therapy for cardiovascular diseases (CVDs) has been hindered by the lack of advanced delivery systems tailored to the unique demands, such as low immunogenicity and targeted delivery. In this study, we designed phase-change perfluorocarbon (PFC) nanodroplets and investigated their properties to transition into microbubbles under ultrasound stimulation, thereby achieving a controlled release of mRNA. Lipid-coated PFC nanodroplets were engineered using three different PFCs—perfluoro-15-crown-5-ether (PFCE), perfluorohexane (PFH), and perfluoropentane (PFP)—through a cutting-edge high-pressure homogenization technique. Resulting emulsion droplets had diameters between 200–300 nm and possessed positive surface charge, rendering them ideal for mRNA delivery. *In vitro* and *in vivo* diagnostic ultrasound imaging demonstrated the trackability of these nanodroplets, positioning them as potential theranostic materials, combining imaging capabilities with mRNA delivery functions. We used eGFP mRNA to directly visualize green fluorescent protein (GFP) after introducing it into Chinese hamster ovary (CHO) cells. Following a direct transfection, we found PFH and PFP nano droplets provided significantly higher GFP expression, as compared to PFCE (46.88, 43.1 vs 9.07, $p<0.0001$) via microscopy or flow cytometry. Using ultrasound stimulus for controlled release study, we observed that transfection efficiency increases of around 20% in PFH and PFP nanodroplet-treated cells, compared to the group without ultrasound burst. In contrast, PFCE nanodroplets exhibited marginal eGFP mRNA transfection efficiency with/without ultrasound. All 3 formulations are highly bio/hemo-compatible in blood and showed no toxicity to cells *in vitro*, hence these fabricated materials are prospective candidates for further development and application *in vivo* (work in progress). In summary, PFC nanodroplets can be visualisation and stimulated for controlled release of their mRNA load via ultrasound, thereby they may provide represent highly promising mRNA delivery systems for the treatment of CVDs.

98. AN OPPORTUNITY TO SEIZE FROM LOW HANGING FRUITS: CAPITALIZING ON INCIDENTALLY REPORTED CORONARY ARTERY CALCIFICATION

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BACKGROUND Incidental Coronary Artery Calcifications (CAC) are frequent findings on non-ECG gated CT Thorax. It is associated with adverse prognosis in multiple patient cohorts.

OBJECTIVES We investigated the prevalence of incidental CAC from non-ECG gated CT Thorax (both contrast and non-contrast) for inpatients. We also assessed for downstream investigation and statin prescription from the inpatient teams.

DESIGN All non ECG-gated CT Thorax done as inpatients from a single centre at Peninsula Health referred from 1 Jan 2022 to 31 Dec 2022 with reported incidental CAC were reviewed for inclusion. Patients who had history of known coronary artery disease, history of coronary stent or bypass, presence of cardiac devices were excluded.

RESULTS Total of 123 patients were included, making the prevalence at 6.2% (123/1980). The median age is 76 (IQR 69 – 85) and predominantly male at 54.5%. Majority of CT chest done were contrasted scan (91.1%). Only 26.8% of CAC were reported on its severity with visual quantification, with 7.3% each reported for both moderate and severe CAC. Only 2.4% of CAC were reported in the conclusion of the CT report. Most these patients were asymptomatic (34.1%). 20.3% of patients had further testings done. Inpatient hospital mortality was 8.1%. About 23.6% and 34.1% of patients were on aspirin and statin therapy respectively at baseline. There was only 1 patient (1.2%) who was prescribed with new statin therapy on discharge.

CONCLUSION Incidental CAC is prevalent in inpatient setting and remains under-recognized by ordering clinicians, with low prescription rate of statin therapy. Practice changing measure to standardize reporting of incidental CAC is needed to identify patients with subclinical coronary disease and initiate preventive interventions.

99. DISENTANGLING THE GENETIC REGULATION OF LIPIDS AND ATHEROSCLEROSIS IN HUMANS AND MICE

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Dysregulated lipid metabolism is intimately linked to the development and progression of coronary artery disease (CAD) risk. However, the role of individual lipid species in CAD remains elusive. Utilising a platform of genetically diverse inbred mice such as the Hybrid Mouse Diversity Panel (HMDP; >100 strains) provides a complementary approach to genetic analyses in humans. Using multiple HMDP cohorts, we performed comprehensive multi-omic integration of multi-tissue transcriptomics, liver/plasma lipidomics and atherosclerotic lesion area, linking results with a recent, comprehensive genetic analysis of the human plasma lipidome that identified genomic variants that co-localise with lipids and CAD susceptibility. Using this translational platform, we prioritised transmembrane-6 superfamily member-2 (*TM6SF2*), which was previously shown to co-localise with plasma phosphatidylcholine (PC) and lysophosphatidylcholine (LPC) lipid species and CAD. We observed significant correlations between the hepatic expression of *Tm6sf2* and hepatic PC lipid signatures across HMDP mice. Furthermore, in atherosclerosis-prone female HMDP mice, hepatic *Tm6sf2* expression was positively correlated with lesion area ($r=0.2537$; $p<0.0001$) and negatively correlated with hepatic steatosis ($r=-0.4615$; $p<0.0001$). We also demonstrated that hepatic *Tm6sf2* abundance was upregulated in atherosclerosis-prone male mice fed a cholesterol-rich western diet (1.8-fold; $P<0.01$). These findings corroborate and extend upon previous reports that link *TM6SF2* with hepatic steatosis, lipoprotein export and coronary atherosclerosis in humans. By performing analysis of complementary human and mouse datasets, we provide insight into conserved lipid endophenotypes that mediate the genetic modulation of atherosclerosis and prioritise *Tm6sf2* as a candidate for the regulation of mammalian lipid metabolism and atherosclerosis, warranting further studies.

100. LEFT ATRIAL SIZE DOES NOT INFLUENCE OUTCOMES FOLLOWING CATHETER ABLATION IN ATRIAL FIBRILLATION WITH SYSTOLIC HEART FAILURE

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BACKGROUND Significant left atrial (LA) enlargement often accompanies both AF and systolic heart failure (HF) and may deter patient selection for AF ablation. However, the impact of LA size on outcomes remains unclear.

OBJECTIVE The present study sought to evaluate the impact of pre-ablation LA size on AF recurrence in patients with and without systolic heart failure following AF ablation.

METHODS Patients undergoing first-time AF ablation from 2014-2021 across 11 centres were stratified by baseline LVEF (left ventricular systolic dysfunction (LVSD) defined as LVEF <50% or without LVSD ≥50%). The impact of LA size on 12-month AF recurrence was determined via remote rhythm monitoring.

RESULTS Among 407 patients (age 63.4±9.8 years; 20% females, LAVI 49±15ml/m2, median continuous AF duration 6 [IQR 2-9] months), 196 had LVSD and 211 had normal LV systolic function. The LVSD group (mean LVEF 36.2±9.6%) were younger (61.7±10.2 vs 64.9 ± 9.1years, p<0.001), with larger pre-ablation LA size (51.5±15.2ml/m2 vs 45.4±13.4ml/m2, p<0.001) and long-standing persistent AF (PsAF) in 22.4% (vs 6.6% without LVSD, p<0.001). Freedom from AF was comparable in those with and without LVSD (60.2% vs 52.1%, respectively; HR 0.78, 95% CI 0.58-1.05, p=0.104). Freedom from arrhythmia recurrence was significantly higher in those with LA enlargement and LVSD (HR 0.82, 95% CI 0.61-0.94, p=0.021) compared to LA enlargement without LVSD, whereas rates of arrhythmia recurrence were comparable in those with normal LA size, irrespective of HF status (p=0.652). At 12 months, 76% with LVSD experienced LV recovery (LVEF>50%; ΔLVEF: +17±13%, p<0.001) with no demonstrable correlation between baseline LA size and extent of LV recovery. Reverse atrial remodeling was significantly greater in the LVSD group (ΔLAVI -8±16 vs -3±11 without LVSD, p=0.006; ΔRA area -5±7 vs -2±5, p<0.001) compared to those without LVSD. On multivariable analysis, pre-ablation LA size (p=0.762) did not predict AF recurrence.

101. ROLE OF HISTONE METHYL TRANSFERASE EZH2 IN ENDOTHELIAL TO MESENCHYMAL TRANSITION IN DIABETES ASSOCIATED ATHEROSCLEROSIS.

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BACKGROUND: Endothelial to mesenchymal transition (EndMT) involves transformation of an endothelial cells to mesenchymal like cellular state. EndMT is known to play role in cardiovascular complications of diabetes. Recently, EZH2, has been implicated in EndMT and the severity of coronary artery disease. However, role of EZH2 in EndMT induction in diabetes associated atherosclerosis is not known.

AIM: To identify role of EZH2 in EndMT in diabetes associated atherosclerosis.

METHODS: (i) An *in-vitro* model of EndMT was generated using high glucose (HG) and TNF-α in human aortic endothelial cells (HAECs). EZH2 methyltransferase activity was inhibited using EZH2 specific inhibitor GSK126. (ii) RNA sequencing was performed in this setting. (iii) EZH2 genetic knockdown (shRNA) in HAECs was also performed. (iv) in addition, EZH2 mediated H3K27me3 and EndMT was assessed in atheroprone diabetic mouse model.

RESULTS: In HAECs, morphological changes as well as gene and protein expression confirmed TNF-α + HG induced EndMT, which was blunted by GSK-126. Elevated EZH2 mediated H3K27me3 activity by the TNF-α and HG stimulation was blunted with GSK-126 treatment. *Furthermore,* RNA sequencing identified several enriched pathways e.g., fluid shear stress and atherosclerosis, directly relevant to EndMT and diabetic complications. *Transcriptomic analysis showed that* 242 genes including MMP2, NOS3 involved in these pathways were regulated by EZH2. Interestingly, expression of 76 dysregulated genes in EndMT were rescued by GSK-126 treatment. EZH2 knockdown studies in HAECs validated the RNA seq data. Furthermore, immunofluorescence staining identified elevated levels of H3K27me3 as well as co-localization of EndMT markers in the aortic endothelial layer of diabetic Apoe $^{-/-}$ mice.

CONCLUSION: This study showed that EZH2 plays a critical role in diabetes induced EndMT in atherosclerosis. Thus, EZH2 inhibition can be a potential new therapeutic target for the disease.

102. PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 INHIBITOR ELIGIBILITY AND PRESCRIPTION RATES IN PATIENTS PRESENTING WITH RECURRENT ACUTE CORONARY SYNDROMES

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BACKGROUND: Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are novel medications for reducing low-density lipoprotein cholesterol (LDL-C) levels. In 2020, the Australian Pharmaceutical Benefits Scheme (PBS) began subsidising PCSK9 inhibitors for secondary prevention of atherosclerotic cardiovascular disease in patients with LDL-C>2.6mmol/L despite statin and ezetimibe therapy. This criteria was expanded to LDL-C>1.8mmol/L in 2022.

METHODS: A retrospective analysis was conducted on patients admitted to a quaternary hospital with acute coronary syndrome (ACS) between 2020-2022. PCSK9 inhibitor eligibility and prescribing patterns were compared between recurrent ACS patients (≥2 events within 5 years) and first-presentation ACS patients. Australian PBS 2020 and 2022 criteria were applied to assess eligibility.

RESULTS: Out of 817 ACS patients with LDL-C>1.8mmol/L, 118 (14.4%) were categorised as recurrent ACS (33.9% female, mean age 67, LDL-C 2.9mmol/L). When compared with first-presentation ACS patients (n=699), recurrent ACS patients had a significantly lower prevalence (14.4% vs 85.6%, p<0.001), but had significantly higher proportions of patients already on statin therapy (49.2% vs 6.0%, p<0.001) and ezetimibe (20.3% vs 2.4%, p<0.001). Recurrent ACS patients had significantly higher proportions of 2020 PBS eligible patients (11.0% vs 1.3%, p<0.001) and 2022 PBS eligible patients (20.3% vs 2.2%, p<0.001). There were no significant differences in PCSK9 inhibitor prescription rates amongst eligible patients (4/13, 30.8% vs 4/9, 44.4%, p=0.51). Univariate binary logistic regression demonstrated that statin intolerance was significantly associated with PCSK9 inhibitor prescription (OR 10, 95% CI 1.3-79.3, p=0.029).

CONCLUSION: Despite significantly higher eligibility rates, PCSK9 inhibitor uptake remains low in high-risk recurrent ACS patients. With the transition from 2020 to 2022 PBS criteria, eligibility rates are now doubled with even more patients potentially being missed for PCSK9 inhibitor initiation. This demonstrates the need to raise further awareness about eligibility criteria and encourage proactive prescription to prevent recurrent cardiovascular events.

103. CROSS-SECTIONAL ASSOCIATIONS BETWEEN MRI-MEASURED CARDIAC INDEX AND BRAIN VOLUME IN THE UK BIOBANK

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Measures of cardiac function are associated with cognitive impairment and dementia in end-stage heart disease, yet the mechanisms of the associated cerebral changes remain unclear.

AIM: We aimed to examine the association between MRI-measured cardiac index (CI) (a measure of cardiac output adjusting for body surface area) and total brain volume (TBV) in a large population-based sample of people in mid-life, and to explore how these associations may be influenced by various dementia risk factors.

METHODS: Cross-sectional health, cardiac and brain magnetic resonance imaging (MRI) data from the UK Biobank (a United Kingdom population-based cohort of people > 40 years old) were analysed. We examined associations between CI and TBV and explored how these associations were altered by modifiable and non-modifiable dementia risk factors using linear regression modelling.

RESULTS: Complete data were available for 22,199 individuals (mean age 64 years (SD 7), 64% women). The mean CI was 2.47 L/min/m2 (SD 0.48) and the mean TBV was 1,499 mm3 (SD 73). Lower CI was associated with lower TBV (β =18.63mm3, 95%CI (16.65 - 20.60), p<2x10-16). When adjusted for age, sex, ethnicity, APOE4 and socioeconomic status, this association was attenuated by 88% (β=2.27mm3, 95% CI (0.60 – 3.95), p=0.007). Further adjustment for cardiometabolic risk factors attenuated the association between CI and TBV by a further 24% (β=1.73mm3, 95%CI (1.89 – 3.45), p=0.048).

CONCLUSION: Lower cardiac index is associated with poorer total brain volume at mid-life and later life. Both modifiable and non-modifiable risk factors appear to play a role in this relationship. Further work is required to understand the mechanisms through which CI contributes to brain health, and whether these pathways are modifiable.

104. THE IMPACT OF LOW POSTERIOR LEFT ATRIAL WALL VOLTAGE ON THE OUTCOMES OF CATHETER ABLATION FOR PERSISTENT ATRIAL FIBRILLATION

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BACKGROUND: Pulmonary vein isolation(PVI) is less effective in patients with persistent atrial fibrillation(PsAF). Adjunctive ablation targeting low voltage areas(LVA) may improve arrhythmia outcomes. LVA are considered surrogate for atrial fibrosis, which is a known trigger and substrate for AF maintenance. However further data is required on the utility of ablation targeting these LVA.

AIM: To compare the outcomes of adding posterior wall isolation(PWI) to PVI, versus PVI alone, in PsAF patients with evidence of posterior wall LVA.

METHODS: CAPLA was the world's largest randomized trial involving PsAF patients who were randomized to PVI alone or PVI with PWI. Voltage mapping done at the time of the ablation procedures were reviewed offline. LVA was defined as bipolar voltage of <0.5mV. The primary endpoint was freedom from any atrial arrhythmia of >30 seconds off anti-arrhythmic medication(AAD) at 12 months, after a single ablation procedure in patients with posterior low voltage area.

RESULTS: 210 patients (average age 64.6+/- 9.2 years, 73.3% males, median AF duration 4.5 months [IQR 2-8]) underwent multipolar left atrial mapping. Posterior LVA was present in 69(32.9%) with median surface area 0.6cm2. The addition of PWI to PVI did not significantly improve freedom from atrial arrhythmia recurrence over PVI alone (PVI with PWI 44.8% vs PVI 41.9%, HR0.95, 95%CI0.51-1.79; p=0.95). Patients with posterior LVA were more likely to have low voltage area in other atrial regions(91.7% vs 57.1%, p<0.01), larger left atrial diameter (4.8cm vs 4.4cm, p<0.01) and significantly increased risk of atrial arrhythmia recurrence at 12 months (LVA 56.5% vs no LVA 41.4%; HR1.51, 95%CI 1.01-2.27, p=0.04) compared to no posterior LVA.

CONCLUSION: In patients with PsAF undergoing catheter ablation, posterior LVA was associated with a significant increase in atrial arrhythmia recurrence. However, the addition of PWI in those with posterior LVA did not reduce atrial arrhythmia recurrence over PVI alone.

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105. A PILOT CASE CROSSOVER STUDY OF THE USE OF PADDED HEADGEAR IN JUNIOR AUSTRALIAN FOOTBALL

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AIM: To explore soft-shell padded headgear (HG) use, player behavior and injuries associated with HG in junior Australian football.

METHODS: Prospective case-crossover with head impact measurement, injury surveillance and video review.

RESULTS: 40 players (mean age: 12.43 years, standard deviation: 1.36) across 15 matches were observed. Frequency of head/neck (p = 0.916) or body (p = 0.883) contact events, and match incidents were similar between HG and no HG conditions. Without HG, females had higher frequency of body contacts compared with males (p = 0.015). Males sustained more body contacts with HG than without HG (p = 0.013).

CONCLUSION: Use of HG in junior football was not associated with injury or head contact rate. Associations between HG use and body contact may differ across sexes.

106. COMPARISON OF PATIENTS' AND HEALTHCARE PRACTITIONERS' EVALUATION OF PATIENT-REPORTED OUTCOMES OF BARIATRIC SURGERY – A MODIFIED DELPHI STUDY

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AIMS: Patient-reported outcomes of bariatric surgery are an important metric increasingly utilised in clinical, research, and registry settings. These outcomes, while vital, are underutilised and require refinement for the specific patient population. This study aimed to investigate and compare how pre-surgical patients, post-surgical patients, and healthcare practitioners evaluate patient-reported outcomes of bariatric surgery to identify those outcomes that are considered most important.

METHODS: A modified Delphi survey was distributed to pre-surgical patients, post-surgical patients and a variety of healthcare practitioners including bariatric surgeons, physicians, nurses, dieticians, psychologists, and researchers. Across two rounds, participants were asked to rate a variety of physical and psychosocial patient-reported outcomes of bariatric surgery on a scale from 0 (Not Important) to 10 (Extremely Important). Items rated 8 – 10 by at least 70% of participants were considered highly important (prioritised). Prioritised items were compared between the three groups as well as between healthcare practitioner subgroups.

RESULTS: 20 pre-surgical patients, 95 post-surgical patients, and 28 healthcare practitioners completed the survey. The three groups prioritised 29, 26, and 44 items, respectively. There were 21 items (out of 90, 23.3%) prioritised by all three groups, 13 by two groups (14.4%), and 18 (20.0%) prioritised by only one group. Unanimously prioritised items include 'Co-morbidities', 'Overall Quality of Life' and 'Overall Mental Health'. Discordant items include 'Fear of Weight Regain', 'Suicidal Thoughts', and 'Addictive Behaviours'.

CONCLUSION: Considerable agreement was seen between groups on several items and domains, however, important differences were also identified between groups including between pre- and post-surgical patients, between patients and healthcare practitioners, and between healthcare practitioner subgroups. By considering the values of all stakeholder groups in identifying the most important patient-reported outcomes of bariatric surgery, we ensure future work and resulting measures will encompass all important outcomes, and will be useful and valid for end users.

107.ALCOHOL-RELATED TRAUMA PRESENTATIONS AMONG OLDER TEENAGERS

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AIM: The objectives of the present study were to report the proportion of older teenagers, including the subgroup operating a motor vehicle, presenting to an adult major trauma centre after injury with a positive blood alcohol concentration (BAC) over a 12-year period.

METHODS: This was a registry-based cohort study, including all patients aged 16-19 years presenting to an adult major trauma centre in Victoria, Australia from January 2008 to December 2019 and included in the trauma registry. A Poisson regression model was used to test for change in incidence of positive BAC associated trauma and summarised using incidence rate ratios (IRRs) and 95% confidence intervals (CIs).

RESULTS: There were 1658 patients included for analysis and alcohol was detected in 368 (22.2%; 95% CI 20.2-24.3). Most alcohol positive presentations were on weekend days (n = 207; 56.3%) and most were males (n = 307). Over the 12-year period, there was a reduction in the incidence of older teenagers presenting with a positive BAC (IRR 0.95; 95% CI 0.93-0.98; P = 0.001). Among patients presenting after trauma in the setting of operating a motor vehicle (n = 545), alcohol was detected in 80 (14.7%) with no significant change in incidence of positive BAC (IRR 0.95; 95% CI 0.89-1.02; P = 0.17).

CONCLUSION: A substantial proportion of older teenagers included in the registry had alcohol exposure prior to trauma. Despite a modest down-trending incidence, the need for continuing preventive measures is emphasised. In particular, preventive efforts should be targeted at male, older teenagers undertaking drinking activities on weekend days and driving motor vehicles.

108. USING STEREO-EEG DATA TO DETERMINE THE OPTIMAL INTRACRANIAL VENOUS SINUS LOCATION FOR AN ENDOVASCULAR SEIZURE DETECTION DEVICE

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INTRODUCTION: Seizure detection and prediction have gained interest in improving quality of life. This study aims to utilise stereo-electroencephalography (SEEG) data to determine the optimal venous location for a seizure detection endovascular device.

METHODS: Post-Stereo-EEG implantation CT scans were aligned with pre-operative MRIs to identify six venous sinus segments (anterior (SS-A), middle (SS-M) and posterior (SS-P) sagittal sinus, straight sinus, ipsilateral (ITS (same-side as seizure originated)), and contralateral (CTS (opposite-side from seizure originated)) transverse sinus). Distances between these sinuses and electrode contacts were measured, with only contacts within 5cm included. Data were categorised into seizure (focal aware, focal impaired awareness, and focal-to-bilateral tonic-clonic seizures (FAS, FIAS, and FBTCS)) and epilepsy (temporal and extra-temporal lobe epilepsy (TLE, ETLE)) levels. Multilevel mixed-effects linear regression and pairwise comparisons were conducted to determine the optimal venous sinus segment or the sinuses that can detect the most seizures.

RESULTS: This study involved 6,707 electrode contacts and 113 seizures (FIAS: 50.44%, FAS: 30.09%, FBTCS: 19.47%) in 40 SEEG patients (TLE: 50%, ETLE: 50%). Seizure type ($p<0.001$) and epilepsy type ($p=0.007$) significantly influenced detectable seizures by venous sinus segments. ITS excelled in detecting seizures for FAS (94.25%), FBTCS (94.44%), TLE (89.92%), and ETLE (90.64%), while the straight sinus performed best for FIAS (88%).ITS detected significantly more seizures than other sinuses for FAS but showed no significant difference with straight sinus ($p=0.649$) for FIAS. For FBTCS, ITS detected more seizures than SS-A ($p=0.015$) but showed no significant difference from other sinuses. However, there was no significant difference from the straight sinus in TLE ($p=0.172$) and SS-M ($p=0.156$) for ETLE.

CONCLUSION: Seizure and epilepsy types influence the optimal venous sinus segment. ITS consistently demonstrated seizure detection capabilities across categories. Other sinuses, like the straight sinus for FIAS and TLE or SS-M for ETLE, should also be considered.

109. WHAT CAN WE LEARN FROM PATIENTS WITH POST-TRAUMATIC EPILEPSY AND HEALTH PROFESSIONALS TO OPTIMISE CARE? A QUALITATIVE STUDY

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Epilepsy is a long-term consequence of traumatic brain injury, occurring within 12 months or up to 10 years or more following injury. The incidence, risk and treatment prophylaxis have been well studied, however its impact in the Australian healthcare setting and community are unknown.
AIM: To understand the current experience of adults and/or their caregivers and health professionals, regarding management of post-traumatic epilepsy in Victoria.

METHODS: A qualitative descriptive study was conducted with seven patients diagnosed with post-traumatic epilepsy (five males, aged 21 – 52 years) and eight health professionals (six males, experience range 6 – 30 years). Semi structured interviews were audio recorded, transcribed, and thematically analysed using a framework approach.

RESULTS: Thematic analysis of patients' interviews found three important categories for post-traumatic epilepsy management - 1) information provision, 2) medication and 3) a well-supported environment. Patients expressed they wanted information about all aspects of epilepsy management and a supportive care team who understood their challenges, including their brain injury. Analysis of health professionals' interviews found the importance of – 1) treating the patient as an individual, 2) involving diverse health professionals and 3) access to specialist care in current management. Several barriers to providing care were identified by patients and health professionals, including limitations in the availability of resources and information provision, and cognitive impairments affecting management. Positive factors Facilitators included providing more written information, having a family member or caregiver attend appointments, greater access to specialist care and long-term follow up, effective communication between all healthcare professionals across settings, greater consideration of patients with cognitive impairments, and connecting to community support services.

CONCLUSION: This study revealed current management of post-traumatic epilepsy requires considering the dual diagnosis. Tailoring management, considering both conditions, and providing accessible information coproduced with stakeholders early are very important to both patients and health professionals.

110. MULTIMODAL LEARNING FOR EMERGENCY DEPARTMENT TRIAGE IMPLEMENTATION: EXPERIENCES FROM PAPUA NEW GUINEA DURING THE COVID-19 PANDEMIC

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BACKGROUND Triage implementation in resource-limited emergency departments (EDs) has traditionally relied on intensive in-person training. This study sought to evaluate the impact of a novel digital-based learning strategy focused on the Interagency Integrated Triage Tool, a three-tier triage instrument recommended by the World Health Organization.

METHODS A mixed methods study utilising pre-post intervention methods was conducted in two EDs in Papua New Guinea. The primary outcome was the mean change in knowledge before and after completion of a voluntary, multimodal training program, primarily delivered through a digital learning platform accessible via smartphone. Secondary outcomes included the change in confidence to perform selected clinical tasks, and acceptability of the learning methods.

RESULTS Among 136 eligible ED staff, 91 (66.9%) completed the digital learning program. The mean knowledge score on the post-training exam was 87.5% (SD 10.4), a mean increase of 12.9% (95% CI 10.7 – 15.1%, p<0.0001) from the pre-training exam. There were statistically significant improvements in confidence for 13 of 15 clinical tasks, including undertaking a triage assessment and identifying an unwell patient.

In an evaluation survey, 100% of 30 respondents agreed or strongly agreed the online learning platform was easy to access, use and navigate, and that the digital teaching methods were appropriate for their learning needs. In qualitative feedback, respondents reported that limited internet access and a lack of dedicated training time were barriers to participation.

CONCLUSION The use of digital learning to support triage implementation in resource-limited EDs is feasible and effective when accompanied by in-person mentoring. Adequate internet access is an essential pre-requisite.

111.SAVING THE LINE: AN EVALUATION OF INTRALUMINAL ALTEPLASE FOR UNBLOCKING CVADS

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Central venous access devices (CVADs) provide reliable, extended intravenous access, however are at risk of occlusion and line malfunction, necessitating resource-intensive replacement. Intraluminal alteplase (IA) is an established thrombolytic for unblocking CVADs following unsuccessful traditional techniques such as mechanical agitation. In 2018, a ready-to-use 2mg alteplase formulation and protocol were added to the hospital formulary of this quaternary referral centre.

AIM: To evaluate use of IA for the management of occluded CVADs and assess the impact on reinsertion rates after guideline implementation.

METHODS: Observational ambidirectional study included a randomly selected sample of patients with CVAD insertions in 2017 (pre-guideline cohort; no thrombolytic) and 2022 (post-guideline cohort; pre-selected 50% IA use). Demographic data, CVAD history, and alteplase-related outcomes were collected from the electronic medical record. The cost of IA is $121 compared with $2458 for CVAD reinsertion. Primary outcome was the incidence of reinsertions. Chi-squared test of independence and unpaired t-test were used to determine statistical significance ($p < 0.05$) for comparison of groups.

RESULTS: Each cohort included 100 patients; 62.5% were male and median age was 59 years (IQR 42,70). Median line dwell time was 20 days (9,38). Overall CVAD reinsertion rates were 21 events per 1000 person-days (16,26) pre-guideline compared with 11 (8.4,15) post-guideline (OR 0.56, 95% CI 0.38-0.82; p=0.0017). Incidence of reinsertion due to thrombosis was significantly reduced from 5.6 to 1.7 per 1000 person-days (OR 0.30, 95% CI 0.11-0.55;p=0.0042). Reinsertions per patient reduced from 2 events pre-guideline to 1.1 in the post-guideline cohort ($p<0.0001$). Restoration of patency was 100% when IA was administered; guideline compliance was 84%.

CONCLUSION: Addition of IA to the formulary, together with a guideline on overall management of occluded CVADs, has resulted in reduced reinsertions in our cohort. This supports the role of IA as an effective cost-saving strategy in supporting CVAD dwell longevity.

112.SUCCESSFUL RECRUITMENT INTO A LARGE MULTI-SITE TRIAL IN AUSTRALIA DURING THE COVID-19 PANDEMIC – LESSONS LEARNED.

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BACKGROUND: The Australian Surgical Antibiotic Prophylaxis (ASAP) trial was a multicentre randomised trial examining the impact of addition of vancomycin to standard prophylaxis with cefazolin in elective joint replacement surgery. The trial commenced recruitment January 2019 and was completed in October 2021 enrolling 4362 patients.[1] The Australia government public health response to prevent and reduce the spread of COVID-19 began in February 2020 with border closures, lockdowns and cancellation of elective surgery.[2.]
This paper examined the effect of the COVID 19 pandemic on recruitment and the strategies put into place to reach the successful enrolment target within the ASAP trial timeframe.

MATERIAL/METHODS: This nested descriptive sub-study examined the impact of the Australian Government response to the COVID 19 pandemic, hospitalisations, international delays, and strategies put into place to facilitate recruitment into the ASAP trial from February 2020 to October 2021.

RESULTS: Australian hospital elective surgery admissions decreased up to 8.7% in 2020[3] including an 8.5% reduction in elective joint replacement surgery[4]. In April 2020, recruitment was suspended due to inability to obtain study drug componentry from the European manufacture due to impact of COVID 19, coinciding with the restrictions placed on elective surgery[5]. Site recruitment in Victoria fluctuated with further elective surgery restriction in August to September 2020[5]. Strategies implemented including the introduction of verbal consent and in spite of the Government COVID-19 responses, overall recruitment to the ASAP trial increased by 10% over the period of interest.

CONCLUSION: The effect of the COVID 19 pandemic on the ASAP trial in Australia was minimal. The key factors that affected this are the low number of COVID 19 hospitalisations in Australia at the time of study recruitment, minimal interruptions to elective surgery and the quick resolution to drug supply. Although the inability of the individual researcher to control the impact of a pandemic on study recruitment, future considerations for similar trials should include securing access to trial components locally or stored locally, and considering verbal consent as an option for sites.

113. IMPROVING HEALTHCARE TEAM HARMONY THROUGH COLLABORATIVE TEAM REFLECTION AND MINDFULNESS

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BACKGROUND: Hospital wards, staffed by the multidisciplinary team, are complex environments where teamwork, communication and psychological safety is essential for coordinated care delivery, yet are faced with challenges such as staffing changes and complex care needs. However, there is little literature on interventions to assist staff connect as a team.

AIM: Investigate the impact of a brief (<10 min) daily (Mon-Fri) group program based on team reflection and mindfulness aimed at a multidisciplinary general medicine team

METHODS: Fifty-one staff members participated in the group program, who self-reported measures of team functioning (effectiveness, communication, and psychological safety) through an online survey. A focus group was conducted to better understand the participants' experiences, which was analyzed with the aid of a thematic map.

RESULTS: We found that participants reported significant improvement in the meeting's effectiveness (U=184, p=0.013), team morale (U=123, p<0.001), and focus (U=183, p<0.001) after the program's commencement. Furthermore, participants who attended the program for at least a week reported they felt more psychologically safe (U=116, p=0.032). We also found significant positive correlation between measures of team functioning and the number of sessions they attended the program (effectiveness of the interdisciplinary meeting r=0.509, p<0.001; team's communication and functioning (r=0.509, p<0.001). The post-intervention focus group highlighted the program helped build relationships within the team, improve psychological safety, and subsequently shifted the team's behaviour to be more supportive of the overall team.

CONCLUSION: A brief daily group program based on mindfulness and team reflection improved the functioning of a multidisciplinary healthcare team.

114. NUTRITIONAL RISK IS ASSOCIATED WITH HOSPITAL RELATED HARMS IN OLDER ADULTS PARTICIPATING IN HOME-BASED REHABILITATION.

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Malnutrition is associated with significant morbidity and mortality amongst hospitalised older adults. The Malnutrition Universal Screening Tool (MUST) is used to identify adults who are malnourished or at risk of malnutrition.

AIMS: Investigate the association between nutritional risk and the incidence of Hospital Related Harms (HRH) in individuals undertaking rehabilitation in a home-based inpatient bed substitution model called Better-at-Home (BAH). To describe the relationship between nutritional risk and HRH in patients enrolled in the rehabilitation and Geriatric Evaluation and Management (GEM) arms of BAH.

METHODS: Single-centre, retrospective cohort study of adults ≥18 years participating in BAH between January 1 to March 31 2021. Those receiving palliative care, living in residential care and readmitted to BAH within 30 days were excluded. Participants were divided into four subgroups: low nutritional risk within GEM, low nutritional risk within rehabilitation, moderate-high nutritional risk within GEM and moderate-high nutritional risk within rehabilitation using the MUST. Outcome measures included delirium, pressure-injuries, falls, transfers and readmission within 30 days. P-value of <0.05 was considered significant.

RESULTS: Of 175 participants, 71 (41.1%) had moderate-high nutritional risk. Patients with moderate-high nutritional risk were more likely to be admitted with delirium (p=0.014) and readmitted to an acute ward (p=0.003) and BAH within 30 days of discharge (p=0.05.) GEM patients, regardless of nutritional risk, were more likely to experience ≥ 1 adverse outcome (p=0.006.)

CONCLUSION: Increasing nutritional risk was associated with HRH in this home-based rehabilitation program. The most common HRHs were falls, transfers to an acute facility and readmissions to hospital. GEM patients, regardless of nutritional risk, were more likely to experience adverse outcomes, compared to rehabilitation patients. Factors such as frailty, chronic disease, functional and cognitive impairment likely confound this relationship. Further prospective studies are required to further characterise this relationship in this inpatient bed substitution model of care.

115. A DIETARY INTERVENTION TO INCREASE COLONIC AND SYSTEMIC SHORT-CHAIN FATTY ACIDS ALTERS GUT MICROBIOTA AND CIRCULATING IMMUNE CELLS IN HEALTHY HUMANS

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BACKGROUND: Short-chain fatty acids (SCFA) produced from microbial fermentation of dietary fibre in the intestine have immune-modulating effects in animal models of disease. However, there is limited evidence of this in humans. This study aimed to determine effects of increased delivery of SCFA via dietary manipulation on the gut microbiota and the phenotype of peripheral blood leucocytes and inflammatory cytokines in healthy humans.

METHODS: Healthy adults (n=20) underwent a blinded, randomized, cross-over dietary intervention, consuming a high SCFA-producing diet (38 g/day fibre) and matched low-SCFA diet (19 g/day fibre) for 21 days with 21-day wash-out in between. Blood and faecal samples were collected at the end of each diet. Gas chromatography was used to measure SCFA. Gut microbiota composition was assessed using shotgun metagenomic sequencing. Flow cytometry was used for peripheral blood immuno-phenotyping. Plasma cytokine levels were quantified using a multiplex assay.

RESULTS: Plasma propionate (9.9 vs 4.7 μmol/L) and faecal SCFA (86.6 vs 75.4 μmol/g) were significantly higher on high-SCFA than on low-SCFA diet. High-SCFA diet associated with elevated expression carbohydrate metabolism and peptidoglycan biosynthesis genes in gut microbiota, and increased differential abundance of *Bifidobacterium adolescentis*, *Anaerostipes hadrus* and *Ruminococcus bromii*. Blood total B cells (184 vs 199 cells/μL), mucosal-associated invariant T (MAIT) cells (62 vs 69 cells/μL) and CD8+ Tfh cells (4.9 vs 5.5 cells/μL) were significantly lower on high-SCFA than on low-SCFA diet. Plasma cytokine levels were similar. Changes in differential abundance of *R. bromii* negatively associated with changes to CD8+ Tfh cells, whilst changes in *Aldercreutzia equolifaciens* relative abundance positively associated with Tfh1 cells.

CONCLUSIONS: Delivery of SCFA using dietary intervention has discrete effects on gut microbiota and circulating immune cells in healthy humans. Further studies are required to determine if these changes alter immune function and have therapeutic benefit to those with inflammatory disease.

116. OUTCOMES OF PATIENTS UTILISING TELE-EMERGENCY CARE IN SOUTHEAST REGION OF MELBOURNE

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BACKGROUND: In January 2022, supported by the State government, three health networks covering the geographical south-east of Melbourne partnered to initiate South East Virtual ED (SERVED), as part of a broader roll-out of already existing emergency telehealth services in Victoria. The aim of this study (SERVED-1) was to report on the initial 5-month experience of the VED service. This report includes all patients assessed through the SERVED over the first 5-months (01 Feb 2022 to 30 Jun 2022).

METHODS: VED consults occurred after referral from Ambulance Victoria paramedics at the pre-hospital setting. Electronic medical records were retrospectively reviewed and demographic, presenting complaint and outcome data extracted. The primary outcome was the count of VED consultations. Secondary outcomes were the proportion of patient in whom a physical ED attendance was prevented within 72 hrs and 7 days. In addition, we presented the proportion of physical ED attendances prevented by sub-groups of primary presenting complaint.

RESULTS: There were 1748 patients who had a VED consultation, of which 1261 (72.1%; 95%CI: 70.0-74.2) patients had a physical presentation to an ED prevented in the 72 hours following the consult. There was a significant increase in utilisation of the service over the 5-month period (IRR 1.27; 95%CI: 1.23-1.31, p<0.001) that was consistent in the three health services. The most common presenting complaints were COVID-19 and shortness of breath, and physical presentation was presented most often among younger patients and those with COVID-19.

CONCLUSIONS: Initial experience of SERVED demonstrated significant increase in adoption of the service and an overall prevention of physical ED attendance by 72% of patients. These results support ongoing VED consultations, supported by ongoing follow-up and health economic evaluations.

117. THE EVALUATION OF GASTRIC EMPTYING USING NUCLEAR SCINTIGRAPHY COMPARED TO THREE-DIMENSIONAL MULTI-DETECTOR COMPUTED TOMOGRAPHY (3D-MDCT) GASTRIC VOLUMETRY IN THE ASSESSMENT OF POOR WEIGHT LOSS FOLLOWING SLEEVE GASTRECTOMY

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Poor weight loss and weight regain are principal challenges following sleeve gastrectomy (SG). There is a lack of standardized assessments and diagnostic tests to stratify the status post-SG and determine whether anatomical or physiological problem exists. We hypothesised, compared to gastric volume, gastric emptying half-time would be a more specific and accurate marker of weight loss post-SG.

AIM: To compare nuclear scintigraphy gastric emptying with CT volumetric analysis of sleeve anatomy and determine the impact of anatomy on physiological function and its correlation with weight loss.

METHODS: Patients >12 months post-SG, were categorised into optimal weight loss (OWL) (n=29) and poor weight loss groups (PWL) (n=50). All patients underwent a protocolised nuclear scintigraphy and Three-Dimensional Multi-detector Computed Tomography (3D-MDCT) Gastric Volumetry imaging.

RESULTS: Post-operative % total weight loss in OWL was 26.2 ± 10.5% vs 14.2 ± 10.7% in the PWL group (p-value <0.0001). The PWL group had significantly more delayed gastric emptying half-time than OWL (34.1 18.8 vs 19.5 4.7, p-value <0.0001). Gastric emptying half-time showed statistically significant correlations with weight loss parameters (BMI; r= 0.215, p-value 0.048, %EWL; r= -0.336, p-value 0.002 and %TWL; r= -0.379, p-value <0.001). The median gastric volume on 3D-MDCT did not differ between the OWL 246 (IQR 50), and PWL group 262 (IQR 129.5) ml, p-value 0.515. Nuclear scintigraphy gastric emptying half-time was the most highly discriminant measure. A threshold of 21.2 minutes distinguished OWL from PWL patients with 86.4% sensitivity and 68.4% specificity.

CONCLUSION: Nuclear scintigraphy is a potentially accurate tool in the functional assessment of sleeve gastrectomy physiology. It appears to perform better as a diagnostic test than volumetric assessment for patients with poor weight loss post-SG. We have established diagnostic criteria of >21 minutes to assess sleeve failure, which is linked to suboptimal weight loss outcomes.

118. USING CENTRAL VENOUS PRESSURE WAVEFORM TO CONFIRM THE PLACEMENT OF AN INTERNAL JUGULAR CENTRAL VENOUS CATHETER IN THE INTENSIVE CARE UNIT

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BACKGROUND: A mobile chest X-ray is traditionally performed to confirm the position of an internal jugular central venous catheter (CVC) after placement in the intensive care unit (ICU). Using chest radiography to confirm CVC position often results in delays in authorising the use of the CVC, requires the deployment of additional human resources, and is costly.

OBJECTIVE: This study aimed to determine the feasibility and accuracy of using the central venous pressure (CVP) waveform to confirm the placement of internal jugular CVCs.

METHODS: This retrospective study was conducted in a single quaternary ICU over a 6-month period. We included adult patients who had internal jugular CVC inserted and CVP transduced as part of their routine care in the ICU. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of CVP waveform analysis in confirming the position of internal jugular CVC relative to chest radiography were calculated.

RESULTS: A total of 241 internal jugular CVCs were inserted (in 219 patients, 35.6% female) and the CVP waveform was assessed. In 231 cases, this suggested adequate placement in a central vein, which corresponded with a correct position on subsequent chest X-ray. On six occasions, the CVP waveforms were interpreted as suboptimal, however, on chest X-rays, the CVCs were noted to be in a suitable position (sensitivity 97.5%). Four suboptimal CVP waveforms were obtained and correctly identified CVC malposition on subsequent chest X-ray (specificity 100%). The average time from CVC insertion to radiological completion was 118 minutes.

CONCLUSION: CVP waveform analysis provides a feasible and reliable method for confirming adequate internal jugular CVC position. The use of chest radiography can be limited to cases where suboptimal CVP waveforms are obtained.

119. 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: There is increasing concern for the potential neurobiological consequences of repeated exposure to head acceleration events (HAEs) in collision sports. No studies have investigated how head impact kinematics from non-concussive impacts aligns with sensitive blood biomarkers of axonal (NfL, p-tau181) and glial (GFAP) pathology.

AIM: To quantify non-concussive head impact exposure and the association with emerging blood biomarkers in male amateur Australian football players.

METHODS: Forty-one amateur male Australian football players from the Victorian Amateur Football Association were recruited and underwent in-season (24h post-match) and post-season blood collections. Twenty-six players wore custom-fitted HitIQ Nexus A9 Instrumented Mouthguards, which measured peak linear (PLA) and rotational (PRA) acceleration per impact. Game footage was used to verify impacts and code the match play situations in which HAEs occurred. Blood biomarker quantification was completed using a Simoa HD-X Analyser.

RESULTS: In-season levels of serum GFAP ($p=0.046$), NfL ($p=0.001$), and p-tau181 ($p<0.0001$) were significantly elevated compared to post-season (n=24). Maximum PLA ($p=0.029$) and PRA ($p=0.046$) in a single game was associated with post-match GFAP levels (n=15). Similarly, cumulative PLA ($p=0.010$) and PRA ($p=0.009$) in a single game was associated with post-match GFAP levels (n=15). No such post-match correlations were observed for NfL and p-tau181; however, cumulative PLA ($p=0.011$) and PRA ($p=0.027$) across two consecutive games correlated with changes in NfL levels across this period (n=11). Tackles accounted for 41% (n=202) of video-verified true positive HAEs (n=484).

CONCLUSION: This data suggests that non-concussive impacts sustained during one or two matches may lead to subtle increases in blood markers linked to brain cell injury. Ongoing validation studies with a larger, diverse sample, including females, are in progress.

120. EMERGENCY NURSE RETENTION: THE INFLUENCE OF JOB STRAIN, ORGANISATIONAL ENVIRONMENT AND SYSTEM PRESSURES.

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Nursing workforce challenges have hit a critical threshold with widespread staff shortages, reduced senior staff, and increasing staff turnover and reduction in contracted hours. This is a critical problem for the sustainability of healthcare systems worldwide.

AIM: To understand factors influencing emergency nurse retention to inform the co-design of interventions to increase emergency nursing staff retention at Alfred Health.

METHODS: A mixed methods study was conducted within Alfred Health Emergency services, based on a framework incorporating the job demands-control-support model and adaptive leadership. This included a survey (n=104) incorporating The Health and Safety Executive's Management Standards Work-Related Stress Indicator Tool (HSE) and Practice Environment Scale of the Nursing Work Index (PES) and questions about intention to leave. Two focus group workshops were also held with nursing leaders to explore job strain and adaptive leadership in the department.

RESULTS: Thirty-seven per cent of nurses were thinking about or planning to leave their position, while 23% intended to reduce their working hours. Nurses experienced high workplace demands, lack of control over key aspects of their work, and lack of support from colleagues many of whom were new and inexperienced. Key tension points affecting job satisfaction and job strain, as described by nurses, are shown in Figure 1.

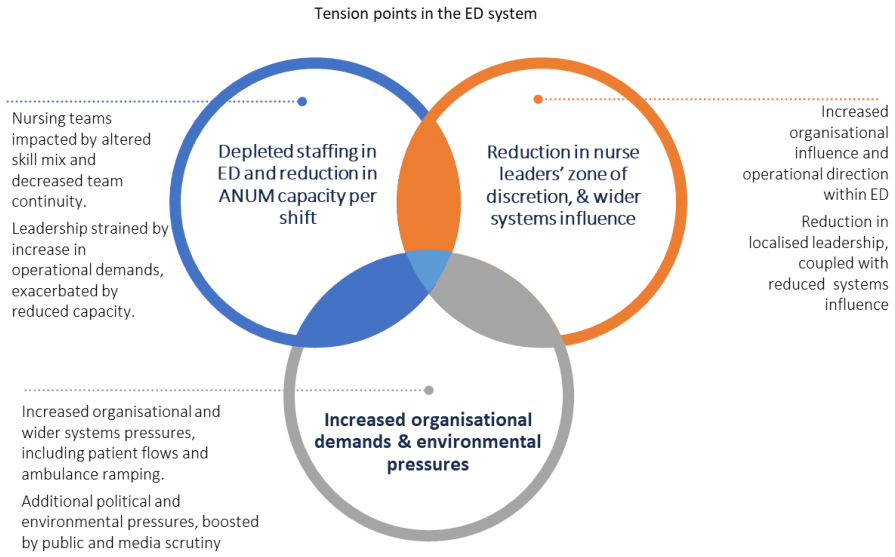

Figure 1 Factors affecting nurse retention

CONCLUSION: The study found that the emergency nursing workforce is experiencing significant job strain due to organisational and system pressures, including ongoing staffing shortages inclusive of skill mix, increased demands, decreased job control and decreased support. Addressing these factors will require multifactorial interventions that are supported by nurses and the organisation. The next steps in this project are to engage nurses to co-design interventions to improve retention, implement interventions and evaluate the effects on staff retention.

121. DEVELOPMENT OF A NEW PAIN-SPECIFIC PATIENT-REPORTED OUTCOME MEASURE IN WOMEN WITH PELVIC FLOOR DISORDERS

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Procedures involving transvaginal mesh implants to treat women with pelvic floor disorders (PFDs), are associated with post-surgical pain. Pain is an important indicator of health-related quality of life, which can be measured using patient-reported outcome measures (PROMs), however, existing PROMs do not capture the different attributes of pain. The Australasian Pelvic Floor Procedure Registry (APFPR) collects PROMs, though currently, it does not include a PROM on pain.

AIM: To develop potential items for a new pain-specific PROM in women with PFDs for inclusion in the APFPR based on women's perceptions of what is important regarding pelvic floor-related pain.

METHODS: We conducted semi-structured interviews with 16 adult Australian and New Zealand women to define a conceptual framework for pain following pelvic floor surgery. One hundred and fourteen potential items were drafted based on the interviews, conceptual framework and existing literature. An online two-round Delphi survey involving 15 international experts, was conducted to rank the items for a new PROM.

RESULTS: Potential items were developed under eight conceptual framework themes on pain including sensation, region, triggers, continuity, intensity, interference, pain relief and management, and comorbidities and complications. From the 114 potential items, a total of 57 were deemed important. Items are currently being revised for clarity and to reduce repetition, then will be validated in the population of women with PFDs.

CONCLUSION: This is the first study to develop items for a new pain-specific PROM for women with PFDs. The complexity of measuring pain including its various characteristics can be overcome with a pain-specific measure explicit to PFDs and pelvic floor surgery. It is anticipated that the new pain-specific measure will be effectively implemented in the APFPR and could also be in clinical practice.

122. LONG-TERM OUTCOMES OF PERSISTENT CRITICAL ILLNESS

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Persistent critical illness (PerCI) describes a growing group of intensive care unit (ICU) patients who initially survive then persist into chronic critical illness. Their long-term functional outcomes are unknown.

AIM: To compare death or new disability in ICU patients with PerCI (defined as 10 days stay in ICU) and without PerCI at six months after ICU admission.

METHODS: Secondary analysis of a multi-centre, prospective cohort study conducted in six metropolitan ICUs. Participants were adults admitted to ICU who received >24 hours mechanical ventilation. The primary outcome was death or new disability at six months, with new disability defined as 10% increase in WHODAS 2.0 score. A significance level of 0.01 was used.

RESULTS: Of the total 888 enrolled patients, the primary outcome was available in 670 (75%) patients, 188 with and 482 without PerCI. The primary outcome was similar between PerCI and non-PerCI patients: 124/171 (72.5%) and 246/457 (53.8%) respectively (risk difference 10.70 [95% CI 0.47–20.90]; p=0.040). At six months, the mortality rate was significantly different between PerCI and non-PerCI patients: 76/252 (30.2%) and 57/547 (10.4%) respectively (risk difference 15.04 [95% CI 9.65–20.39]; p=<0.001). In survivors, there was no difference in the incidence of new disability: 48/95 (50.5%) PerCI and 100/311 (32.2%) non-PerCI patients (risk difference 9.98 [95% CI -0.27–20.20]; p=0.056).

CONCLUSION: At six months, the incidence of death or new disability was not statistically different in patients with and without PerCI, but patients without PerCI were more likely to survive to six-months.

123. RIGHT BRACHIOCEPHALIC VEIN ORIGIN INTRAVENOUS ACCESS FOR THE RESUSCITATION OF ADULT TRAUMA PATIENTS

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INTRODUCTION: Severe blood loss (haemorrhagic shock) is the most common cause of preventable death after injury. Obtaining intravenous access for volume replacement in shocked trauma patients is challenging due to circulatory collapse. Central venous access can be obtained via the brachiocephalic vein origin (BCVO) with ultrasound guidance. The BCVs appear to be stabilized by the clavicle and sternum, and are less likely to collapse in shock. The right BCVO (RBCVO) is preferred for access in adults as it is more superficial, larger, and straighter. A literature review of BCV access, a biometric analysis of CT scans patients, and a prospective ultrasound study all suggest that RBCVO access is feasible in resuscitation of shocked trauma patients.

AIMS: This research aims to investigate the clinical effectiveness of RBCVO access in trauma resuscitation, whilst maintaining cervical spine alignment. This includes investigating how RBCVO access integrates into trauma resuscitation and the comparative success rates, complication rates and procedural difficulties of RBCVO and subclavian vein (SCV) access.

METHODS: This study is a prospective randomised control trial comparing central venous access gained via the RBCVO and SCV in shocked trauma resuscitation. The study was approved by the Alfred Human Research Ethics Committee (ID 312/22) and is registered with the Australian New Zealand Clinical Trial Registry (ACTRN12623000916640).

RESULTS: RBCVO access has been successful during trauma resuscitation. To date, 40 patients have been recruited, with an 83% success rate, 65% first attempt success rate and 1.4 mean attempts required for RBCVO access compared to a 61% success rate, 48% first attempt success rate and mean 2.0 attempts required for SCV access.

CONCLUSION: Preliminary results demonstrate that RBCVO access is feasible in trauma resuscitation. It may provide another, potentially more reliable venous access route. This may enhance resuscitation of haemorrhagic shock and lead to improved outcomes after injury.

124. HUMAN FACTORS ASSESSMENT OF THE USABILITY OF FOUR MODERN ANAESTHESIA MACHINES

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Human Factors is the scientific discipline that aims to improve system efficiency and safety through design. Anaesthesia machines are a major, safety critical investment, but procurement processes rarely include consideration of usability and safety. Usability is the extent to which a product can be used with effectiveness, efficiency, safety and satisfaction in a specified context of use.

AIM: The aims of this study were to assess the overall usability and safety of four anaesthesia machines being considered for purchase, and recommend next steps in the evaluation and procurement process.

METHODS: Participants were clinicians from Alfred Health, and were invited to view and interact with each machine during February-March 2023 with vendor representatives and a human factors researcher present. A mixed methods approach was used, comprising heuristic evaluation, task analysis, observations, and surveys.

RESULTS: Over 40 hours of observations and 53 surveys were collected. Usability and safety concerns, such as poor feedback, mode errors, difficulty solving problems, unclear/misleading labels and difficulty performing tasks were identified in two machines and indicated that they should be eliminated from further consideration. Two machines showed a good level of usability, with clear displays, support for task performance and problem solving, and good safety features, and were recommended to be tested in a simulated setting. User preferences aligned with these safety and usability findings.

CONCLUSION: Four modern anaesthesia machines differed in usability despite all being approved for use. Usability assessments identified safety concerns and indicated that two machines should be eliminated from consideration. Simulated testing of the remaining machines should be done to quantitatively assess task performance and user experience, particularly in emergencies. Usability and safety evaluation, along with mechanisms for feedback to manufacturers should be integrated into healthcare procurement processes.

125. ASSOCIATION OF NEUROCRITICAL CARE UNITS WITH PATIENT OUTCOMES FOR ADULTS WITH BRAIN INJURY IN AUSTRALIAN INTENSIVE CARE UNITS FROM 2016 TO 2020

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Background: Neurocritical care (NCC) services is associated with improved mortality in brain-injured patients. However, this has not been examined in the Australian population. This observational cohort study compares outcomes in adults with brain injuries admitted to Australian intensive care units (ICUs) with and without NCC services.

Methods: A nationwide survey was conducted in 2020 examining NCC services in Australian ICUs. ICUs were categorised as NCC units if they identified as a neurocritical care unit (NCCU) and/or employed a neurointensivist. ICUs were included if they routinely treated acute brain-injured adults. Data linkage was undertaken with a registry comparing outcomes for patients managed in NCCUs or general ICUs from 2016 to 2020 inclusive. The primary outcome of interest was in-hospital mortality, reported as an odds ratio (OR). Results was adjusted for the Australian New Zealand Risk of Death score, year of admission and source of admission. Secondary outcomes included discharge destination, reported as OR, and ICU and hospital length of stay (LOS), reported as median difference (MD).

Results: 17,383 brain-injured adults were treated across 8 NCCUs (n=9561) and 35 general ICUs (n=7822) over 5 years. Hospital mortality was lower in the NCCU group (16.4%) compared to general ICUs (19.3%) with an unadjusted OR of 0.82 (95% CI 0.76-0.89, *p*-value <0.001), favouring NCCUs. Adjusted OR did not identify a statistically significant correlation (OR 0.93, 95% CI 0.85-1.03, *p*-value 0.194). Patients had an increased odds of discharge to rehabilitation following an NCCU admission (OR 1.58, *p*-value <0.001, 95% CI 1.42-1.76). ICU and hospital LOS was longer in NCCU admissions with an adjusted MD of 0.47 (*p*-value <0.001, 95% CI 0.34-0.58) and 0.65 (*p*-value 0.011, 95% CI 0.14-1.15) respectively.

Conclusion: Brain-injured adults treated in NCCUs in Australia were correlated with a lower in-hospital mortality. However, this was not statistically significant when adjusted for other variables.

126. MORAL DISTRESS AND BURNOUT IN HEALTH CARE WORKERS AT ALFRED HEALTH AT THE START OF THE COVID-19 PANDEMIC: QUANTITATIVE RESULTS.

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Moral distress(MD) arises when we feel compelled to act or witness acts that challenge our values. Described in military conflict and healthcare workers(HCW), validated scales exist to measure MD in HCW, Moral Distress Scale – revised(MDS-R). Ongoing MD can lead to burnout. Soon after COVID-19 was first detected people in Victoria, The Alfred Health Staff Wellness Survey was conducted.

AIM: To examine MD and burnout in HCW at Alfred Health.

METHOD: An online survey collected demographic data and included measures of burnout and MD. All staff across Alfred Health had access. Statistical analysis was undertaken in Jamovi® and R.

RESULTS: 406 staff participated in the survey, 150(37%) scored both frequency and level of distress for all 25 MDS scenarios. Mean MDS scores were calculated. Most participants were female(83%), nurses(44%) and allied health(37%). Equal numbers of staff worked in frontline(49%) and non-frontline(51%) settings. MD was high in COVID-19 care areas (p=0.008) and nurses(p=0.04). MD correlated with burnout (p<0.001). MD levels were highest in nurses(p=0.01) and allied health workers(p=0.01). Predictors of higher levels of MD were nursing profession (p<0.001) and burnout(p=0.02).

The 5 top root causes of MD were:
- Witness diminished patient care quality due to poor team communication.
- Watch patient care suffer because of lack of provider continuity.
- Work with nurse and other healthcare providers who are not as competent as patient care requires.
- Balance your own physical and mental healthcare needs with those of patients.
- Provide less than optimal care due to pressures from administrators or insurers to reduce costs.

CONCLUSION: The impact of COVID-19 on staff at The Alfred was significant. Moral distress and burnout, particularly in nurses and allied health staff, was evident. Further research into, and efforts to mitigate the impacts of, the root causes of MD is recommended.

127.CUMULATIVE RADIATION DOSE FROM CT IN AN AUSTRALIAN TEACHING HOSPITAL

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The International Atomic Energy Agency in collaboration with the World Health Organisation have identified that there is a considerable number of patients who receive "concerningly high" cumulative doses from recurrent diagnostic imaging. This recognition has largely arisen due to the sizable datasets now available through automated dose monitoring systems.
AIM: While dose monitoring software are not widespread in Australia and New Zealand, it is important to gain a better understanding of the distribution, frequency and magnitude of recurrent imaging.

METHODS: The cumulative dose from computed tomography (CT) scans across two hospitals, including six CT scanners, were assessed. The Radiology Information System (RIS) was used to extract data on CT scans, patient demographics and dose length product (DLP) over a two-year period (2019-2020). Effective dose was determined using a DLP conversion coefficient and were cumulated per individual.

RESULTS: Over the two-year period, 97,765 CT scans were undertaken on 49,623 patients. On average patients received 1.97 scans. The most frequent type of scan was a non-contrast scan of the brain (18%), followed by scans of the abdomen-pelvis (9.9%). The majority (79%) of patients received less than 25 millisieverts (mSv) of CT radiation exposure, while 1.1% (554 patients) received more than 100 mSv. Almost 30% of patients with cumulative doses greater than 100 mSv were less than 50 years old.

CONCLUSION: This analysis only captured CT scans for individuals within a two-year period that were performed at two hospitals. Therefore, the cumulated doses may be significantly underestimated for any single individual's actual exposure. The clinical indication of the scan was not extracted and would be useful to correlate with high recurrent imaging doses for future optimisation. Despite limitations, it is evident that some patients within the public health system are receiving many CT scans and high cumulative radiation doses.

128.ESTABLISHING AN MR SAFETY COMMITTEE

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Introduction: Recently we have established a committee for oversight of Magnetic Resonance Imaging (MRI) safety. The aim of the committee is to provide a forum for discussion of incidents and device safety as well as the development of MR safety guidelines. Implementing the committee is part of a larger safety framework aligning with the RANZCR MRI Safety Guidelines.

Method: The Safety of MRI Advisory Committee (SMAC) was established in 2019 with a multi-disciplinary team of radiographers, radiologists and medical physicists, fulfilling the roles of MR Medical Director (MRMD), MR Safety Officer (MRSO) and MR Safety Expert (MRSE). Incidents relating to MR safety are collected and reviewed and safety is considered for implants which have not been tested. Incidents have been categorised into 1) failure to indicate a contraindication to MR on the request, 2) safety, 3) incorrect patient, 4) incorrect request and 5) incomplete implant documentation.

Results: There has been an average of 50 MR incidents per year for the past three years (2020-2022) across five MRI scanners including inpatients, outpatients and participants in research and clinical trials. The incident rate ranged from 3.4 to 4.7 per 1000 MR patient visits. Of these incidents, 81% are due to failures to indicate contraindications, 13% are MR safety related, and 6% are equally attributable to incorrect patient, request and implant documentation.

The vast majority of requestor failures to indicate contraindications are for pacemakers, with aneurysm clips, coils, stents, shunts and filters also contributing to this category. Specific device assessments have been undertaken for deep brain stimulators, embolisation coils and an infusion pump.

Conclusion: The implementation of an MR Safety Committee has provided important oversight for incident reporting. It is integral to developing a more comprehensive safety framework for the MR environment. Furthermore, it provides an appropriate forum for assessment of device safety.

129. THE ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND FRAILTY IN COMMUNITY-DWELLING OLDER ADULTS

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Background: Frailty is a common and increasingly prominent condition as the global older-adult population increases. Physical activity (PA) is a promising potential preventive strategy for frailty during older age. This study explores the association between physical activity intensity and frailty among community-dwelling older adults aged 70 years or older.

Methodology: This prospective cohort study utilises data from 11,570 participants in the ASPirin in Reducing Events in the Elderly (ASPREE) clinical trial and the ASPREE Longitudinal Study of Older Persons (ALSOP). Adults (70+ years) self-reported maximal usual PA intensity (never/rarely, light, moderate, vigorous). Frailty was defined in two ways; i) according to the Fried Phenotype criteria (Fried phenotype) (having 3+ of: shrinking, slowness, weakness, exhaustion, low activity); and ii) scoring >0.21 on a 67-item deficit accumulation index (Index). Cox proportional hazards regression explored the association between PA and frailty over a maximum of 6 years, after adjustment for age, sex, education, smoking and alcohol status, living status, area-level socio-economic status, annual income status, remoteness, BMI, diabetes mellitus, dyslipidaemia, hypertension, and baseline frailty status. A competing risk regression was also conducted, adjusting for death. Hazard ratios and 95% confidence intervals (CI) were reported.

Results: 11,570 adults (mean age (SD) = 75.1 (4.2) years, 53.4% females) were followed for a median of 5.2-years during which time 1,202 adults (10.4%) developed frailty according to the Fried phenotype and 3,097 (26.8%) according to the frailty index. Compared with light PA, the risk of developing frailty was greater among those who reported rarely/never engaging in PA (Fried phenotype: 1.55 (1.18-2.03); Index: 1.12 (0.91-1.37)) and lower among those engaging in moderate PA (Fried phenotype: 0.68 (0.59, 0.77)); Index: 0.87 (0.80, 0.93)) or vigorous PA (Fried phenotype: 0.47 (0.36, 0.60); Index: 0.70 (0.61-0.81)). The results of the competing risk regression analysis were similar.

Conclusions: The study results suggest that PA in older age at any intensity may lower frailty risk in older adults.

130. ASSESSING THE NECESSITY OF INTRAVENOUS CONTRAST FOR COMPUTED TOMOGRAPHY IN THE ACUTE UNDIFFERENTIATED ABDOMEN

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BACKGROUND: Undifferentiated abdominal pain in the emergency setting is frequently investigated with an intravenous contrast enhanced CT as a first line diagnostic test. However, global contrast shortages restricted the use of contrast for a period in 2022, altering standard practice with many scans performed without intravenous contrast. Whilst IV contrast can be useful to assist with interpretation, its necessity in the setting of acute undifferentiated abdominal pain is not well described. In addition, the use of IV contrast comes with its own risks including mandating an IV cannula, contrast nephropathy, allergy, and death.

AIM: This study aimed to assess the shortcomings of omitting IV contrast in an emergency setting, by comparing the rate of CT scans with "indeterminate" findings with and without the use of IV contrast.

METHODS: Retrospective case-control study from presentations to our emergency department for undifferentiated abdominal pain prior to and during contrast shortages in June 2022. The primary outcome was the rate of diagnostic uncertainty, where the presence or absence of intra-abdominal pathology could not be ascertained.

RESULTS: 12/85 (14.1%) of the unenhanced abdominal CT scans provided an uncertain result, compared with 14/101 (13.9%) of control cases performed with intravenous contrast, p = 0.96. There were also similar rates of positive and negative findings between the groups.

lipid atlas of human a demonstrated no significant difference in the rate of diagnostic uncertainty. There are significant potential patient, fiscal and societal benefits as well as potential improvements to emergency department efficiency with the reduction of unnecessary intravenous contrast administration.

131. THE ASSOCIATION BETWEEN PATIENT CHARACTERISTICS AND REHABILITATION OUTCOMES FOR ADULTS ENROLLED IN A METROPOLITAN REHABILITATION IN THE HOME PROGRAM

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An increasing proportion of rehabilitation services are now being delivered in a patient's home such as the Better at Home Program at Alfred Health as part of patient-centred care. However, little is known about what patient characteristics are associated with successful outcomes in a home-based program.

AIMS: To investigate patient level characteristics associated with successful rehabilitation in a home-based inpatient bed substitution model of care (Better at Home).

METHODS: Retrospective cohort study of patients aged ≥18 years admitted to Better at Home between 01 January 2021 to 30 March 2021. The primary outcome ('successful rehabilitation') was a composite score (out of 3) of: (1) patient remaining at home at discharge, (2) no readmissions within 7 days of discharge, and (3) improvement in FIM score. Patients were dichotomised into those scoring 0-2 and 3. Characteristics of each group were compared. Secondary outcomes included the rates of pressure injuries, falls, and transfers to ED.

RESULTS: Of the 175 patients included, 70 (40%) scored 0-2 and 105 (60%) scored 3. There were significant differences between the groups in Charlson Comorbidity Index (7.5 vs 6.7, p=0.05), number of admission medications (11.1 vs 9.5, p=0.02), and having a MyAgedCare package (38.5% vs 17.1%, p<0.01). There were no statistically significant differences between the groups in age, sex, nutritional status, living arrangements, cognitive impairment, IDC presence, or with routine screening tools (FRASS, BRADEN, MUST). A MyAgedCare package and lower admission FIM were associated with increased falls. A lower BMI was associated with increased transfers to ED and a higher MUST with readmission.

CONCLUSION: A higher number of comorbidities, medications, and presence of formal supports were associated with poorer outcomes in the Better at Home Program. Larger prospective studies are needed to identify targeted interventions for those recognised at risk of poorer outcomes.

132. A COMPARISON OF DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF OPIOIDS USERS AND PATIENTS ON OPIOID AGONIST TREATMENT REFERRED TO AUSTRALIAN PAIN MANAGEMENT SERVICES FROM 2016 TO 2021

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INTRODUCTION: Opioids have been widely used to manage chronic pain (CP). While opioid use disorder (OUD) often co-occurs with CP, little is known about the differences in demographic and clinical characteristics among people who are taking different dosages of opioids and those receiving treatment for OUD with opioid agonist treatment (OAT).

AIM: This study aims to compare the demographic and clinical characteristics of patients attending Australian pain management services receiving conventional opioids and OAT.

METHODS: This cross-sectional study uses a national database from the electronic Persistent Pain Outcomes Collaboration (ePPOC) in Australia. Data were collected for adult patients from 1 January 2016 to 31 December 2021. Patients were divided into an OAT group and other three conventional opioid use groups from low to high doses (low: <40 mg/d, moderate: 40-100 mg/d, high: >100 mg/d). Differences between groups on variables including age, gender, employment, physical comorbidities, mental health symptoms and pain-related characteristics were analysed using multiple logistic regression.

RESULTS: A total of 42,182 participants were included. Most were female (56.8%), and the mean age was 51.70 years (SD: 0.07, 95% CI: 51.56 – 51.84, range: 18 – 102). The largest group was the low-dose group (48.64%), which formed the reference group in the logistic regression analyses. After adjusting for all characteristics, people on OAT and high-dose opioids were more likely to be male, not working, have more severe anxiety and depression symptoms and have had CP for more than 5 years. It is noted that there was no significant difference in pain severity between the OAT and low-dose groups.

CONCLUSION: People on OAT and high-dose opioids have relatively similar demographic and clinical characteristics, with low employment, and poorer mental health, than people on low opioid doses.

133.IMPLEMENTATION OF A RADIATION ONCOLOGY CT REFERENCE LEVEL REVIEW PROCESS

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INTRODUCTION: Diagnostic Reference Levels (DRLs) have been published in Australia for computed tomography (CT) since 2012, and comparison against DRLs is a regulatory [1] and accreditation requirement [2]. No such requirement exists for planning scans performed in a Radiation Oncology (RO) context, however, global interest is growing in the auditing and benchmarking of planning CT scans [3]. From a radiation detriment perspective, reducing unnecessary dose to patients undergoing RO planning scans via CT optimization is prudent.

METHOD: At our organization, a cross-disciplinary collaboration comprising of diagnostic and RO medical physicists, radiation therapists and radiographers across two clinics was established to discuss CT dose optimization. Annual diagnostic CT patient dose surveys are collected and compared with established ARPANSA DRLs. For RO, dose data for planning scans is collected and compared with the reference levels proposed by IPEM as a guide [4]. The collected RO and diagnostic dose data are also compared.

RESULTS: CT dose data for radiation oncology patients were collected for seven protocols across two sites in 2022 and compared to IPEM proposed planning scan reference levels (Table 1). Several RO protocols exceeded planning scan reference levels. Key differences between RO and diagnostic protocols were noted, as well as causative factors for differences between oncology clinics (e.g. kV, use of iterative construction, image quality indicators), yielding opportunities for optimization changes.

TABLE 1 – MEDIAN VOLUMETRIC COMPUTED TOMOGRAPHY DOSE INDEX (CTDIVOL) AND DOSE LENGTH PRODUCT (DLP) VALUES FOR AUDITED SCANNING PROTOCOLS, AND THE PROPOSED IPEM REFERENCE LEVELS.

Scan protocol	Clinic 1		Clinic 2		IPEM proposed reference level	
	CTDIvol (mGy)	DLP (mGycm)	CTDIvol (mGy)	DLP (mGycm)	CTDIvol (mGy)	DLP (mGycm)
Brain	38	998	21	704	50	1500
Neck	12	424	10	388	49	2150
Chest/Breast	6	218	14	459	10	390
Lung 4D	73	2109	--	--	63	1750
Abdomen 4D	132	4126	--	--	N/A	N/A
Pelvis	11	398	14	577	N/A	N/A
Abdomen	7	268	--	--	N/A	N/A

CONCLUSION: This pilot attempt at RO CT protocol dose auditing allowed comparison to international proposed refence levels. Collecting and sharing patient dose data from both radiation oncology and diagnostic contexts allowed for fruitful communication between the disciplines and sharing of skills.

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134. THE ASSOCIATION BETWEEN PLANT AND ANIMAL PROTEIN INTAKE AND DISABILITY-FREE SURVIVAL IN COMMUNITY-DWELLING OLDER ADULTS: THE RESULTS OF THE ASPREE LONGITUDINAL STUDY OF OLDER PERSONS (ALSOP)

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Evidence on the impact of protein sources on health in older adults is limited.

AIM: This study aimed to investigate the link between plant and animal protein consumption and disability-free survival (DFS) in older individuals.

METHODS: The study included 9,951 adults aged ≥70, participants in the ASPirin in Reducing Events in the Elderly (ASPREE) study and the ASPREE Longitudinal Study of Older Persons (ALSOP). DFS was a composite of all-cause mortality, dementia, or persistent physical disability. Participants reported their intake of protein subtypes: red meat, fish, poultry, and plant protein, with consumption frequency ranging from rarely/never to several times daily. A composite variable integrating plant and animal protein was created. Cox proportional hazards regression models, adjusted for various covariates, were used to analyse the relationship between protein types and DFS.

RESULTS: Over an average follow-up of 6.4 years, 1,011 DFS events occurred (546 Men & 465 women). Men who consumed plant protein several times daily had a 57% lower risk (HR 0.43 [95%CI: 0.20-0.90]) of reaching the DFS endpoint compared to those who rarely/never consumed it. Similarly, regular fish consumption (monthly, weekly, and several times weekly) was associated with significantly lower DFS risk in men (0.50[0.32-0.76]; 0.53 [0.34-0.81]; 0.47[0.24-0.92]). No significant association was found between red meat or poultry consumption and DFS in either sex. When considering composite variables, women who consumed poultry and plant-based protein weekly had a 64% lower risk (0. 36[0.25-0.96]) of reaching the composite DFS endpoint compared to those who rarely/never consumed these proteins. In men, a lower risk of the DFS endpoint was observed when monthly and weekly red meat consumption was combined with weekly plant-based protein consumption (HR.034[0.13-0.92]; 0.42[0.19-0.95]).

CONCLUSION: The regular consumption of fish and plant-based protein in community-dwelling men 70 years and over, is associated with prolonged survival free from disability

135.UPSCALING AUTOLOGOUS ENGINEERED FULL-THICKNESS SKIN FOR BURN WOUND CLOSURE

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INTRODUCTION: The treatment of patients with severe burns covering a large total body surface area (TBSA) presents a significant challenge due to a lack of available donor sites. The Skin Bioengineering Lab has developed and demonstrated that a dermal/epidermal composite Human Skin Equivalent (HSE) is capable of closing full-thickness wounds in mice. The HSE manufacturing process has been upscaled in preparation for a prospective feasibility study (phase I) from 2023-2026 to evaluate the safety and efficacy of this novel skin graft in burns patients.

METHODS: A biopsy of < 10 cm^2 was obtained from elective plastic surgery patients to simulate the limited size of available healthy skin that may be obtained from severe burns patients. Fibroblasts and keratinocytes were then expanded using previously reported methods.[1-2] Cells were seeded into a crosslinked platelet precipitate hydrogel, developed in-house, and grown for five days to form the HSE.[3]

RESULTS & DISCUSSION: Immunofluorescence analysis shows that HSEs exhibit characteristics of native skin, including the presence of a basement membrane, stratified epidermis and collagen-rich dermis. The process of manufacturing HSEs has now successfully been upscaled wherein a minimum of nine 12 cm x 12 cm grafts can be prepared within the four-week window in which burns patients typically recover between debridement and grafting surgeries.

CONCLUSION: Limiting the size of the donor site, using fully autologous cells, and matching the engineered graft manufacturing process with the timing of routine burns surgeries allows for HSEs to potentially replace the need for split skin grafting. Unlike cultured epithelial autografts, the HSE is capable of closing a deep burn wound intrinsically without the need to combine with other grafting methods.[4]

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136. INCIDENCE OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH MAJOR BURNS RECEIVING STANDARD DOSE THROMBOPROPHYLAXIS: A RETROSPECTIVE STUDY

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AIM: To evaluate thromboprophylaxis prescribing and incidence of venous thromboembolism (VTE) in patients with burns >20% total body surface area (TBSA).

METHOD: Retrospective cohort study conducted at a state-wide provider for adults with complex burns. Adult patients admitted between Jan-2019 and Oct-2021 with burns >20% TBSA were identified from the Victorian Adult Burns Service registry. Data retrieved from the registry and electronic medical records included demographic and clinical parameters (length of stay (LOS), %TBSA burns, thromboprophylaxis prescribed, dosing, time to administration, VTE). The primary outcome was the incidence of VTE. Data were analysed descriptively; chi-squared or Mann-Whitney U test determined statistical significance (p-value <0.05), comparing those with VTE to those without.

RESULTS: Seventy-eight patients met inclusion criteria. Majority of patients were male (73.1%), median age was 42.5 years (IQR: 32.0-58.0) and LOS 24.4 days (IQR: 10.8-42.9); 3.8% of patients had history of thrombophilia and mortality rate was 24.4%. The median TBSA burns was 33.0% (IQR: 23.6-49.8), with a high proportion of patients (94.9%) experiencing a flame burn injury. All patients received pharmacological prophylaxis. Five patients (6.4%, 95% CI 2.1-14.3%) developed VTE whilst inpatients. Patients experiencing VTE were less likely to receive standard-dose VTE prophylaxis (40% vs 95%, P=0.0001), the time to first administration of VTE prophylaxis was longer (27.2 hours vs 23.7 hours, p=0.002) and they had a significantly increased LOS (90.9 vs 20.9 days, p=0.0002), compared to those who did not develop VTE. There were no differences in %TBSA.

CONCLUSION: A low incidence of VTE was identified in patients with major burns. There were statistically significant differences in time to first administration of thromboprophylaxis and optimal dosing of VTE prophylaxis, in patients with VTE compared to those without. Larger prospective studies will inform future guidelines on the use of increased dose thromboprophylaxis in patients with major burns.

137.PREVALENCE OF ALCOHOL AND OTHER DRUG USE IN VIOLENCE-RELATED INJURIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Alcohol and/or other drug (AOD) use increases the risk of being a perpetrator and a victim of violence. The aim of this systematic review was to report on the prevalence of acute pre-injury AOD exposure in patients presenting to hospital with violence-related injuries.

METHODS: Systematic database (Medline, Embase, CINAHL, PsycINFO) and grey literature searches were used to identify observational studies of patients aged ≥15 years who presented to hospital with violence-related injuries that used biological samples (e.g., blood, breath, urine) to measure AOD exposure. Screening, data extraction, and risk of bias assessments were completed by two independent reviewers. Studies were grouped based on injury cause (any violence, assault, firearm, and other penetrating injuries including stab or incised wounds) and substance type (any AOD use, alcohol only, drugs other than alcohol only). Where appropriate, meta-analyses were completed using Stata.

RESULTS: Of the 10,756 records screened, 28 met inclusion criteria. The prevalence of AOD exposure varied across injury groups. Alcohol was detected in 13-66% of violence-related injuries (5 studies), 4-71% of assaults (13 studies), 21-45% of firearm injuries (6 studies; pooled estimate=41%, 95%CI: 40-42, n=9,190), and 9-66% of penetrating injuries (9 studies; pooled estimate=60%, 95%CI: 56-64, n=6,950). The prevalence of drugs other than alcohol was 37% for violence-related injuries (1 study), 39% for firearm injuries (1 study), 7-49% for assaults (5 studies), and 5-66% for penetrating injuries (3 studies). Any AOD use was identified in 76-77% of violence-related injuries (3 studies), 40-73% of assaults (6 studies), and 26-45% of penetrating injuries (4 studies; pooled estimate=30%, 95%CI: 24-37, n=319).

CONCLUSIONS: AODs were frequently detected in cases of violence-related injury, highlighting the need for innovative approaches to preventing violence-related injuries involving AOD use. Prevalence estimates of AOD involvement in violence-related injury events provide a benchmark for future harm reduction and injury prevention strategies.

138.A PROSPECTIVE CROSS-SECTIONAL STUDY ASSESSING TEACHING OF INTERVENTIONAL RADIOLOGY ACROSS 20 AUSTRALIAN MEDICAL SCHOOLS, ENDORSED BY THE AUSTRALIAN MEDICAL STUDENTS ASSOCIATION

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BACKGROUND: Existing literature from several countries around the world has shown that teaching of Interventional Radiology (IR) to medical students is suboptimal. In Australia, despite calls for improvement at a "grass-roots" level, most IRs find that junior doctors have limited or no knowledge of IR, and thus reduced awareness of potential IR treatments for their patients or contemplating IR as a future career.

AIM: The aim of this study was to survey current medical students to assess perception of whether a wider variety of medical schools are integrating IR into their curriculum, from universities all across Australia.

METHODS: Prospective cross-sectional study of members of the Australian Medical Students Association (AMSA) from across Australia. Students were given a link to 14-question electronic survey of current university teaching and students' knowledge of the discipline of IR. The primary outcome was perception of current teaching and knowledge of IR. Secondary outcomes include awareness of technical, clinical, and other duties of IRs. The survey link was sent in a newsletter and posted on the AMSA Facebook page to their members.

RESULTS: Responses were received from 82 students, representing 20 out of 23 Australian medical schools. 61% of students described poor or no knowledge of IR and 88% of students perceived teaching of IR as either poor or absent. Teaching of IR was significantly worse than diagnostic radiology ($p < 0.001$), and 99% suggested that IR teaching could be improved. Only 11% of students would consider a career in IR.

CONCLUSION: Medical student perception of exposure to IR teaching is poor compared to diagnostic radiology. Better awareness may lead to improved referral patterns for patients and more career interest in IR.

139.AN INVESTIGATION INTO DOSE RATE METERS PROMPTED BY LONG DISCHARGE TIMES POST-ADMINISTRATION OF LU-177 PSMA

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Introduction: Lutetium-177 prostate-specific membrane antigen (Lu-177 PSMA) therapy has been delivered as an outpatient service in our department through the participation in three research trials. Self-sufficient participants are discharged when their external dose rates at two metres reach the threshold of 9 microsieverts per hour (μSv/h). Participants at our department typically remained above the threshold for more than four hours post-administration (after six to eight bladder voids), which is longer compared to other two sites enrolled in the same trials (Sites A and B). It prompted a review of the dose rate meter, a Cypher survey meter (model 5000), used at our department.

Method: A literature review of dose rate levels and discharge times for Lu-177 PSMA therapy, and a direct comparison of readings between our equipment and those from Site A were undertaken. Consequently, dose rate correction factors for Lu-177 and other relevant radionuclides were derived for the Cypher survey meter through the assessment of its calibration factor curve and comparisons of dose rate measurements with published dose rate constants.

Results: From the literature, the recommended discharge threshold [1] for similar prescribed activities were reached between one to four hours post-administration [3, 4]. Direct measurements of a research participant at Site A showed that readings from Cypher survey meters were similar, but were about 55% lower with their Berthold LB134 Umo II monitor. Correction factors of 0.5, 0.8 and 0.9 were derived for dose rate measurements using the Cypher survey meter for Lu-177, Technetium-99m and Iodine-131, respectively. The discharge times post-administration of Lu-177 PSMA, henceforth, dropped to one to two hours.

Conclusion: The Cypher survey meter (Model 5000) at our disposal overestimates the dose rate for Lu-177 roughly by a factor of two. The use of a correction factor for measurements during Lu-177 PSMA therapies was successfully implemented.

140.RESEARCH OUTPUT OF RADIOLOGISTS IN AUSTRALIA AND NEW ZEALAND: STRENGTHS, WEAKNESSES AND FUTURE DIRECTIONS

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BACKGROUND: Clinical radiology is a popular career. However, academic radiology in Australia and New Zealand (ANZ) has not traditionally been a strength of the specialty which has a focus on clinical medicine and has been influenced by corporatisation of the specialty.

AIM: The aim of this study was to review the source(s) of radiologist-led research in Australia and New Zealand, to identify areas of relative deficiency and propose plans to improve research output.

METHODS: A bibliometric study was performed of all manuscripts in seven popular ANZ journals: Journal of Medical Imaging and Radiation Oncology, Journal of Medical Radiation Sciences, Medical Journal of Australia, New Zealand Medical Journal, Internal Medicine Journal, Emergency Medicine Australasia and the ANZ Journal of Surgery. Manuscripts were included where a radiologist from Australia or New Zealand was the corresponding or senior author. Publications between January 2017 and April 2022 were included.

RESULTS: There were 285 manuscripts from ANZ radiologists during the study period. This equates to 10.7 manuscripts per 100 radiologists based on RANZCR census data. Radiologists in Northern Territory, Victoria, Western Australia, South Australia and the Australian Capital Territory all produced manuscripts above the corrected mean incidence rate of 10.7 manuscripts per 100 radiologists. However, locations including Tasmania, New South Wales, New Zealand and Queensland were below the mean. The majority of manuscripts arose from public teaching hospitals with accredited trainees (86%), and there were a higher proportion of manuscripts published by female radiologists (11.5 compared to 10.4 per 100 radiologists).

CONCLUSION: Radiologists in ANZ are academically active; however, interventions aimed at increasing output could be targeted at certain locations and/or areas within a busy private sector. Time, culture, infrastructure and research support are vital, but personal motivation is also extremely important.

141.PREHOSPITAL TRANEXAMIC ACID FOR SEVERE TRAUMA

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The effect of early tranexamic acid (TXA) administration among patients with major trauma and suspected trauma-induced coagulopathy being treated in advanced trauma systems is uncertain.

AIM: To assess the effectiveness of pre-hospital TXA on functional outcome and survival after major trauma

METHODS: We randomly assigned adults with major trauma who were at risk for trauma-induced coagulopathy to receive TXA (administered intravenously as a 1g bolus before hospital presentation, followed by a 1g infusion over 8 hours in hospital) or matched placebo. The primary outcome was favourable functional outcome at 6 months after injury, assessed using the Glasgow Outcome Scale–Extended (GOS-E), with favourable outcome defined as GOS-E level of 5 ("lower moderate disability") or higher. Secondary outcomes included death within 28 days and within 6 months after injury.

RESULTS: A total of 1310 patients were recruited by 15 emergency medical services in Australia, New Zealand, and Germany; 661 were assigned to receive TXA, and 646 were assigned to receive placebo; unknown trial group assignment for 3 patients. A favourable outcome at 6 months was observed in 307 of 572 patients (53.7%) in the TXA group and in 299 of 559 (53.5%) in the placebo group (risk ratio (RR) 1.00; 95% confidence interval [95%CI]: 0.90 to 1.12; p=0.95). At 28 days after injury, 113 of 653 patients (17.3%) in the TXA group and 139 of 637 (21.8%) in the placebo group had died (RR 0.79; 95%CI: 0.63 to 0.99). The number of serious adverse events did not differ meaningfully between the groups.

CONCLUSIONS: Among adults with major trauma and suspected trauma-induced coagulopathy who were being treated in advanced trauma systems, prehospital administration of TXA followed by an infusion over 8 hours did not result in a greater number of patients surviving with a favourable functional outcome at 6 months than placebo.

142. A RETROSPECTIVE OBSERVATIONAL STUDY ASSESSING MORTALITY AFTER PELVIC TRAUMA EMBOLISATION.

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BACKGROUND: Trauma to the pelvic ring and associated haemorrhage represent a management challenge for the multidisciplinary trauma team. In up to 10% of patients, bleeding can be the result of an arterial injury and mortality is reported as high at 89% in this cohort.

AIM: This study aimed to assess mortality rate after pelvic trauma embolisation and whether earlier embolisation improved mortality.

METHODS: Retrospective observational study at single tertiary trauma and referral centre, between 1 January 2009 and 30 June 2022. All adult patients who received embolisation following pelvic trauma were included. Patients were excluded if angiography was performed but no embolisation given.

RESULTS: During the 13.5-year time period, 175 patients underwent angiography and 28 were excluded, leaving 147 patients in the study. The all-cause mortality rate at 30-days was 11.6% (17 patients). The median time from injury to embolisation was 6.3 hours (range 2.8-418.4). On regression analysis, time from injury to embolisation was not associated with mortality (OR 1.01, 95%CI 0.952-1.061). Increasing age (OR 1.20, 95%CI 1.084-1.333) and increasing ISS (OR 1.14, 95%CI 1.049-1.247) were positively associated with all-cause 30-day mortality, while non-selective embolisation (OR 0.11, 95%CI 0.013-0.893) was negatively associated with mortality.

CONCLUSION: Time from injury to embolisation was not associated with all-cause 30-day mortality. However, the overall mortality rate in this study was lower than in many published studies. This may be a type 2 error due to the sample size and low incidence of the outcome. AS such, it is likely that improving embolisation times in unstable patients is still an important governance process particularly if hospital mortality rates exceed those quoted in literature.

143. SEX DIFFERENCES IN THE LINK BETWEEN DNA METHYLATION-DERIVED BIOLOGICAL AGEING AND HEALTH IN OLDER INDIVIDUALS

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DNA methylation (DNAm) derived biological age, also known as epigenetic age, is one of the most promising ageing biomarkers. Females live longer than males and there are sex disparities in physical health and disease incidence. However, sex differences in biological ageing have not been consistently reported and may differ depending on the measure used.

AIM: This study aimed to determine the correlation between different generations of epigenetic age acceleration (AA) measures, with a system-wide deficit-accumulation frailty-index (FI) ageing and brain-predicted-age-difference (brain-PAD), separately in males and females aged ≥70 years. We additionally explored the extent to which these AA measures were associated with clinical measures and chronic conditions.

METHODS: Epigenetic age (HorvathAge, HannumAge, PhenoAge, GrimAge, GrimAge2, and DunedinPACE) was estimated in blood from 560 Australians (females, 50.7%) enrolled in the ASPREE study. AA is the residual from regressing epigenetic age on chronological age. FI was comprised of 67 items covering a broad range of biological systems. Brain age was estimated from T1-weighted MRI.

RESULTS: Females had significantly lower epigenetic ageing than males, but higher FI, and there was no difference in brain-PAD. FI had the strongest correlation with the newest AA (DunedinPACE; r >0.21 in both sexes). Brain-PAD was not correlated with any biological ageing measures. Significant correlations between AA and health markers including grip strength and gait speed were more commonly found in females (e.g., for DunedinPACE; r range: -0.23 to 0.24) than in males. GrimAA and Grim2AA were significantly associated with obesity and depression in females, while in males, hypertension, diabetes, and chronic kidney disease were associated with these clocks, as well as DunedinPACE ($p<0.05$).

CONCLUSION: Our findings suggest that epigenetic AAs could be useful clinical indicators of overall age-related deficits, even in relatively healthy older people, and highlight the importance of considering sex differences when using these biomarkers.

144.'DEMYSTIFYING' POPS: A QUALITATIVE CASE STUDY TO UNDERSTAND THE CORE ELEMENTS OF THE PERIOPERATIVE MEDICINE FOR OLDER PEOPLE UNDERGOING SURGERY (POPS) SERVICE

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BACKGROUND: Perioperative medicine for older people undergoing surgery (POPS) services deliver a complex model of care that improves outcomes for older people contemplating or undergoing surgery. Complex models of care may be difficult to implement without understanding the elements that comprise the service delivering that model of care. One way of describing these elements is with a logic model, which can be used to aid implementation by visually depicting theoretical relationships between elements of the service.

AIM: To understand the key core elements of the POPS service, required for the successful delivery of a perioperative model of care for older people undergoing surgery.

METHODS: A qualitative case study at three hospitals in the United Kingdom was undertaken. The hospital differed across contextual factors (population, workforce, size) and stages of POPS service implementation maturity. Semi-structured interviews (n=56) with purposively sampled clinicians (medical, nursing, allied health, and pharmacy) and managers were conducted.The interviews were analysed using inductive and deductive methods.

RESULTS: We developed a multiple-site logic model with themes that described the core elements of the POPS service, across seven logic model domains. These domains included the inputs or resources required to deliver the POPS service, core components of the service, process changes needed to implement POPS, contextual factors that affected implementation, short- and long-term outcomes of the POPS service, and the wider impact of the POPS service. We found the POPS service could be adapted to 'fit' local context and still achieve its desired outcomes if it remained true to the principles of comprehensive geriatric assessment and optimisation (CGA), and was delivered by staff with expert skills and attitudes.

CONCLUSION: Our multiple-case logic model provides generalisable information about the key core elements of the POPS service. This information can be used to aid the implementation of POPS in new healthcare settings.

145. PRE-HOSPITAL FREEZE-DRIED PLASMA FOR CRITICAL BLEEDING AFTER TRAUMA: A PILOT RANDOMIZED CONTROLLED TRIAL

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Objectives: Transfusion of a high ratio of plasma to packed red blood cells (PRBC), to treat or prevent acute traumatic coagulopathy, has been associated with survival after major trauma. However, the effect of pre-hospital plasma on patient outcomes has been inconsistent. The aim of this pilot trial was to assess the feasibility of transfusing freeze-dried plasma with red blood cells (RBC) using a randomized controlled design in an Australian aeromedical pre-hospital setting.

Methods: Patients attended by Helicopter Emergency Medical Service (HEMS) paramedics with suspected critical bleeding after trauma managed with pre-hospital RBC were randomized to receive two units of freeze-dried plasma (Lyoplas N-w) or standard care (no plasma). The primary outcome was the proportion of eligible patients enrolled and provided the intervention. Secondary outcomes included preliminary data on effectiveness, including mortality censored at 24 hours and at hospital discharge, and adverse events.

Results: During the study period of 01 June to 31 October 2022, there were 25 eligible patients, of whom 20 (80%) were enrolled in the trial and 19 (76%) received the allocated intervention. Median time from randomization to hospital arrival was 92.5 mins (IQR 68- 101.5). Mortality may have been lower in the freeze-dried plasma group at 24h (RR 0.24 95%CI: 0.03 - 1.73) and at hospital discharge (RR 0.73; 95%CI: 0.24 - 2.27). No serious adverse events related to the trial interventions were reported.

Conclusions: This first reported experience of freeze-dried plasma use in Australia suggests pre-hospital administration is feasible. Given longer prehospital times typically associated with HEMS attendance, there is potential clinical benefit from this intervention and rationale for a definitive trial.

146. MID-ARM POINT IN PAEDIATRICS (MAPPAED): AN EFFECTIVE PROCEDURAL AID FOR SAFE PLEURAL DECOMPRESSION IN TRAUMA

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Objective: Life-threatening thoracic trauma requires emergency pleural decompression and thoracostomy and chest drain insertion are core trauma procedures. Reliably determining a safe site for pleural decompression in children can be challenging. We assessed whether the Mid-Arm Point (MAP) technique, a procedural aid proposed for use with injured adults, would also identify a safe site for pleural decompression in children.

Methods: Children (0–18 years) attending four EDs were prospectively recruited. The MAP technique was performed, and chest wall skin marked bilaterally at the level of the MAP; no pleural decompression was performed. Radio-opaque markers were placed over the MAP-determined skin marks and corresponding intercostal space (ICS) reported using chest X-ray.

Results: A total of 392 children participated, and 712 markers sited using the MAP technique were analysed. Eighty-three percentage of markers were sited within the 'safe zone' for pleural decompression (4th to 6th ICSs). When sited outside the 'safe zone', MAP-determined markers were typically too caudal. However, if the site for pleural decompression was transposed one ICS cranially in children ≥4 years, the MAP technique performance improved significantly with 91% within the 'safe zone'.

Conclusions: The MAP technique reliably determines a safe site for pleural decompression in children, albeit with an age-based adjustment, the Mid-Arm Point in PAEDiatrics (MAPPAED) rule: 'in children aged ≥4 years, use the MAP and go up one ICS to hit the safe zone. In children <4 years, use the MAP.' When together with this rule, the MAP technique will identify a site within the 'safe zone' in 9 out of 10 children.

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147. ACUTE AND SUB-ACUTE BLOOD BIOMARKERS TO ASSIST DIAGNOSIS IN CT NEGATIVE ISOLATED MILD TRAUMATIC BRAIN INJURY

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Objectives: Blood biomarkers GFAP and UCH-L1 have recently been FDA approved as predictors of intracranial lesions on CT after mild traumatic brain injury (mTBI). However, the vast majority of mTBI cases are CT negative, and no biomarkers are approved to assist diagnosis in these individuals. Here we aimed to determine the optimal combination of biomarkers to assist mTBI diagnosis in otherwise healthy adults aged under 50 presenting to an ED within 6h of injury. We also assessed how sex, presence or absence of loss of consciousness and/or post traumatic amnesia (LOC/PTA), and delayed presentation, affected classification performance.

Methods: Blood samples, symptom questionnaires and cognitive tests were conducted prospectively for mTBI participants recruited from The Alfred Hospital Emergency & Trauma Centre and uninjured controls. Follow-up testing was conducted at 7 days. Simoa® quantified plasma GFAP, UCH-L1, Tau, NfL, IL-6 and IL-1β. AUC analysis assessed classification accuracy and logistic regression models identified optimal biomarker combinations.

Results: Plasma IL-6 (AUC=0.91, 95%CI=0.86-0.96), GFAP (AUC=0.85, 95%CI=0.78-0.93) and UCH-L1 (AUC=0.79, 95%CI=0.70-0.88) best differentiated mTBI (n=74) from controls (n=44) acutely (<6h), with NfL (AUC=0.81, 95%CI=0.72-0.90) the only marker to have such utility sub-acutely (7 days). Biomarker performance was overall similar between sexes and for participants with and without LOC/PTA. Acute IL-6 (R^2=0.50, 95%CI=0.34-0.64) outperformed GFAP and UCH-L1 combined (R^2=0.35, 95%CI=0.17-0.50), with the best acute model featuring GFAP and IL-6 (R^2=0.54, 95%CI=0.34-0.68).

Conclusions: Adding IL-6 to a panel of brain-specific proteins such as GFAP and UCH-L1 might assist in the acute diagnosis of mTBI in adults under 50. Multiple markers had utility in participants without LOC/PTA. When compared with the best performing acute markers, sub-acute measures of plasma NfL resulted in minimal reduction in classification accuracy. Future studies will investigate the optimal time frame over which plasma IL-6 might assist diagnostic decisions and how extracranial trauma affects utility.

148. SIGNIFICANT IMPROVEMENTS IN SAFETY AND OPERATIONAL EFFICIENCY IN THE INTENSIVE CARE UNIT (ICU) BY AN ADVANCED CLINICAL NURSE CONSULTANT (CNCLT)

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Background: The increasing number of critically-ill patients being admitted into ICU has led to longer waiting periods for urgent central venous accesses (CVADs) as well as immediate Intra-Hospital Transports (IHT) for diagnostic and procedural interventions. These led to bottlenecks in time-sensitive treatments, oftentimes, decisive and vital for optimal patient care and outcome.

Aim: To evaluate the efficacy and safety of a fully dedicated CNC in ICU for both CVAD Insertions and Intra-Hospital Transports (CNCLT) of critically-ill intubated patients.

Results: From 2018, the CNCLT has inserted over 1,500 CVADs independently and supervised over 700 occasions for Junior/Senior Medical Officers (JMOs/SMOs). Since 2020, he has competently performed more than 700 IHT critically ill intubated patients without medical escort and supervised over 200 occasions for JMOs. Together, this equates to over 1,700-hours of procedural patient-contact without medical intervention and 1,000-hours of JMO/SMO accreditation time.

This role has produced some major benefits through:

1. Implementing various stringent and standardised practices that have reduced CLABSI rates and adverse events (2018-2023)
2. Reducing malpositions and post-procedural CXRs by 20-30% and 70-80% respectively through Sherlock-PICC System with cost-savings >$30,000/year (2018-2020)
3. Expediting patient care with accreditation of >300 PIVC-competent nurses, ensuring prompt treatment delivery, saving invaluable time (2018-2023)
4. Initialising Co-infusion protocol in reducing blocked lumens by 20-40% (2020-2021) with cost-savings (>$75,000/year)
5. Launching CVP guideline leading to 4-6 hours of time saved to treatments (sample of 250 IJ CVCs, 2021/2023)
6. Accrediting JMOs/SMOs in CVAD and IHT, thereby reducing adverse events and vastly improving medical-nursing workflows and easing workloads
7. Reducing multiple distractions to ICU rounds.

Conclusion: Milestones have been achieved through the introduction of this specialised CNCLT role. This is the FIRST such initiative ever taken by any hospital in Victoria, if not in Australia. With adequate support and funding, this advanced nursing role can be well replicated.

149.PONTANEOUS RETROPERITONEAL HAEMORRHAGE: EFFICACY OF CONSERVATIVE MANAGEMENT AND EMBOLISATION

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BACKGROUND: Spontaneous retroperitoneal haemorrhage (SRH) has a low published incidence of under 0.6% but a relatively high mortality of up to 22% based on case series published to date. There has been recent uptake of embolisation as a minimally invasive endovascular treatment option for these patients, however conservative (medical) measures including fluid resuscitation, blood transfusion, and cessation or reversal of anticoagulation are the mainstay of management and are highly successful.

AIM: To assess the efficacy of conservative management and embolisation in patients with spontaneous retroperitoneal haemorrhage.

METHODS: Single-centre retrospective case–control study of patients with spontaneous retroperitoneal haemorrhage between 1 January 2012 and 2022. Patients aged ≥ 18 years were identified from CT imaging reports. Exclusion criteria included recent trauma, surgery, retroperitoneal vascular line insertion, or other non-spontaneous aetiology.

RESULTS: A total of 54 patients met inclusion criteria, who were predominantly anticoagulated (74%), male (72%), older adults (mean age 69 years), with active haemorrhage on CT (52%). Overall mortality was 15%. Clinical success was more likely with conservative management (36/38) than embolisation (9/16; $p < 0.01$), and all-cause (1/38 vs 7/16; $p < 0.01$) and uncontrolled primary bleeding (1/38 vs 5/16; $p < 0.01$) mortality were higher with embolisation. However, embolised patients more commonly had active bleeding on CT (15/38 vs 13/16; $p < 0.01$), shock (5/38 vs 6/16; $p < 0.04$), and higher blood transfusion volumes (mean 2.2 vs 5.9 units; $p < 0.01$). After one-to-one propensity score matching, differences in clinical success ($p = 0.04$) and all-cause mortality ($p = 0.01$) remained; however, difference in uncontrolled primary bleeding mortality did not ($p = 0.07$).

CONCLUSION: Conservative management of SRH is likely to be effective in most patients, even in those who are anticoagulated and haemodynamically unstable, with variable success seen after embolisation in a more unstable patient group, supporting the notion that resuscitation and optimisation of coagulation are the most vital components of treatment.

150. A SIMPLE SCORING MODEL TO DIFFERENTIATE INFLAMMATORY BOWEL DISEASE FROM NON-INFLAMMATORY BOWEL DISEASE AETIOLOGIES OF ACUTE DIARRHOEA IN PATIENTS ADMITTED TO HOSPITAL

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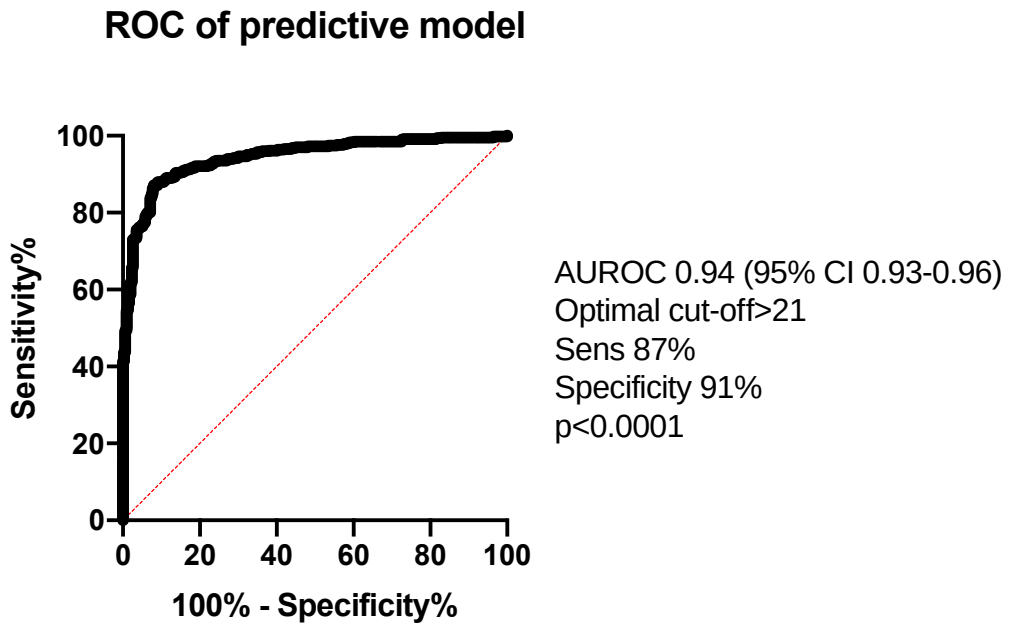
INTRODUCTION: In patients admitted to hospital with acute diarrhoea, differentiating between inflammatory bowel disease (IBD) and infectious gastroenteritis/non-infective aetiologies is challenging and important, as management differs significantly.

AIM: To explore the role of the platelet count in this population and identify predictive factors which could further aid in the diagnosis of IBD flare vs infectious/non-infectious diarrhoea.

METHODS: We retrospectively identified patients admitted to the Alfred Hospital with acute diarrhoea 2000-2018 from medical records. Patients with non-IBD were classified as infectious with positive stool cultures, or non-infectious. Clinical and biochemical parameters were compared using univariate and multivariate analysis and differences in platelet count in IBD flare was compared to non-IBD. A simple scoring tool to predict IBD was created. This model was then validated in an external cohort.

RESULTS: Of 858 patients, 506 had IBD (43% UC) and 352 infectious/non-infectious. Median platelet count was higher in patients with IBD flares, (349 vs 220, p<0.001); notably 0.9% of non-IBD flares had a thrombocytosis. On multivariate analysis, factors independently associated with IBD flare included age (OR 0.95; 95%CI 0.2-0.9), platelet count (OR 1.0), blood in faeces (OR 9.04; 95%CI 2.1-46.7) and longer duration of diarrhoea (OR 1.23; 95%CI 1.1-1.5), all p<0.001. On backward stepwise regression, a model adding the value of the platelet/albumin ratio, diarrhoea duration (+1 for each day diarrhoea) and blood in faeces (yes=score+1) identified an optimal cut-off score >21 to diagnose IBD, with an AUROC of 0.94 (sensitivity 87%, specificity 91%). The model performance was excellent when validated in an external cohort (sensitivity 94.9%, specificity 87.6%, positive predicative value 90.1%, negative predictive value 93.1%)

CONCLUSION: Thrombocytosis is rare in patients admitted to hospital with acute diarrhoea due to non-IBD flares. A simple scoring model can be employed to diagnose IBD from non-IBD causes on presentation to hospital.



151. THE USE OF WHOLE-BODY TRAUMA CT SHOULD BE BASED ON MECHANISM OF INJURY: A RISK ANALYSIS OF 3920 PATIENTS AT A TERTIARY TRAUMA CENTRE

Findakly S [1], Zia A [1], Kavnoudias H [1,2], Mathew J [3,4,5], Varma D [1,2,3], Di Muzio B [1], Lee R [1], Moriarty HK [5], Joseph T [1], Clements W [1,2,3].

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BACKGROUND: Mechanism of injury (MOI) plays a significant role in a decision to perform whole-body computed tomography (CT) imaging for trauma patients. Various mechanisms have unique patterns of injury and therefore form an important variable in decision making.

AIM: Identify the relationship between specific MOI and the finding of traumatic injuries on WBCT imaging at the time of presentation, and thus inform implementation of evidence-based CT scanning based on MOI.

METHODS: Retrospective cohort study including all patients >18 years old who received WBCT between 1 January 2019 and 19 February 2020. The outcomes were divided into CT 'positive' if any internal injuries were detected and CT 'negative' if no internal injuries were detected.

RESULTS: 3920 patients met the inclusion criteria, of which 1591 (40.6%) had a positive CT. The most common MOI was fall from standing height (FFSH), 23.0%, followed by motor vehicle accident (MVA), 22.4%. Covariates significantly associated with a positive CT included age, MVA >60 km/h, motor bike, bicycle, or pedestrian accident >30 km/h, prolonged extrication >30 min, fall from height above standing, penetrating chest or abdominal injury, as well as hypotension, neurological deficit, or hypoxia on arrival. FFSH was shown to reduce the risk of a positive CT overall, however, sub-analysis of FFSH in patients >65 years showed a significant association with a positive CT (OR 2.34, $p < 0.001$) compared to <65 years.

CONCLUSION: Mechanism of injury has a significant predictive impact on identifying subsequent injuries. In high energy trauma, we should consider the need for WBCT based on MOI alone regardless of the clinical examination findings. However, for low-energy trauma, including FFSH, in the absence of clinical examination findings which support an internal injury, a screening whole-body CT is unlikely to yield a positive result, particularly in the age group <65yo.

NURSING

152. BEHAVIOUR OF CONCERN MANAGEMENT IN AN ADULT INTENSIVE CARE SETTING

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Behaviours of concern (BOC) are defined as actions which cause physical harm or distress. BOC directed towards health staff is a complex issue with significant consequences. Intensive care (ICU) is a unique setting therefore potential exists that BOC management strategies are unique.

AIMS: To describe the management strategies implemented for BOC incidents, to identify variations in management related to patient demographic or health status and to establish compliance with unit policy.

METHODS: A one-month, prospective, twice daily audit of the intensive care unit was conducted to identify BOC episodes within the intensive care unit. If an episode was identified on the audit, the nurse involved was invited to complete a questionnaire.

RESULTS: Male patients were more likely to be involved in BOC events than female patients (74% and 26% respectively). 46% of patients involved in BOC events were ventilated at the time of the event. 90% of BOC events were managed combined strategies. Verbal reassurance and chemical restraint were the most common strategies (n=74 and n=71 respectively). 93% of BOC events involving females and 77% BOC events involving males were managed with verbal reassurance.

Patients managed with verbal reassurance and or chemical restraint had higher rates of pre admission substance abuse (n=75 and n=81). CAM-ICU completion was consistent across all strategies (averaged 74%). History of alcohol abuse in the verbal reassurance group was recorded as n=12, however only n=2 had AWS recorded.

CONCLUSIONS: Male patients are more likely to be involved in a BOC event. BOC events were commonly managed with a combination of management strategies. Hands off management strategies were more likely to be utilized than hands on management. Gender influenced the management strategy implemented. Screening tools were under-utilized which may have contributed to initial and recurring BOC events in this sub-population.

153.NDIS HEALTH SUPPORT LETTER (HSL): PROSPECTIVE QUALITATIVE STUDY

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The HSL aims to identify clients with comorbid physical/mental health conditions and provide an appropriate funding structure within a NDIS plan. These plans can promote sustained community access with long term physical health interventions leading to positive outcomes and improved quality of life, however the HSL is currently underutilised in practice

AIM: To determine whether the HSL is useful in practice to improve clients access to support including Exercise Physiology, Dietician (and dietary supports) and support worker allocation, and to determine the barriers and facilitators to improved HSL use across AMAH community-based staff.

METHODS: Qualitative interviews were conducted 7 staff members who were identified as working with clients who could benefit from the use of the HSL. Questions addressed issues such as knowledge of the HSL, eases of access to and completion of the HSL, barriers to its use and examples of success.

RESULTS: Thematic analysis of the interview data indicated themes; Funding received (through using HSL), ease of use. Flexibility/adaptation (depending on individual clients and requests), usefulness for clinicians and consumers, barriers and applicability. Examples of success included some changes in funding allocation within NDIS plans through use of the HSL and applicability particularly with Dietary supports in clients with Eating Disorders. Examples of things that weren't successful included inconsistent funding allocation and challenges with linkage to recommended primary care supports through the NDIS.

CONCLUSION: The project demonstrated that the use of the HSL can improve outcomes for clients in accessing support through the NDIS, however practical barriers to increased use remain, including inconsistent funding allocation and linkage to recommended primary care supports through the NDIS. Addressing the barriers to implementation will improve the ways AMAH delivers services in the future and strength community linkages within primary care.

154.EVALUATING STAFF PERCEPTIONS OF A NURSE LED MULTIDISCIPLINARY HARM PREVENTION 'HUDDLE' PROGRAM WITHIN AN ACUTE STROKE SERVICE

Kinsella D[1], David A[1], Eaton M[1], Lobo R[1], Chalke P[1], Fowler D[2], Hamson E[1], Cloud G[1,3]

[1] Stroke Service, Alfred Hospital; [2] Nursing Quality & Clinical Projects, Caulfield Hospital; [3] Department of Neuroscience, Central Clinical School, Monash University

Hospital-acquired complications including falls, infections, delirium, shoulder-injuries, pressure-injuries, and malnutrition are common in hospitalised acute stroke patients. Implementation of *prevention* strategies are integral for patient safety and *avoiding* catastrophic outcomes, warranting their inclusion in Australia's national stroke clinical care recommendations. Patient safety huddles have been identified as effective intervention in other settings. However, nurse-led multidisciplinary patient safety huddles addressing aggregated patient risk have not been trialled on acute stroke units. Assessing staff perceptions of implementing a patient safety huddle intervention are important as these form a strong predictor of staff engagement and longevity of successful implementation.
AIMS: To evaluate staff perceptions of a nurse-led acute stroke unit multidisciplinary patient safety huddle 'Risk Assessment and Management Plan' *(RAMP)* implementation.

METHODS: A pre-and post-trial evaluation questionnaire involving staff demographics, the modified Hospital Survey on Patient Safety Culture (mHSOPS) Likert questionnaire and open-ended questions. The multidisciplinary stroke team consisted of nursing, dietitian, occupational therapy, physiotherapy, speech pathology, allied health assistants, and medical staff.

RESULTS: From 82-questionnaire responses (pre-trial n=32, post-trial n=50), nursing was the largest professional group 67% (n=55), undergraduate degree was the highest level of education for 90% (n=74), and clinical-experience ranged from 2-months to 25-years (median3.5-years). The mHSOPS evaluated staff perception /25 in each domain pre-and post-trial; (i)implementing patient safety strategies (IPSS) (pre-14, post-19 p=<0.0001), (ii)consistent approach to assessing for IPSS (pre-14, post-19 p=<0.0001), (iii)culture of IPSS (pre-13, post-19 p=<0.0001), (iv)standardised documenting of IPSS (pre-12, post-19 p=<0.0001), (v)positive communication of IPSS (pre-12, post-19 p=<0.0001), and (vi)team work opportunity to evaluate performance (pre-12, post-19 p=<0.0001).

CONCLUSION: The results of this real-world nurse-led multidisciplinary patient safety quality improvement trial are highly encouraging. Demonstrating a significant improved patient safety culture through building capacity of multidisciplinary teamwork and IPSS completion. Further evaluation of the patient impact of RAMP on acute stroke units is now warranted.

155. UNEXPECTED DEATH AND SERIOUS PATIENT DETERIORATION IN HOSPITAL: AN EXAMINATION OF COMMUNICATION AND DECISION-MAKING IN SENTINEL EVENTS

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[1] Deakin University, [2]Alfred Health, [3] Barwon Health

BACKGROUND: Patients in acute hospitals can deteriorate unexpectedly. Prompt recognition, escalation, and treatment of deteriorating patients is necessary to ensure safe, quality care. If the signs of deterioration are missed, or appropriate treatment is delayed or foregone, adverse outcomes including critical illness, unplanned intensive care admissions, cardiac arrest, and death can ensue.

AIM: To explore evidence of antecedent events in coronial inquest transcripts of patients who died in acute hospitals after unexpected deterioration.

METHOD: Fifteen coronial inquest transcripts of patients who died in acute hospitals between 2010-2019 following unexpected deterioration were obtained from the Coroner's Court of Victoria, Australia. Narrative analysis was used to determine storylines and narrative threads.

RESULTS: Two overarching narratives were evident: 'The unexpected diagnosis' and 'making mistakes'. Incorrect diagnosis could be due to an unusual presentation of a common condition, misunderstanding of test results or symptoms, very rare conditions, or presenting symptoms that were unrelated to the core problem. Clinicians made mistakes because of communication failures, lack of education, inadequate supervision or education, cognitive bias or unmanageable workload.

CONCLUSIONS: Correctly diagnosing a patient's health problem is fundamental to successful treatment decisions, but influences on diagnostic decisions can be multifactorial and complex. Actively seeking alternative explanations for patient symptoms when new information comes to light is crucial. Meaningful partnerships with patients and family carers have been identified previously as a contributor to accurate diagnosis and management of illness. Listening carefully to the observations and concerns of patients and families, and taking them into account when diagnosing and managing illness would improve clinician understanding and accuracy. Further research exploring the use of structured communication and decision algorithms in clinical diagnosis is recommended.

156. AN EXPLORATION OF INTENSIVE CARE NURSES' PERCEPTIONS OF WORKLOAD IN EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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BACKGROUND: There is increasing use of Extracorporeal Membrane Oxygenation (ECMO) in intensive care and nurses provide the majority of the ongoing care. There is limited information from the nursing perspective around the experiences and challenges in relation to workload in the provision of ECMO care.
AIM: To investigate intensive care nurses' perceptions of workload in providing specialist ECMO care in a high-volume ECMO centre.

METHODS: The study employed a qualitative descriptive methodology through semi-structured interviews. Data were analysed using an inductive thematic analysis approach. This study was conducted at a public, quaternary, university-affiliated hospital which provides specialist state-wide service for ECMO.

RESULTS: Our study consisted of a convenience sample of 30 participants who were all critical care trained registered nurses and had completed an ECMO specific training program. The majority of nurses were female (n = 21, 70%), had >5 years ICU experience (n = 24, 80%), and cared for on average >5 ECMO patients per year (n = 29, 97%). This study identified four key themes: (1) nurses' professionalism, (2) the art and science of nursing, (3) nursing ECMO responsibilities, and (4) the importance of teamwork impacting on ICU ECMO specialist nurses' workload in an ICU led high-volume ECMO centre.

CONCLUSION: Critical care trained registered nurses are motivated and engaged to learn and acquire ECMO skills and competency as part of ongoing professional development. ECMO specialist trained nurses identified the need for advanced clinical and critical thinking skills. Providing bedside ECMO management requires constant monitoring and surveillance from nurses to care for the one of the most critically unwell patient populations in the ICU setting. ECMO nurses described the need for a suitably trained and educated workforce of critical care trained registered nurses. ECMO services provide opportunities to increase nursing scope of practice and create advance practice specialist roles.

157.A DELPHI STUDY TO OBTAIN CONSENSUS ON MEDICAL EMERGENCY TEAM (MET) STAND-DOWN DECISION MAKING

Natalie A. Kondos[1,2], Jonathan Barrett[2], Jo McDonall[1] and Tracey Bucknall[1,2]

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This Delphi study provided expert consensus to optimise MET stand-down decision-making and the ultimate decision to end a MET call. It offers clinical and MET staff a process to support handing over clinical responsibility, and clarification of management plans to reduce repeat MET calls and improve patient outcomes.

AIM: A medical emergency team (MET) stand-down decision is the decision to end a MET response and hand responsibility for the patient back to ward staff for ongoing management. Little research has explored this decision. This study aimed to obtain expert consensus on essential elements required to make optimal MET call stand-down decisions and the communication required before MET departure.

METHODS: An expert panel of ten members were recruited based on their expert knowledge and recent clinical MET responder experience in acute hospital settings. Participants were emailed a consent form and an electronic interactive PDF for each survey. Two rounds were conducted with no attrition between rounds. The CREDES guidance on conducting and reporting Delphi studies was used to report this study.

RESULTS: Consensus by an expert panel of 10 MET responders generated essential elements of MET stand-down decisions. Essential elements comprised of two steps: 1) the stand-down decision that was influenced by both the patient situation and the ward/organisational context; and 2) the communication required before actioning stand-down. Communication after the decision required both verbal discussions and written documentation to hand over patient responsibility. Specific patient information, a management plan and an escalation plan were considered essential.

CONCLUSION: The Delphi surveys reached consensus on the actions and communication required to stand down a MET call. Passing responsibility back to ward staff after a MET call requires both patient and ward safety assessments, and a clearly articulated patient plan. Observation of MET call stand-down decision-making is required to validate the essential elements.

158. THE TOP 100 CITED NURSE PRACTITIONER PUBLICATIONS: A BIBLIOMETRIC ANALYSIS

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Background: Development of the Nurse practitioner role and the specialisation of practice is an increasing focus in healthcare. To date, a bibliometric evaluation of scholarly work referring to Nurse Practitioners, has not been located in the published literature.

Objective: With the aim of identifying the top 100 cited articles in the Nurse Practitioner domain, the Scopus™ database was searched for Nurse Practitioner studies during 2007–2021. Using bibliometric analysis we identified prolific authors; annual trend; citation rates; countries of origin; study designs and journals.

Results: There were 1768 papers identified across 360 peer reviewed journals in 33 countries. The Top authors ranked by publication count, ranged from authors who had published a minimum of 10 through to 30 NP related papers. The top author was Poghosyan, et al (period 2012 - 2021) with a total of 30 papers and followed by Donald, F. et al (period 2007 – 2020) with 22 papers respectively. There were 10 Australian authors featured in the top 20 authors by publication.

Conclusions: This study affirms the existing body of knowledge within the NP domain and can enhance the future contributions in high quality health care evidence. An awareness of citation metrics and collaboration between authors, may help to enhance NP future research. Australia has the potential to be a leader, gaining research capacity within this domain, as this review has identified that 10 of the top 20 authors by publication reside in Australia.

159. THE ACUTE SCREENING OF SWALLOW IN STROKE/TIA (ASSIST) TOOL IN COMPARISON TO A SPEECH PATHOLOGY ASSESSMENT IN A COMPREHENSIVE STROKE CENTRE

Hamson E[1], Mok Z[1], Chalke P[1], McCormack S[1], Mahoney J[1], Cloud G[1,2]

[1]Stroke Service, The Alfred; [2] Department of Neuroscience, Central Clinical School, Monash University

Background: The Australian Stroke Foundation clinical guidelines strongly recommend all stroke and TIA patients have their swallow screened within four hours of admission prior to any oral medications, diet or fluids. The Acute Screening of Swallow in Stroke and Transient Ischaemic Attack (ASSIST) is a commonly used bedside nursing screening tool to determine the risk of dysphagia and resultant aspiration after stroke. It comprises of four stages of assessment; if all stages are passed, the patient can recommence their premorbid diet and oral medications. Failure at any stage deems the patient nil by mouth until a formal speech pathology assessment is completed.

Aims: To assess the positive predictive value of the ASSIST tool against gold-standard, bedside speech pathology assessment.

Methods: We retrospectively reviewed demographics, ASSIST and speech pathology assessments for all patients with a diagnosis of acute stroke admitted to The Alfred Hospital, Melbourne, Australia between April 2021 and March 2022.

Results: Of the 390 patients who had an ASSIST completed, 249/390 (64%) passed the ASSIST and commenced their pre-morbid diet. 141/390 (36%) failed the ASSIST. Of the 141 who failed the ASSIST, only 75/141 (53%) were diagnosed with dysphagia by the speech pathologist assessment. 66/141 (47%) did not have dysphagia. The positive predictive value is 53%.

Conclusion: The ASSIST may result in a prolonged period of inadvertent fasting for patients who could safely commence oral medications, a diet and fluids. Further investigation is warranted to understand the clinical utility of the ASSIST, including nurse training and inter-rater reliability. A prospective study of sensitivity and specificity using a modified ASSIST pilot tool would be the next step to improve dysphagia screening tools in acute stroke.

160. EVALUATION OF A CARE BUNDLE TO SUPPORT HEALTHCARE WORKERS WEARING N95 MASKS

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N95 masks are required to protect healthcare workers from COVID-19, however, they are known to increase the risk of facial skin injuries.

AIM: This study aims to assess adverse outcomes, staff knowledge and behaviour in relation to a care bundle, designed to prevent and manage facial skin injury in healthcare workers wearing N95 masks.

METHOD: A quasi-experimental study design was used to compare outcomes for staff who were required to wear N95 masks and had access to a care bundle at a major metropolitan health service during the COVID-19 pandemic, compared to those who did not. Staff were invited to participate in an anonymous survey.

RESULTS: The convenience sample included 758 participants and of these 31.3% accessed the care bundle. Post introduction of the care bundle, 59.8% developed facial injury compared to 72.7% who did not use the care bundle ($p = 0.03$). Of staff who accessed the care bundle, 28.7% developed acne, compared to 49.5% who did not access the care bundle ($p = 0.001$). Statistically significant improvements in uptake of prevention and treatment strategies were found in those who accessed the care bundle, compared to those who did not.

DISCUSSION: This study has demonstrated the benefits of a care bundle to support healthcare workers wearing N95 masks. The bundle improved staff knowledge and reduced minor facial skin injuries.

CONCLUSION: Ongoing COVID-19 cases necessitates that healthcare workers continue to wear N95 masks for long and indefinite periods and as such the field remains an area for future research.

161. THE NURSE-LED INTERVENTION AIMED TO OPTIMISE CARE FOR PATIENTS IN ISOLATION AT AN ACUTE HOSPITAL- A PILOT FEASIBILITY STUDY

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Isolation in a health setting has been considered the gold standard practice for many decades to reduce and prevent the spread of bacterial and viral infections. However, studies showed adverse outcomes were often associated with patients in hospital isolation. At the same time, there was limited evidence of multi-factorial interventions in practice to reduce risk and improve isolated patient outcomes in hospitals.

AIM: The primary aim was to examine the feasibility of implementing a nurse-led intervention to optimise care for patients in strict isolation at an acute hospital. Secondly, to measure anxiety, depression, loneliness, nutrition, activity, adverse events, quality of life and length of stay between the two groups.

METHODS: A non-randomised control trial design was conducted. Individuals in the control group received standard isolation care. The intervention group received twice daily visits by a registered nurse, seven days per week, in addition to their usual care. Intervention group patients were assessed for mood and physical activity, unmet needs and adverse events. Patient assessments were communicated to the nurse-in-charge and escalated to the medical team if appropriate. Data was analysed descriptively, with the difference between groups compared using a t-test for parametric and a Mann Whitney test for non-parametric data.

RESULTS: After screening 300 hospitalised patients who were in isolation, 20 patients were recruited in each group. The main reasons for patients being in isolation were droplet precaution and enteric precaution. It was feasible to provide a nurse-led intervention, with over 75% of patients' needs addressed or action facilitated by research nurses. Most unmet needs reported were comfort requests such as toiletries, water jug refills and assistance with meal orders and delivery. Patients in both groups were very inactive, with the majority of patients having a step count of less than 1000 steps per day. There were no significant differences found between groups for the secondary outcomes.

CONCLUSION: It is feasible to provide a nurse-led intervention in an acute hospital for isolated patients. The intervention group patients were pleased to have their unmet needs addressed. Future trials need to be conducted to test the effectiveness of the intervention on patient outcomes and improve patient isolation experience.

162. MULTIDISCIPLINARY EARLY ACCESS CARE MODEL TO OPTIMISE OUTCOMES IN ATRIAL FIBRILLATION MANAGEMENT.

Azzopardi S [1,2], Segan L [1,2], Warner V [3], Duong J [3], Rush L [3], Prabhu S [1,2], Kaye D [1,2], Kistler P [1,2], Patel H [1].

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Integrated care models for atrial fibrillation (AF) management reduce all-cause mortality and cardiovascular-related hospitalisations and improve adherence to guideline-directed therapies.

AIM: Establish a nurse and pharmacist-led rapid access AF (RAAF) clinic to bridge the gap from the Emergency Department (ED) to specialist service. Objectives include reduce time to specialist care, improve adherence to guideline directed anticoagulation, and enhance patient education.

METHODS: From August, 2022 - February, 2023, patients attending ED with AF were referred to the RAAF clinic for comprehensive assessment. Subsequent follow up was triaged to Arrhythmia or General Cardiology outpatient clinics. Patient satisfaction and acceptability was sought using a Net Promotor Score (NPS) metric (rating 1 to 10).

RESULTS: Fifty-three patients attended clinic (60% first presentation AF, median CHA_2DS_2-VA 1 (IQR 0-2.5)). Rhythm at clinic review was AF in 23%; all of whom proceeded to expedited Direct Current Reversion (DCR). Thirty-six patients had a CHA_2DS_2-VA ≥1, of these 27 (75%) were anticoagulated upon ED discharge and a further nine (25%) commenced anticoagulation in clinic. One third of the cohort had additional comorbidities detected. Six patients (11%) had new AF and concurrent heart failure (HF) and received HF education and guideline-directed HF pharmacotherapy. Five patients had new dyslipidaemia and four patients had Diabetes Mellitus detected on blood results ordered in clinic. Two patients were diagnosed with coronary artery disease, needing revascularization procedures. All patients received individualised education regarding AF and risk factor modification. Time to specialist care was reduced by > 80% (≈ 16 days from ≈ 102 days with standard care). Thirty-two patients completed the survey (response rate 60%) with 100% reporting an NPS promotor score of 9 or 10.

CONCLUSION: An integrated care model delivered through a nurse and pharmacist-led RAAF clinic enhanced AF management through patient education, optimising guideline-directed anticoagulation and reduced time to specialist care.

163. THE FAMILY LIAISON NURSE ROLE: STRENGTHENING FAMILY COMMUNICATION IN INTENSIVE CARE DURING COVID-19

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BACKGROUND: The visitor restrictions introduced during the COVID-19 pandemic across healthcare created challenges for family visitation and traditional communication methods. In response to these challenges the Family Liaison Nurse (FLN) role was created to provide support and information for families.
AIM: To investigate the activity of the FLN within an Intensive Care Unit (ICU) during the COVID-19 pandemic.

METHODS: We conducted a retrospective review of FLN activity for patients admitted between July 2020 and November 2022 to a tertiary ICU in Australia. Descriptive statistics were used to explain FLN activity.

RESULTS: The FLN role provided ICU coverage from Mon-Sun within normal business hours. A total of 6,536 (99%) post ICU admission contact calls to family and/or carers of 6608 patients admitted to ICU were made during the study period. The first contact call involved a mean call-time of 11.95 minutes, with the maximum call length recorded 120 minutes. Unknown patient identity, no next of kin, and FLN role sickness accounted for the missing 72 (1%) admissions.

The FLN responsibilities involved making first contact with, and recording of first contact details, clarified visitation restrictions, communication avenues, identified any issues around next of kin, and communication with the ICU nursing and medical team, regarding formal family/carer updates. For the first 12 months of the FLN role, any identified issues received a further 72-hr follow up call (n = 841) with a mean time of 8.17 minutes, however this additional workload was not sustainable with the increased ICU bed capacity and subsequent ICU admissions during the remainder of the study period.

CONCLUSION: The FLN provided an important communication role for families and carers of patients admitted to ICU during the COVID-19 pandemic. The FLN vitally helped distribute and offload workload from the ICU healthcare team involving communication and restriction updates throughout COVID-19.

164. 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 anaesthesia 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 anaesthesia 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

Reference: Wallace SKA, Bucknall TK, Myles PS. Consumer Engagement in Perioperative Clinical Trials. Anesth Analg. 2022 Nov 1;135(5):1001-1010. doi: 10.1213/ANE.0000000000006209. Epub 2022 Sep 22. PMID: 36135337..

PSYCHIATRY

165. REDUCING FALLS ON AN OLDER PERSON'S ACUTE MENTAL HEALTH INPATIENT UNIT: IMPLEMENTATION OF A FALLS RISK ROUND TO REDUCE THE NUMBER AND SEVERITY OF FALLS

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Falls among hospital inpatients are a particular risk for older adults. The older adults' mental health inpatient setting represents a nexus of factors that elevates risk for falls: including the impact of mental disorders e.g. depression, anxiety and psychosis; neurodegenerative disorders or cognitive impairment; comorbid physical health conditions such as cardiovascular disorders; and the use of psychotropic medications. This study reports on the implementation of a multidisciplinary falls risk assessment and risk management strategy, to determine if implementation reduced the number and severity of falls. The study used an audit approach to examine routinely collected falls data as well as falls responses on an older adults' acute mental health inpatient unit. The audit examined the rates, characteristics and severity of falls prior to and again following the implementation of the falls risk round in line with the recommendations of the NICE (UK) guidelines. A standard two tailed T-test was used to determine significance of change between pre-implementation and post-implementation.

The study found that the risk round resulted in a non-significant reduction in number of falls and a significant reduction in falls related harm. The biggest reduction in falls was amongst women and amongst the oldest age groups, which are the most pertinent risk factors identified in current literature. There was no effect of the risk round on improving staff adherence to the organisational guideline in regards to post-fall management. Despite a small cohort size and time period, the implementation of the falls risk round resulted in improvement in outcomes for these vulnerable older patients. Further evaluation would be beneficial to further understand the factors associated with falls risk in this particular cohort and the impact of strategies such as the falls risk round.

166. THE RELATIONSHIP BETWEEN EARLY LIFE TRAUMA AND EMPATHY IN ADULTS WITH BORDERLINE PERSONALITY DISORDER

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Borderline Personality Disorder (BPD) is a highly heterogeneous psychiatric condition that is often best characterised by interpersonal dysfunction. Though increasing empirical support has established childhood trauma as a salient trigger, a paucity of research exists specifically relating experience of trauma to BPD's social cognitive symptoms. Empathy, which involves a cognitive and affective component, functions as an ideal framework for understanding the aberrant social cognitive capacity in BPD.

Aim: The current study aims to compare cognitive and affective empathy in BPD patients and healthy controls. It will also explore the relationship between childhood trauma type/severity and empathic capacity in BPD patients.

Methods: This study analysed participant responses on the retrospective, self-report Maltreatment and Abuse Chronology of Exposure (MACE) questionnaire, in addition to performance on the computer-based Multifaceted Empathy (MET) test.

Results: A total of 70 patients with BPD and 52 healthy controls were included in the study. Preliminary results have revealed that BPD patients had poorer performance in the MET than healthy controls when inferring mental states, indicating a deficit in cognitive empathy. However, there did not seem to be a significant difference in affective empathy across the two groups. Data on early life trauma to be analysed.

Conclusion: These findings support the notion that deficits in empathy, particularly in the cognitive domain, may partially account for the turbulent interpersonal relationships associated with BPD

167. A SYSTEMATIC REVIEW OF THE FACILITATORS AND BARRIERS FOR THE IMPLEMENTATION OF CODESIGNED YOUTH SUICIDE AND SELF-HARM INTERVENTIONS.

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Background: Co-designed interventions targeting youth suicide and self-harm are starting to emerge, however, few studies discuss the barriers and facilitators for implementing such interventions.

Objective: The aim of this systematic review was to synthesise the literature regarding barriers and facilitators to the implementation of co-designed inventions for suicidal and self-harming young people.

Method: A systematic literature review was conducted in March 2023. From the 645 initial papers, a final sample of seven papers met eligibility criteria and were included in the review. Thematic analysis was used to identify barriers and facilitators to implementation in the included studies.

Results: A total of four barriers were identified (team member burden, lack of team communication and support, mismatch between co-design outcomes and implementation factors and COVID-19) and three facilitators were identified (effective team structures, co-design promoted intervention implementation and flexible delivery approaches).

Conclusion: Co-design is increasingly being used to develop tailored interventions to address suicide and self-harm in young people, but evaluation of the implementation of these interventions remains limited. This study has identified a range of factors such as clear communication, training, support, adaptability, and flexibility which may act as facilitators or barriers to the implementation of co-designed interventions. Awareness of these factors may improve intervention implementation in the future.

168.MEMANTINE – A NOVEL TREATMENT FOR BORDERLINE PERSONALITY DISORDER

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Borderline Personality Disorder (BPD) is a highly prevalent and complex psychiatric illness. The neurobiological pathophysiology of BPD is related to chronic stress-inducing glutamate dysregulation and overactivity. Therefore, a treatment capable of regulating glutamate excitotoxity would be promising. Memantine is an uncompetitive, low-affinity glutaminergic N-methyl-D-aspartate (NMDA) receptor antagonist that selectively blocks excessive NMDA receptor activation.

AIM: To determine if memantine can improve BPD symptoms.

METHODS: This 12-week, double-blind, placebo-controlled trial of adjunctive memantine recruited adults with BPD from 2017 to 2022. Participants were randomly assigned to receive placebo or daily oral memantine 10mg for 7 days, with subsequent titration to daily oral memantine 20mg. The primary outcomes included Zanarini Rating Scale for Borderline Personality Disorder and the Borderline Evaluation of Severity over Time (BEST). The secondary outcomes included the Borderline Personality Disorder Severity Index, fourth edition (BPDSI-IV) and Cogstate. Primary outcome assessments were done at weeks 0, 2, 4, 6, 8, 10, 12, while the secondary outcomes assessments were done at weeks 0 and 12.

RESULTS: Of 114 included participants, 99 received the intervention and were included in intent-to-treat analyses; of these, 86 (86.9%) were female, and the mean (SD) age was 33.7(11.2) years. 56 participants were randomised to memantine and 43 to placebo. Significant longitudinal improvement was found on 'affective' subscale in ZANBPD, 'thoughts and feelings' and 'total score' in BEST, and 'affective instability' in BPDSI-IV in both memantine and placebo. A significant improvement was found in the memantine group only on the 'cognitive and disturbed relationship' subscales, as well as 'total score' in the ZAN-BPD; 'negative behaviours' in BEST; and 'abandonment' and 'total score' in BPDSI-IV. No serious adverse event was found.

CONCLUSION: Memantine is a well-tolerated drug that can improve BPD symptoms. It is a promising novel treatment for BPD as it targets glutamate dysregulation.

169.THETA BURST STIMULATION IMPROVES PREMENSTRUAL DYSPHORIC DISORDER SYMPTOMS: A PILOT STUDY

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Premenstrual Dysphoric Disorder (PMDD) is a depressive disorder that occurs in a cyclical pattern due to hormonal changes in the menstrual cycle, with symptoms most severe during the premenstrual phase. Existing treatments provide no or only partial symptomatic relief, highlighting the clear need for effective and safe treatment. Brain stimulation, specifically theta burst stimulation (TBS), has demonstrated efficacy in treating depression, and may be a promising approach to treating PMDD mood symptoms.

AIM: To evaluate the effectiveness of prolonged intermittent TBS (piTBS) for treating mood and other psychological symptoms in PMDD.

METHODS: Eight participants completed the Daily Record of Severity of Problems (DRSP), a measure of daily PMDD symptoms, every day for a three-month period. Months 1 and 2 were defined as the pre-treatment phase. At the start of Month 3, the treatment phase, participants received 10-minute sessions of piTBS over 5 continuous days while in the premenstrual phase (determined by an ovulation test). Stimulation intensity was at 120% of the individual's calibrated resting motor threshold. Percentage elevation (i.e. symptom elevation during premenstrual compared to postmenstrual phase) was calculated using by (premenstrual DRSP-postmenstrual DRSP)/range of scale x 100.

RESULTS: There was a marked decrease in total DRSP mean percentage elevation from pre-treatment to treatment phase (20.26% to 10.10%). Looking at the different DRSP symptom domains, there was a decrease in mean percentage elevation from pre-treatment to treatment phase across all domains; depression (19.60% to 8.11%), anxiety (13.26% to 3.05%), mood lability (25.23% to 13.45%), anger (20.19% to 10.49%), interest (24.83% to 13.67%), concentration (22.90% to 11.10%), lethargy (25.25% to 7.92%), appetite (24.50% to 12.97%), sleep (25.01% to 4.48%), overwhelmed (13.22% to 8.61%) and physical symptoms (16.05% to 12.99%).

CONCLUSION: These preliminary findings demonstrate that piTBS improves symptoms during the premenstrual phase, and is a promising treatment for PMDD patients.

170. BEHAVIOURS OF CONCERNS (BOC): RAPID MENTAL HEALTH ASSESSMENT IN THE EMERGENCY DEPARTMENT. FIRST HAND CLIENT EXPERIENCES.

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Alfred Health introduced the BOC (Behaviours of Concern) callout system in 2017, a paging system that alerts multiple emergency department clinicians to patient presentations that may pose some risk towards staff or the clients themselves due to behavioural disturbances. When a callout is activated, the client is taken to the BOC annex for the assessment and management of behaviours of concern (BOC) in the Emergency Department. The client is attended by a member of the emergency psychiatry team, the ED medical officer, the west wing RN, the security team, and the nurse in charge of the ED (resource nurse). This enables a swift assessment of the clients' needs and the development of a suitable plan of care during their stay in the ED.

BOC may refer to any behaviour of a verbal, physical, psychological, or sexual nature in clinical settings in which staff are at risk from threatening, abusive, or assaultive behaviour arising out of, or in the course of their employment. Commonly used terminology to describe BOC in local guidelines and the broader literature is 'clinical aggression' or 'acute behavioural disturbance,' which can be defined as a behavioural syndrome with the potential to escalate to dangerous behaviour and violence. It is characterized by a variety of symptoms, including excessive motor or verbal activity, irritability, uncooperativeness, vocal outbursts, and threatening gestures. As a precaution, patients presenting via police under Section 232 of the Mental Health and Wellbeing Act 2022 are initially assessed in the BOC Assessment Room.

The purpose of this research is to explore the experiences of consumers managed by Alfred Health's BOC process to develop an understanding that enhances the ability to improve standards of care in alignment with the Mental Health and Wellbeing Act 2022. The project aims to evaluate the experiences of consumers whose mental health was initially managed in the Alfred Health BOC Annex/Assessment Room. It will seek additional insight into areas that could be improved in the BOC process and explore potential alternative management strategies to enhance their outcomes and minimise unintentional harm.

The primary goal of this research is to promote and lead reform in the provision of mental health and wellbeing services, with a consumer-focused approach that enhances and removes barriers to seeking mental health services.
Data collection will aim to obtain this information via self-reporting surveys posted to identified clients or delivered to them by their community team case manager, with the aim of including up to 30 clients experience relating to the BOC process.

171.CLOZAPINE SAFETY IN PREGNANCY – A CLINICAL STUDY

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Aim: To evaluate obstetric and neonatal outcomes of a cohort of Australian perinatal patients diagnosed with psychotic disorders and treated with clozapine.

Method: The National Register of Antipsychotic Medication in Pregnancy (NRAMP) is the first global prospective observational study collecting data about antipsychotic medication use in pregnancy. Pregnant women (n=14) prescribed clozapine who were enrolled in NRAMP from its inception in 2005 to 2019 were compared with two NRAMP subsamples of pregnant women: medication-free group (n=24) and quetiapine-treated group (n=53). Primary and secondary outcomes included neonatal outcomes, maternal gestational diabetes assessment and obstetric outcomes.

Results: More miscarriages were found in the clozapine group (n=3; 21.4%), compared to the quetiapine (n=1; 2.1%) or drug-free groups (n=0; 0%). The early pregnancy BMI (32.36±5.94) was higher in the clozapine group than in medication-free (25.55±4.85) and quetiapine-treated (28.65±6.93) group with a significant p value (< 0.01). The overall weight gain through pregnancy was lower in clozapine group (10.36kg±6.48kg) than in the groups of medication-free (17.73kg±9.49kg) and quetiapine-treated (16.34kg ± 9.4kg). The diagnosis of gestational diabetes in the clozapine group was significantly higher compared to other groups (OR = 1.67; 95% CI, 1.32 to 2.10; p < 0.001). 72.7% of clozapine-exposed babies were admitted to an SCN/NICU compared to 45.5% quetiapine-exposed babies and 60.9% babies in the no-medication group. The baby birth weight was significant lower (3177.27g±458.76g) in clozapine exposed babies than in no-drug group (3317.21g±804.29g) and quetiapine exposed group (3452.60g±561.48g). Neonatal gestational age, birth weight, and Apgar scores were comparative between the groups without any significant differences.

Conclusion: Women of childbearing age with schizophrenia-spectrum disorders are at increased risk of a number of adverse pregnancy outcomes. Clozapine might be associated with a greater risk of certain adverse outcomes for both mother and baby, including gestational diabetes mellitus, and SCN/NICU admission.

172.COMMUNITY MENTAL HEALTH NURSE TRANSITION TO SPECIALITY PRACTICE FRAMEWORK: THE BENEFITS AND BARRIERS IN THE FRAMEWORK IMPLEMENTATION.

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There is a growing focus in Australian policy of providing mental health care in a community setting. A key feature of the Royal Commission into Victoria's mental health system tabled in Parliament 2021, was to prioritise community-based care "a system with community at its core". Developing a skilled, flexible and competent nursing workforce is a key objective for any community based mental health service as nurses provide a vital role in health care delivery.

The three-year comprehensive nursing qualification has little to no mental health curriculum leaving nursing graduates unprepared for work in mental health, while hospital-based training for graduate nurses doesn't prepare them for the realities of community-based work. Significant work has been undertaken in Victoria to develop, refine and implement a competency framework for transition from acute inpatient settings into community-based services.

AIM: To better understand the effectiveness of this framework in preparing nurses for the community workforce, as well as the barriers and enablers of implementation.

METHOD: A qualitative method investigated experiences of AMAH staff who had participated in the transition program in either aged, adult or a homeless outreach team. Interviews were conducted with transition nurses (n=5), mentors(n=4), Clinical managers(n=3) educators/coordinator(n=2).

RESULTS: The framework structure helped mitigate role stress, allowed for consolidation of theory into practice providing learning opportunities, provided clinical oversight for safe practice, supported autonomous practice, critical thinking, staff wellbeing and demonstrated positive outcomes for consumers and carers. It also had a positive impact on retention and recruitment. Whilst there were limited barriers, the framework implementation relied on organisational support with staff resourcing.

CONCLUSION: Evaluation findings demonstrate the importance of this framework. This structured program helped facilitate professional development with an integration of knowledge, skills, attitudes and confidence along with staff wellbeing, leading to enhanced clinical practice and outcomes for clients and carers.

173. TAKE HOME NALOXONE PROVISION AT A MAJOR METROPOLITAN HOSPITAL: EVALUATING GAPS IN ACCESS

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An increasing rate of opioid-related harm has demanded focus on harm reduction strategies including Take-Home Naloxone (THN) provision following hospitalisation.

Aim: To identify gaps in provision of THN in the emergency department (ED) and inpatient wards at a metropolitan tertiary referral healthcare organisation prior to implementation of a Commonwealth THN program.

Methods: A retrospective audit of naloxone provision on discharge for January-December 2022 was undertaken. Potentially eligible patients were identified using ICD10-AM coding for opioid-misuse disorder diagnosis, opioid overdose in the 30 days prior to presentation or current opioid replacement therapy (ORT). Naloxone provision at discharge was identified. For data verification, results were compared to prescribing, dispensing and automated dispensing machine records.

Results: There were 302 patients who met eligibility criteria, median age 43years (IQR 32-52), 179 (59.3%) were male. Forty (13.2%) patients received THN (22 prescriptions for community dispensing, 18 dispensed naloxone products). Of patients eligible for THN, 240 had active opioid-misuse disorder (39 received THN), 137 recent opioid overdose (17 received THN) and 113 on ORT (22 received THN). Using ICD10-AM coding alone identified a significantly higher proportion of inpatients receiving THN than from ED (21.1% vs 5.8%, p<0.0001). Potential contributing factors for low provision among ED patients were the short length of stay (ave. 7.8 hours), discharge against medical advice (DAMA) (9%) and discharge outside pharmacist working hours (31%). Inpatient factors included DAMA (7.5%), and discharge to another facility (14.8%). Data validation identified THN provision to a total of 126 cases, (indicating that 86 (68.3%) cases of THN provision were not coded for eligible conditions.

Discussion: Naloxone provision on discharge was underutilised prior to implementation of the Commonwealth THN program in March 2023. Challenges exist in identifying eligible patients using ICD-10AM coding. Further research is required to determine barriers and enablers for THN provision.

RESPIRATORY

174. ADULT WARD OXYGEN GUIDANCE IN AUSTRALIAN HOSPITALS

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Introduction/Aim: Conventional oxygen therapy (COT) is used routinely in adult ward acute hypoxaemic respiratory failure management. We aimed to review COT guidance documents used in Australian hospitals, to identify any variations and to generate standardised core recommendations to support implementation.
Methods: A systematic review of hospitals COT guidelines, protocols, procedures and policies for use in adult inpatients were identified via the PROMPT database and other networks. Data extracted included initiation, maintenance, weaning, escalation and processes of care.

Results: Of the 17,331 documents identified, 37 were included; 36 Victorian hospitals (97.3%), 21 (56.7%) rural, 9 (24.3%) regional, and 7 (18.9%) metropolitan. Majority focused on medical wards (n=36, 97.3%). TSANZ acute oxygen guidelines were referenced infrequently (n=11, 29.7%). Pulse oximetry (n=23, 62.2%) was recommended more often than arterial blood gas (ABG) (n=13, 35.1%) for assessing hypoxaemia. None required an ABG prior to COT initiation

(n=37, 100%), 3 (8.1%) documents recommended ABG be performed to monitor COT use. Oxygen saturation (SpO2) targets for initiation and maintenance was common (n=29, 78.4%), 6 (16.2%) did not specify a SpO2 value to define hypoxaemia. Medical staff were most often recommended to prescribe COT (n=21, 56.7%), followed by nurses (n=14, 37.8%) and physiotherapists (n=4, 10.8%). Guidance on monitoring and up titration occurred frequently (n=29, 78.3%), however, 15 (40.5%) documents did not specify criteria for clinical review and weaning guidance was rarely included (n=9, 24.3%). A system to detect patient deterioration was often stated (n=19, 51.3%), commonly MET criteria (n=17, 45.9%). Documentation guidance of COT delivery systems and vital signs components, including frequency was high variable.

Conclusion: Australian health services COT guidance contained substantial variation in recommendations of process of care. Implementation of standardised core recommendations may assist clinical decision making across health services, and lead to reduction in variations of care and improved patient safety and outcomes.

175.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 CLAD development prior to the irreversible decline in lung function.

METHODS: We performed untargeted metabolomics, lipidomics and bulk transcriptomics on longitudinal broncho-alveolar lavages (BAL) from 13 CLAD and 16 CLAD-free lung transplant recipients over the first 30 months post-transplant.

RESULTS: Prior to a diagnosis, CLAD patients had significantly increased vascular endothelial barrier dysfunction, neutrophil recruitment and altered metabolism of ceramides and carboxylic acids (FDR < 0.05). Importantly, metabolites and lipids were already differentially expressed (DE) at 3 months post-transplant (FDR < 0.05), prior to any decline in lung function. DE metabolites, lipids and genes were further correlated with neutrophil levels in the BAL (Pearson, r > 0.3, adj-p < 0.05), but not with peripheral blood neutrophils, indicating CLAD-associated signatures to be exclusive to immune responses within the allograft. Application of a machine learning model trained on all DE features predicted CLAD onset as early as the first 2 months post-transplant (ROC = 0.85), and consistently thereafter until a CLAD diagnosis (ROC = 0.83).

CONCLUSION: We have identified important key immunological processes that underlie CLAD development, and metabolites, lipids and genes able to predict CLAD prior to its clinical manifestation. 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.

176.INNATE IMMUNE CELLS DRIVE CHRONIC INFLAMMATORY LUNG DISEASE THROUGH IL-17A SIGNALLING

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INTRODUCTION: Chronic Obstructive Pulmonary Disease (COPD) is a heterogenous, progressive lung disease presenting with pulmonary inflammation, chronic bronchitis and emphysema. It is the third leading cause of death worldwide and existing treatments only manage the symptoms or slow progression, therefore further insights into its mechanisms are needed.

AIM: To use a novel COPD mouse model called the $Hck^{F/F}$ mouse to explore the cellular and molecular mechanisms of lung disease.

METHODS: $Hck^{F/F}$ mice spontaneously develop lung inflammation, mucus overproduction (chronic bronchitis) and alveolar destruction (emphysema), mimicking COPD. Lung disease was investigated through assessing lung pathology by histological staining, immune cell mediators by flow cytometry and inflammatory genes by qPCR.

RESULTS: Increased myeloid cells and neutrophils was observed in the lungs of $Hck^{F/F}$ mice, correlating with increased levels of the neutrophilic growth factor, G-CSF in the lung. IL-17A, a pro-inflammatory cytokine which is a potent inducer of G-CSF production, was examined and found to be upregulated and secreted by innate IL-17A-producing gamma delta (γδ) T cells. γδ T cells were hypothesised to be drivers of disease and a genetic deletion of γδ cells from $Hck^{F/F}$ mice was performed. Interestingly, deletion of γδ cells did not reduce lung disease. Instead, a niche-filling effect occurred, with innate IL-17A-producing MAIT cells expanding in the absence of γδ T cells in the lungs, driving disease. Lastly, a genetic deletion of IL-17A from $Hck^{F/F}$ mice was performed and this ablated COPD-like lung disease, indicating that IL-17A is a key mediator of disease.

CONCLUSION: IL-17A, alongside G-CSF may be attractive therapeutic targets for the treatment of COPD patients with more neutrophilic lung disease. Furthermore, targeting specific immune cells themselves may be not effective for reducing disease as other cell types can compensate to produce inflammatory molecules.

177. SINGING FOR BREATHING IN COPD AND ILD PATIENTS: QUALITATIVE LONGITUDINAL INTERVIEW STUDY

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Introduction: In response to COVID-19, singing for lung health programs have transitioned from in person to online delivery in order to facilitate participation. However, there remains insufficient evidence regarding the accessibility and effectiveness of these online singing programs for participants. "SINFONIA: A clinical trial examining the benefits of SingINg For breathing in COPD aNd ILD pAtients" was undertaken in Melbourne using this novel online approach.

Aim and Methods: Qualitative longitudinal interviews were undertaken to determine the attitudes and knowledge of people with chronic obstructive pulmonary disease or interstitial lung disease and their carers regarding SINFONIA to understand how such views may change over time, alongside any barriers and enablers to participating online. Qualitative data was extracted and analysed, which generated descriptive and analytical themes.

Results: Themes identified from 43 patient and six carer interviews consisted of anticipation and reluctance to participate; mastery of condition; the power of music; group singing and social dynamics; delivery of SINFONIA. The themes were categorised into three time points to examine participants' perspectives before, during and after the singing program. Over time participants transitioned from anxiety to mastery of their chronic condition with progression of the singing program. In addition to their engagement with music, participants were also able to share their knowledge and experiences with others who have similar CRDs and symptoms.

Conclusion: The findings from this study indicate that participants, including those who were technologically challenged but received support, were able to experience psychological, social and health benefits from the online singing program. Future work should involve people with advanced CRD in the design and development of singing for lung health programs to gain further insight into the acceptability and feasibility to inform broader implementation of the intervention.

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Competing interests: None declared.

178. NEBULISED GM-CSF IN AUTOIMMUNE PULMONARY ALVEOLAR PROTEINOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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Background: Autoimmune Pulmonary Alveolar Proteinosis (aPAP) results from impaired macrophage mediated clearance of alveolar surfactant lipoproteins. Whole lung lavage has been first line treatment although recent reports suggest efficacy of nebulised GM-CSF. We aimed to review efficacy and safety of nebulised GM-CSF in aPAP.

Methods: We conducted a systematic review and meta-analysis searching EmBase, CINAHL, MEDLINE and Cochrane Collaborative databases (1946 - 1st April 2022). Studies included patients aged >18 years with aPAP receiving nebulised GM-CSF treatment and a comparator cohort. Exclusion criteria included secondary or congenital PAP; GM-CSF allergy; active infection or other serious medical conditions. The protocol was prospectively registered with PROSPERO (CRD42021231328). Outcomes assessed were St George's Respiratory Questionnaire (SGRQ), 6-minute walk test, gas exchange (DLCO% predicted) and arterial-alveolar oxygen gradient (A-a gradient).

Results: Six studies were identified for review and 3 for meta-analysis revealing SGRQ (Mean Difference -8.1 (-11.9—4.3) p<0.0001), functional capacity (6-minute walk test) (MD 21.72 (-2.8-46.2) p=0.08), gas diffusion (DLCO % predicted) (MD 5.09 (2.1-8.1) p=0.001), and arterial-alveolar gradient (MD -4.36(-7.2- -1.5) p=0.003) all significantly improved in GM-CSF treated patients with minor statistical heterogeneity (I2=0%). No serious trial-related adverse events were reported.

Conclusions: Patients with aPAP treated with inhaled GM-CSF demonstrated significant improvements in symptoms, dyspnoea scores, lung function, gas exchange, and radiology indices after treatment with nebulised GM-CSF of varying duration. There is an important need to review comparative effectiveness and patient choice in key clinical outcomes between the current standard of care, whole lung lavage with the non-invasive treatment of nebulised GM-CSF in aPAP.

179. EFFECT OF PULMONARY REHABILITATION ON EXERCISE CAPACITY, DYSPNEA, FATIGUE AND PERIPHERAL MUSCLE STRENGTH IN PATIENTS WITH POST-COVID-19 SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: There is a lack of high-level of evidence on the effect of Pulmonary Rehabilitation (PR) on symptoms and physical function in post-COVID-19 patients and which is the most effective delivery modality and duration of PR to achieve results.
Objective: To establish the effects of pulmonary rehabilitation (PR) in patients with persistent symptoms following COVID-19 infection. In addition, to compare the modalities of PR services (face-to-face and telerehabilitation) and the duration of PR in weeks (≤8 weeks and >8 weeks).

Methods: This systematic review and meta-analysis was conducted following the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.

Results: The literature search retrieved 1,406 articles, of which seven studies explored the effects of PR on patients with post-COVID-19 syndrome, with 188 patients randomised to PR. The mean age of participants was 50 years and 49% were female. Meta-analysis showed an increase in exercise capacity with PR compared to control (six-minute walking test: Mean difference: 60.56 m, 95% confidence interval: 40.75 to 80.36), a reduction in fatigue (Fatigue Severity Scale: -0.90, -1.49 to -0.31) but no change in dyspnea (-0.57, -1.32 to 0.17) and muscle strength (3.03, -1.89 to 7.96). There were no differences between telerehabilitation and face-to-face PR regarding effects on peripheral muscle strength (p=0.42), dyspnea (p=0.83) and fatigue (p=0.34). There were no differences between programs ≤8 weeks and >8 weeks regarding exercise capacity (p=0.83), peripheral muscle strength (p=0.42), and dyspnea (p=0.76).

Conclusions: PR improves exercise capacity and reduces fatigue in patients with post-COVID-19 syndrome. Telerehabilitation programs have similar outcomes to face-to-face programs, with 4-8 week programs showing similar outcomes to longer programs.

Key Words: COVID-19, Pulmonary rehabilitation; Telerehabilitation; Exercise capacity; Dyspnea; Fatigue; Peripheral muscle strength.

The review was registered with PROSPERO (CRD42022310788).

180.ARE SpO2 RECORDINGS FROM TWO OXIMETERS ON THE SAME HAND OF A PARTICIPANT DURING AN OVERNIGHT SLEEP STUDY SIGNIFICANT?

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Accurate non-invasive oxygen saturation (SpO_2) measurement is crucial in healthcare, however is challenged by numerous devices using variable algorithms[1]. We compared two commonly used oximeter devices worn simultaneously in patients during an overnight polysomnogram.

Aim: To assess (1) differences between two SpO_2 recording devices and (2) SpO_2 accuracy against SaO_2.

Methods: SpO_2 data of two devices were recorded, downloaded and analysed with corresponding software: device 1 (Rad7 [Masimo, Irvine, CA, USA] set at 2-4sec averaging time) with software 1 (PSG 4 [Compumedics, Melbourne, Australia]) and device 2 (Wrist-Ox2® [Nonin Medical Inc, Plymouth, MN, USA] set at 3 sec averaging time) with software 2 (Noxturnal [Nox Medical Inc, Reykjavik, Iceland]). Responsiveness of each oximeter to changes in the patients' desaturations associated with apnoeas and hypopnoeas overnight was assessed. In addition, both device SpO_2 values were compared with SaO_2 from simultaneous arterial blood gas sampling.

Preliminary Results: 7 patients (age 56.4±7.1 years, BMI 31.6±2.2 kg/m^2, 100% male, 87% light skinned) were studied. The mean SpO_2 with RAD7 was higher than the Nonin (95.9±1.6 vs 94.2±1.4%, mean difference 1.6±1.0%). Differences in the responsiveness of the oximeters during overnight desaturations were also observed. However, both device SpO_2 values were found to be within ±2% of SaO_2.

Conclusions: Discrepancies in SpO_2 measurement do occur between devices and may have important clinical implications especially when it comes to the measurement of hypoxemic burden during sleep.

1. *Blanchet MA et al. Accuracy of Multiple Pulse Oximeters in Stable Critically Ill Patients. Respir Care. 2023 May;68(5):565-574.*

181. LONGITUDINAL IMMUNOPHENOTYPING OF CLAD+ LUNG TRANSPLANT PATIENTS SHOWS BROAD CHANGES IN B CELLS OVER TIME

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Lung transplantation (LTx) survival outcomes are impeded by chronic lung allograft dysfunction (CLAD), occurring in approximately 50% of recipients by 5 years post-LTx. CLAD is diagnosed once recipient pulmonary function has begun to decline and the graft is already failing. As such, there is a need to identify early biomarkers of the disease.

AIM: To study peripheral lymphocytes and identify early biomarkers of CLAD in LTx recipients.

METHODS: We present a prospective longitudinal study of B and T cells from the blood of LTx performed at the Alfred Hospital (Australia). LTx recipients were monitored for CLAD development out to 3 years from transplant and a total of 39 LTx recipients (CLAD-free n=26; CLAD+ n=13) were analysed and peripheral lymphocytes were compared across several time points from pre-LTx to 12 months post-LTx.

RESULTS: CLAD+ recipients had significantly ($p < 0.05$) lower total B cell counts (mean=53.3, 95%CI:29.2-77.5) compared to CLAD-free individuals (mean=204.2, 95%CI:142.7-265.8) at pre-LTx. Early post-LTx, CLAD+ recipient B cell count remained significantly lower than their CLAD-free counterparts, with this difference peaking at 1.5-months post-LTx (CLAD+ 102.8, 95%CI:52.1-153.4; CLAD-free 257.7, 95%CI:172.8-342.7; $p < 0.01$). By 6 months post-LTx, the B cell counts of CLAD-free recipients began to decline with no significant difference in counts between the groups out to 12 months post-LTx. Sub-setting of the B cell compartment revealed that this difference in B cells was specifically driven by a lack of naïve B cells.

CONCLUSIONS: This study is the first of its kind and shows low B cell counts prior to and early post-LTx may be associated with CLAD development by 3 years post-LTx. Measurement of B cells may have utility as prognostic biomarkers of eventual CLAD development. This study suggests that B cells may be key participants in long-term LTx survival.