ABSTRACT BOOK

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CONTENTS

POPULATION HEALTH AND EPIDEMIOLOGY 60

ALLERGY, ASTHMA AND IMMUNITY

1. FUNCTIONAL EVALUATION OF COMMON NOD2 GENE VARIANTS IN PATIENTS WITH ANTIBODY DEFICIENCY AND GASTROINTESTINAL COMPLICATIONS

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Background: Predominantly antibody deficiency (PAD) is the most common inherited immunodeficiency and presumed to be caused by rare genetic mutations. Despite genomic advances, >70% remain genetically undiagnosed. Approximately 20% of PAD patients suffer from gastrointestinal disease. Common genetic variants (minor allele frequency >1%) in the *NOD2* gene (R702W, G908R, and L1007fsX1008) are the three major risk alleles for gastrointestinal disease. NOD2 is a pattern recognition receptor that recognises peptidoglycan fragment muramyl dipeptide (MDP) and is critical for defence against bacteria. In this study, we examined whether *NOD2* variants are associated with PAD and whether these impact on NOD2 function.

Methods: Carriership for three *NOD2* variants (R702W, G908R, and L1007fsX1008) was determined in 75 PAD patients from whole exome sequencing data, and using Sanger sequencing in 75 healthy adult controls. NOD2 function was determined through *in vitro* stimulation of peripheral blood mononuclear cells with L18-MDP and detection of intracellular TNFα by flow cytometry. Stimulation with LPS and media only were used as positive and negative controls, respectively.

Results: The R702W variants was detected in 8 controls and 8 patients, G908R in 2 controls and 1 patient, L1007fsX1008 in 2 patients. No homozygotes were detected. Monocytes from healthy adults with and without the R702W showed similar TNFα production (medians)(P=0.43) in L18-MDP-induced TNFα production in individuals with or without R702W.

Conclusion: Our PAD cohort did not display increased presence of *NOD2* variants. The R702W does not impact on NOD2 function in healthy controls. In ongoing studies, NOD2 signalling will be examined in PAD patients with the R702W and L1007fsX1008 variants. This will give new insights into the functional consequences of *NOD2* variants and their association with gastrointestinal disease in PAD. If an effect is confirmed, this would provide a rationale for the use of anti-TNF therapies in these patients.

2. INCREASED BASAL AND INDUCED PHOSPHOINSITOL-3-KINASE SIGNALLING IN B- AND T-CELLS OF HEALTHY ADULTS CARRYING THE PTPN22 R620W MUTATIONS

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Background: The non-synonymous common variant c.1858C>T (p.R620W) in *PTPN22* is a risk variant for autoimmunity. Furthermore, prevalence is higher in patients with predominantly antibody deficiency (PAD), a primary immunodeficiency with increased incidence of autoimmunity. PTPN22 is a phosphatase that restricts signal transduction downstream of B- and T-cell receptors. Whether this mutation enhances or impairs PTPN22 function is currently disputed. Here, we addressed this by studying phosphoinositol-3-kinase (PI3K) signalling in B- and T-cells from healthy adults with and without the c.1858C>T variant.

Methods: Peripheral blood was collected from 63 healthy adults for Sanger sequencing for *PTPN22* c.1858C>T variant identification, detailed B- and T-cell immunophenotyping, and *in vitro* stimulation of antigen receptor signalling for S6 phosphorylation.

Results: 6/63 healthy controls were heterozygous for *PTPN22* c.1858C>T, at an allele frequency of 4.8%. Heterozygous carriers had significantly higher CD27+IgM+IgD+ B-cell numbers. Carriers expressed higher CD19 and lower CD21 levels on transitional and naïve-mature B-cells, and higher CD8 levels on cytotoxic T-cells. Additionally, their naïve B-, CD4+ and CD8+ T-cells exhibited higher basal phosphorylated-S6 levels. Finally, antigen receptor stimulation resulted in higher phospho-S6 levels in B-cells (anti-IgM) and T-cells (anti-CD3) compared to individuals without the variant.

Conclusion: Here, we showed for the first time that PTPN22 R620W results in increased PI3K signalling in B- and T-cells, demonstrating that the mutation inhibits the repressive function of PTPN22. PI3K signalling in lymphocytes is tightly balanced with increased activity resulting from *PIK3CD* and *PIK3R1* mutations leading to antibody deficiency and autoimmunity. Our results indicate that this variant has similar effects but to a milder degree, which would explain the predisposition to autoimmunity. Thus, a common variant can directly impact an individual's immune profile. Future studies, will address the functional consequences of this variant in PAD patients and whether this functions as a first genetic hit for developing disease.

3. DURABILITY OF B-CELL MEMORY TO SARS-COV-2 INFECTION AND VACCINATION

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Background: Lasting immunity following SARS-CoV-2 infection or vaccination is questioned because serum antibodies decline in convalescence. However, functional immunity is mediated by long-lived memory T and B (Bmem) cells, which we hypothesise are more accurate markers of long-term immunity.

Objective: To determine the immunophenotype and durability of SARS-CoV-2-specific Bmem cells in individuals after infection or vaccination for SARS-CoV-2.

Methods: Recombinant Spike receptor binding domain (RBD) and Nucleocapsid (NCP) proteins were produced for ELISA-based serology, and biotinylated for fluorescent tetramer formation to identify SARS-CoV-2-specific Bmem cells by flow cytometry. Cells were obtained from 29 convalescent patients and repeat samples were taken from individuals up to one-year post-infection. In addition, samples were collected from healthy adults immunised with the Pfizer mRNA (n=32) and AstraZeneca vector (n=37) SARS-CoV-2 vaccines at three time points: pre-vaccination, 1-month post-prime and 1-month post-boost.

Results: All recovered COVID-19 patients had serum IgG that specifically recognised recombinant RBD and NCP proteins, with levels declining beyond 20 days post-infection. Vaccination induced anti-RBD antibodies, which were increased after boost, whereas no anti-NCP antibodies were formed. In recovered COVID-19 patients, RBD- and NCP-specific Bmem cell numbers peaked after 50 days and remained stable at 1.25-170 cells/ml of blood (0.008-0.1% of total B cells) in all patients for >240 days post-infection. RBD- and NCP-specific Bmem cells predominantly expressed IgM or IgG1.

Conclusion: Detailed immune profiling revealed durable RBD- and NCP-specific Bmem cells in COVID-19 convalescent individuals. We will now quantify the serological and antigen-specific Bmem cell response in vaccinated individuals. This will allow us to compare the generation of durable immunological memory between natural infection and vaccination, as well as between mRNA and vector-based SARS-CoV-2 vaccinations. This could inform on the need for future booster vaccinations and levels of protection to emerging variants of concern.

4. IDENTIFYING RESPONDERS TO HOME AND HOSPITAL-BASED PULMONARY REHABILITATION IN PEOPLE WITH COPD: ANALYSIS FROM THE HOMEBASE TRIAL

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Introduction/Aim: Studies suggest that people with COPD gain similar improvements in exercise capacity and health-related quality of life following home and hospital-based pulmonary rehabilitation (PR). However, the proportion of participants who achieved clinically significant gains with each model has not been reported. The aim of this analysis was to compare the proportion of responders achieving clinically significant improvements in home and hospital-based PR, using data from a randomised controlled trial.

Methods: The numbers of home and hospital-based PR responders who achieved the minimal clinically important difference (MID) for changes in the 6-minute walk test (6MWT) and chronic respiratory disease questionnaire (CRQ) total score at end rehabilitation and 12 months later were compared using chi-square tests. Binary logistic regression was used to detect predictors of responders for 6MWT and CRQ including location of PR (home vs hospital), participant demographics and baseline performance.

Results: 166 participants were included (80 Hospital, mean±SD age 68±11years, FEV_1 50±19%predicted). Responders rates for 6MWT were 41% of total participants at end rehabilitation and 37% at 12 months. No between-group difference was found in numbers of responders for 6MWT at end rehabilitation (Home n=32(46%) vs Hospital 26(37%),p=0.24) or at 12 months (Home 19(35%) vs Hospital 22(39%),p=0.71). CRQ responders were 48% of participants at end rehabilitation and 44% at 12 months. Responders for CRQ were similar at end rehabilitation (Home 40(56%) vs Hospital 33(42%),p=0.11) and at 12 months (Home 28(45%) vs Hospital 26(43%),p=0.78).

Lower mMRC score at baseline was identified as a predictor for achieving MID for 6MWT at end rehabilitation with an odds ratio 0.48 (95%CI 0.27-0.79). No other predictors of response were detected.

Conclusion: Similar numbers of responders to home and hospital-based PR were identified. A large proportion of participants were non-responders to PR, and it is challenging to predict responders to PR for either model.

5. NEBULISED SARGRAMOSTIM IN PULMONARY ALVEOLAR PROTEINOSIS

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BACKGROUND: Pulmonary alveolar proteinosis (PAP) is a rare diffuse respiratory condition, characterised by accumulation of surfactant apoproteins within distal air spaces. Traditional treatment has been restricted to whole lung lavage (WLL), but in recent years, minimally invasive nebulised treatment has become available.

AIM: To evaluate the safety and effects of nebulised sargramostim (GM-CSF) treatment on exercise capacity, pulmonary function, and radiographic imaging in patients with pulmonary alveolar proteinosis

METHODS: Five patients with PAP (60% Male, aged 26-62 years) with mean baseline FEV_1 (%predicted) of 2.23 (70.25%) underwent 9 courses of nebulised sargramostim between 2013 to 2020. Clinical variables collected included; age, sex, diagnosis validation, tobacco exposure, prior WLL, presence of anti GMCSF antibody, subjective assessments (cough, sputum, exertional dyspnoea), pulmonary function testing at three, six, and twelve months (FEV_1 %predicted, FVC %predicted, FEV_1/FVC, TLCO corrected %predicted and six minute walk test), readmission times, mortality and computed

tomography (CT) imaging. CT Images were scored using the procedure described by Tokura *et al* by a subspecialty trained thoracic radiologist with six years of experience. Descriptive statistics was used to describe the data.

RESULTS: Four patients reported subjective improvements in symptoms. There was less than 5% mean change in pulmonary function tests (FEV_1, FVC, FEV_1/FVC, TLCO) at three, six and twelve months in the cohort. The 6MWT was increased by a mean of 11.6 meters at 3 months in the cohort. Radiological improvement was observed for the majority of patients with pre-treatment CT score mean 37.4 (SD 9.4) and post treatment score 28.4 (14.4) (p=0.055 Wilcoxon paired t-test). No adverse drug events or safety issues were reported, no patient was admitted to hospital for exacerbation of PAP or escalated to WLL, no patient required lung transplantation or died from PAP related illness.

CONCLUSIONS: Nebulised GM-CSF enabled minimally invasive treatment of this cohort with some symptomatic improvement, minimal lung function response and trend to radiological improvement. Nebulised treatment allowed patients to be treated at home, preventing hospitalisation and avoiding invasive WLL for exacerbations. The role, timing, effectiveness and patients acceptance of nebulised GM-CSF and WEEL demand further study in PAP.

6. SPATIAL RESPONSE TO SMALL AND LARGE PARTICLE BRONCHODILATOR IN ASTHMA

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INTRODUCTION: Topical treatment of asthmatic airways relies on effective delivery of inhaled medication. It is unclear if small particle sizes that penetrate the lung periphery are more effective.

AIMS: This study aimed to assess response to large and small particle short-acting $\beta_2$agonist (SABA) with the hypothesis that subjects with more peripheral airway dysfunction would respond better to small particle.

METHODS: 8 subjects with asthma completed spirometry, multi-breath nitrogen washout to measure conductive (Scond) and acinar (Sacin) ventilation heterogeneity, and phase resolved functional lung MR imaging (PREFUL) to measure the spatial heterogeneity of ventilation. Tests were performed at baseline and post SABA delivered via vibrating mesh nebuliser twice; a large (6.2μm) and small (2.6μm) particle visit.

RESULTS: The cohort had elevated Sacin $0.181\pm0.079L^{-1}$ (ULN:$0.120L^{-1}$). Small particle SABA resulted in greater improvement in: $\Delta FEV1\%$ 10±13 (large) vs 22±13 (small) p=0.01; $\Delta FVC\%$ 4±6 vs 9±14 p=0.04; $\Delta SacinL^{-1}$ 0.000±0.022 vs -0.028±0.023 p=0.03. Reduction in low ventilation areas (C2, the low ventilation spatial cluster) from PREFUL correlated with increase in FEV1; $\Delta C2\%$ and $\Delta FEV1mL$ r=-0.55 p=0.03.

CONCLUSION: Asthma subjects with peripheral airway dysfunction had a greater reduction in peripheral ventilation heterogeneity with small particle bronchodilator and the reduction in spatial regions of low ventilation correlated with change in FEV1.
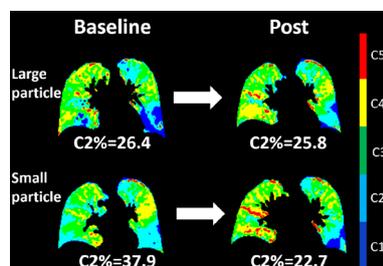
Figure. K-means quantified PREFUL ventilation images for an example subject

Reference

1. Verbanck, S., et al., The functional benefit of anti-inflammatory aerosols in the lung periphery. J Allergy Clin Immunol, 2006. 118(2): p. 340-6.

7. DIAGNOSTIC AND THERAPEUTIC OUTCOMES FOLLOWING SYSTEMATIC ASSESSMENT OF PATIENTS WITH CONCURRENT SUSPECTED VOCAL CORD DYSFUNCTION AND ASTHMA

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BACKGROUND: Vocal Cord Dysfunction (VCD) is present in 25-50% of patients with asthma. When mistaken for asthma, VCD has been associated with high asthma medication usage and invasive interventions. When both diagnoses are suspected, accurate diagnosis and targeted management represent a clinical challenge because of overlapping symptomatology.

OBJECTIVE: To evaluate diagnostic and therapeutic outcomes following systematic assessment for patients with concurrent suspected vocal cord dysfunction and asthma.

METHODS: Patients underwent systematic assessment by clinical evaluation and validated questionnaires, followed by multidisciplinary management. VCD was confirmed by visualisation of paradoxical vocal fold motion during laryngoscopy either at baseline or following provocation. Asthma was confirmed by demonstrating variable airflow obstruction (VAO). Asthma medications were de-escalated in those with low clinical probability of asthma and no VAO. Response to ≥2 sessions of speech therapy was assessed by subjective report and standardised questionnaires.

RESULTS: Among 212 consecutive patients, 60 (28%) patients had both VCD and asthma, 56 (26%) had VCD alone, 50 (24%) had asthma alone and 46 (22%) had neither. Expert clinician assessment and the Laryngeal Hypersensitivity Questionnaire both predicted laryngoscopy-confirmed VCD. De-escalation or discontinuation of asthma therapy was possible in 37/59 (63%) of patients without VAO, and was most successful (OR 5.5) in the presence of laryngoscopy-confirmed VCD (24/30, or 80%). Patients with VCD responded subjectively to ≥2 sessions of speech therapy, but laryngeal questionnaire scores did not improve.

CONCLUSION: Physicians experienced in the evaluation and management of middle airway disorders and the Laryngeal Hypersensitivity Questionnaire predict the presence of laryngoscopy-confirmed VCD. In patients with a low clinical probability of asthma without variable airflow obstruction, confirmation of an alternative diagnosis of VCD supports diagnostic de-labelling and de-escalation or discontinuation of unnecessary asthma medications. Subjective symptom improvement following speech therapy was not paralleled by laryngeal questionnaire scores in this cohort.

BURNS

8. PLATELET LYSATE CAN SUPPORT DEVELOPMENT OF A 3D SKIN ORGAN CULTURE FOR CLINICAL APPLICATION

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Platelet lysate (PL) contains a range of growth factors that are involved in spontaneous wound repair. *In vitro*, in the absence of fully defined media for expansion of a variety of cell types, PL has been used as a source of stimulatory growth factors and an effective substitute for foetal bovine serum (FBS) in a variety of cell therapies. Replacing FBS with PL as a cell culture supplement, improves the regulatory concerns by reducing the risk of prions and virus transmission. It also has ethical and animal welfare benefits by eliminating the requirement for bovine foetuses. Furthermore, PL is often prepared from outdated platelets collected for clinical applications, which would otherwise be disposed of, and, therefore, reduces waste.

HYPOTHESIS: PL can be utilised to produce serum-free 3D skin organ culture, containing dermal / epidermal components, for clinical application.

METHODS: Primary human adult fibroblasts and keratinocytes, isolated from donor skin samples, were cultured and processed for 3D skin organ culture. Flow cytometry was employed to assess fibroblast marker profiles. Expression of growth factors and extracellular matrix (ECM) proteins was measured in PL-expanded fibroblasts.

RESULTS: PL supported short-term (1-2 weeks) fibroblast expansion and keratinocyte stratification plus maturation in a 3D skin organ culture. Basement membrane was formed within 5 days, evident from collagen IV deposition. We found interleukin-6 (IL-6) and collagen I (Col I) upregulation in PL-expanded fibroblasts. PL-expanded fibroblasts were phenotypically separated into three subpopulations, based on CD90 and FAP expression. Data suggested that PL drove expansion of CD90^{+}FAP^{+} fibroblasts, which may have a reduced fibrotic effect, compared to CD90^{+}FAD^{-} once grafted.

CONCLUSION: Our findings support the concept of PL as a safe and effective serum alternative for skin cell therapies and provides a novel approach for bioengineering a serum-free 3D skin organ culture.

9. A PLATELET-DERIVED HYDROGEL IMPROVES NEO-VASCULARISATION IN FULL THICKNESS WOUNDS

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Platelets are a reservoir of growth factors, cytokines and chemokines involved in spontaneous wound repair. In this study, a platelet-rich and fibrin-rich hydrogel was generated from expired platelet components that would have otherwise been transfused.

AIM: To develop a non-autologous platelet-derived hydrogel to study its benefits on full-thickness wound healing in a mouse model.

METHODS: The hydrogel was prepared from apheresis platelet components on day 6 post-collection and wound repair was studied in a mouse model. The concentration of platelet-derived growth factors was measured in the platelet components using ELISA and mechanistic properties of hydrogels by rheology. A full thickness mouse wound model was established and platelet-derived hydrogel effect on wound repair studied using real-time PCR, and histological analysis.

RESULTS: The material contained physiological concentrations of transforming growth factor β1 (TGF-β1), platelet-derived growth factor AB (PDGF-AB), PDGF-BB, insulin-like growth factor-1 (IGF-1), fibroblast growth factor 2 (FGF-2), and epidermal growth factor (EGF). The effect of the hydrogel on wound repair was investigated in SKH-1 mice. Full thickness dorsal wounds were created on the mice and treated with the hydrogel at various concentrations. Immunohistochemical staining with CD31 (endothelial cell marker) revealed that wounds treated with the hydrogel showed significantly enhanced vascularisation in the wound bed. Moreover, low levels of interleukin-6 (IL-6) and KC (IL-8 functional homologue) in treated wounds were sustained over a longer period of time, compared to untreated wounds.

CONCLUSION: We postulate that sustained IL-6 is a driver, at least partly, of enhanced vascularisation in full thickness wounds treated with platelet-derived hydrogel. Further analysis of the hydrogel in large animal models and in clinical settings is needed to investigate its efficacy as a wound dressing treatment option when vascularisation is a critical limitation.

CANCER RESEARCH

10. PERIPHERAL BLOOD T-CELL PROFILING IN METASTATIC MELANOMA PATIENTS AS A MARKER FOR RESPONSE TO COMBINATION TREATMENT WITH IMMUNE CHECKPOINT INHIBITORS AND RADIOTHERAPY

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Background: The addition of stereotactic ablative radiotherapy (SABR) to immune checkpoint inhibitors (ICIs) has the potential to significantly improve outcomes in the treatment of metastatic melanoma. We analysed peripheral blood immune cells of patients receiving combination SABR and ICI to detect the effect of treatment and identify potential biomarkers that predict outcome.

Methods: 24 metastatic melanoma patients participated in the SABR IMPACT trial, receiving standard dose immunotherapy with anti-PD-1 and/or anti-CTLA-4, and a single dose stereotactic ablative radiotherapy to one metastatic site. Comprehensive immunophenotyping of T-cells was performed with flow cytometry on blood samples from 13 patients at baseline and following the first 4 cycles of treatment.

Results: Following four cycles of immunotherapy and SABR the proportion of naïve subsets were reduced within both the CD4 and CD8 T-cell lineages. Independently, SABR resulted in increased expression of PD-1 (p=0.019) and ICOS (p=0.46) on CD8+ T-cells, accompanied by a reduction in regulatory T-cell frequencies (p=0.048). A multivariate discriminant analysis revealed a baseline signature of low CD8+ naive T-cells and high levels of TIM-3 on regulatory T-cells and memory T-cells best predicted response to treatment.

Conclusion: The combination of immunotherapy and SABR changed the immunophenotype of blood T cells, with some shifts attributable to SABR. Importantly, we identified a T-cell signature at baseline that best predicted response. Validation of these findings in an independent cohort could confirm these as biomarkers at baseline or early during treatment, and whether these can be utilised to stratify patients for high or low intensity treatment to reduce toxicity.

11. NEW RECOMMENDATIONS FOR THERMAL ABLATION OF RENAL CELL CARCINOMA (RCC). A NON-THERMAL ABLATION OPTION: IRREVERSIBLE ELECTROPORATION (IRE) FOR THE TREATMENT OF RENAL TUMOURS

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Thermal ablation has been shown to be as effective with fewer complications than nephrectomy for T1a RCC. The 2020 SIR position statement recommends that thermal ablation should be offered over active-surveillance for T1a, and be offered to selected T1b RCC patients.

AIM: To report on IRE ablation of renal tumours close to vital structures that are unsuitable for thermal ablation.

METHODS: An ethics approved prospective study to investigate IRE tumour treatment safety and efficacy was undertaken. Nineteen patients with renal tumours deemed unresectable and poor candidates for thermal ablation were treated between 2008 -2015. A second IRE was performed if complete ablation was not achieved in the first procedure. Patients were followed up clinically and with CT for adverse events and recurrence-free survival for at least 5 years.

RESULTS: Nineteen patients underwent 29 procedures for 27 tumours. 16/19 (84%) were treated for RCC, 8/29 (42%) had a solitary kidney and 18/19 (94%) had lesions adjacent to thermally-sensitive structures. Success was correlated to tumour size; 15/16 (94%) of <3cm tumours were successfully ablated versus 7/11 (63%) of tumours ≥3cm.

Stratification by follow-up duration (short-term 1-2 years; medium-term >2-5 years; long-term >5 years) showed complete ablation post ≤2 rounds of IRE in 100% of short and medium term patients and 58% of long term patients. One patient with Von Hippel-Lindau had multiple ablations for multiple lesions and five-year recurrence-free-survival was observed for two lesions.

AEs: Partial ureteric stenosis was seen in 1 patient, thought to be related to previous thermal-ablation of the same tumour. No other major complications were observed.

CONCLUSION: IRE is a nephron-sparing, safe ablation option for treatment of renal tumours, including tumours close to vital structures not suitable for thermal ablation. Success was higher for tumours <3cm.

12. A NOVEL METHYLTRANSFERASE-INDEPENDENT FUNCTION OF EZH2 IN PROMOTING MELANOMA PROGRESSION VIA GTP PRODUCTION

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Cellular heterogeneity in cancer is linked to disease progression and therapy response, although the mechanisms are not well understood that regulate distinct cellular states within tumours. To address this, we identified melanin pigment content as a major source of phenotypic and functional heterogeneity in melanoma, and compared protein and RNAseq data from high (HPC) and low pigmented melanoma cells (LPC), revealing the polycomb repressor complex protein, EZH2, as a master regulator of these states. EZH2 protein, but not RNA expression, was found to be upregulated in LPCs and inversely correlated with melanin in pigmented patient melanomas. Surprisingly, conventional EZH2 methyltransferase inhibitors, GSK126 and EPZ6438, had no effect on LPC survival, clonogenicity and invasion, despite fully inhibiting methyltransferase activity. In contrast, EZH2 silencing by siRNA or DZNep reduced total EZH2 protein and conferred significant inhibition of cell growth and invasion in LPCs. Notably, the EZH2 knockdown phenotype was rescued by both WT-EZH2 as well as methyltransferase-deficient H689A mutant EZH2 overexpression. This indicates a methyltransferase independent role of EZH2 in melanoma cell tumorigenicity and invasion.

To identify potential methyltransferase-independent mechanisms of EZH2 function, we performed LC/MS on EZH2 immunoprecipitates and identified an interacting protein complex with inosine monophosphate dehydrogenase 2 (IMPDH2), the rate-limiting enzyme in de-novo GTP synthesis, a purine nucleoside that mediates essential requirements of cancer cells such as ribosome biogenesis and G-protein coupled receptor signalling. Biochemical studies showed that EZH2 interacts with IMPDH2 mostly in cytosol through the IMPDH2-CBS domain in a methylation-independent manner. EZH2 silencing localizes IMPDH2 into nuclei and reduces IMPDH2 tetramerization/activity and cellular GTP levels. Guanosine, which replenishes GTP, stabilized ribosomal function and Rho-ROCK-Myosin II activity, thereby promoted invasive and clonogenic cell states even in siEZH2-treated cells. This indicates methyltransferase-independent and GTP-dependent non-canonical mechanisms of EZH2 regulation of the malignant cell state.

13. MALNUTRITION DEFINED BY GLIM CRITERIA ASSOCIATES WITH AN INCREASED RISK OF ADVERSE OUTCOMES AFTER OESOPHAGO-GASTRIC CANCER SURGERY, COMPARED TO ICD-10 DEFINED MALNUTRITION

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Background: Low muscle mass is associated with poor outcomes after oesophago-gastric (OG) cancer surgery. The 2019 Global Leadership Initiative on Malnutrition (GLIM) criteria includes muscle mass, a measure not incorporated in the International Classification of Diseases, 10th Revision, (ICD-10) criteria. We aimed to determine the prevalence of preoperative GLIM and ICD-10 malnutrition and assess the impact on postoperative outcomes after OG cancer surgery.

Methods: Patients who underwent radical OG cancer surgery with preoperative abdominal computed tomography (CT) imaging were included. Low skeletal muscle index (SMI, cm^2/m^2) was measured by CT using predefined cut-points[1.] Additional nutrition parameters (BMI, weight loss) were retrospectively collected to diagnose malnutrition using ICD-10 and GLIM definitions.

Malnutrition was assessed against prospectively collected oncological, surgical, and survival data. All patients met the GLIM aetiologic criterion of an inflammatory condition. McNemar's test assessed differences between malnutrition definitions (total and severe). Logistic and Cox regression determined predictors of complications and survival, respectively.

Results: 108 patients were included. Malnutrition prevalence was significantly higher using GLIM criteria compared to ICD-10 (n=75, 69.4% vs n=44, 40.7%, p <0.001), including severe malnutrition (30.6% vs 11.1%, p <0.001). The predominant phenotypic criterion for GLIM-malnutrition was low SMI (n = 66, 61%), followed by preoperative weight loss (n=46, 43%) and low BMI (n= 1, 10%). GLIM malnutrition was associated with postoperative pneumonia (26.9% vs 6.7% well-nourished, p = 0.010) and was an independent predictor (p=0.038, OR 5.7, CI 1.1-29). Severe GLIM malnutrition independently predicted poorer 5-year overall survival (p=0.025, HR 2.39, CI 1.15-5.11). ICD-10 malnutrition was not associated with postoperative complications or survival.

Conclusion: GLIM-malnutrition is more prevalent than malnutrition defined by the ICD-10 classification and is an independent predictor of postoperative pneumonia and poorer survival. Muscle mass is a key GLIM criterion and an important component of preoperative nutrition assessment in OG cancer surgery.

References: Prado C et al. Lancet Oncol. 2008.

14. EFFECT OF FOLLOW-UP SURVEILLANCE AFTER CURATIVE-INTENT TREATMENT OF NSCLC ON DETECTION OF NEW AND RECURRENT DISEASE, RE-TREATMENT AND SURVIVAL: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Patients with NSCLC may be treated with curative intent, yet these patients remain at high risk of both disease recurrence and second primary lung cancer and are at increased risk of early death. Various guidelines provide recommendations for follow up but there is little consensus and review of available evidence is necessary.

Hypothesis: The use of a systematic follow up strategy for the detection of disease recurrence or second primary lung cancer (SPLC) after curative intent treatment of NSCLC may increase the proportion of patients available for retreatment and increase survival for screen detected patients.

Methods: We performed a systematic review and meta-analysis of prospective studies on follow up of NSCLC after curative intent treatment to answer three questions. What is the effect of follow up on detection of recurrence or SPLC? What is the effect of surveillance detection on curative intent retreatment? What is the survival impact?

Results: Recurrence/SPLC was observed in 17.8-71% of patients. Scheduled imaging detected recurrence in 60-100% of cases, yet neither CT-based (OR 2.31; 95% CI 0.27-19.49, p=0.44) nor PET-CT-based follow up (OR 1.431; 95% CI 0.92-2.22, p=0.12) were statistically superior to standard follow up strategies. Detection of disease recurrence/SPLC significantly increased the odds of curative intent retreatment (OR 1.431; 95% CI 0.92-2.22, p=0.12). Five studies described survival outcomes suggesting poor survival following symptomatic presentation, trends to longer survival following scheduled surveillance, CT and PET detected recurrence and longer survival for those able to undergo curative intent retreatment.

Conclusions: The early detection of disease recurrence/SPLC may increase likelihood of curative intent retreatment and prolong survival. There is clear need for prospective randomised controlled studies of follow up to confirm effectiveness of available follow up modalities.

15. IRREVERSIBLE ELECTROPORATION (IRE) FOR THE TREATMENT OF THE RARE CANCER, HEPATIC EPITHELIOID HEMANGIO-ENDOTHELIOMA (HEHE): LONG-TERM RESULTS OF TWO CASE STUDIES AND PROTOCOL FOR AN INTERNATIONAL PATIENT-LED STUDY

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HEHE is a rare, malignant vascular cancer. Untreated, it has a low 5% 5-year survival-rate. It affects young people and current treatments effect a high morbidity or are unsuitable for 80% of patients. IRE has been shown to be a safe, effective treatment for hepatic tumours and to modulate immune responses by releasing tumour-cell antigens and decreasing tumour protective Treg-cells.

AIM: To report on long-term treatment outcomes of two HEHE-patients treated with IRE and to present the protocol for an international patient-led project.

METHODS: An ethics approved prospective study to investigate IRE tumour treatment safety and efficacy was undertaken. Two HEHE-patients with tumours unsuitable for resection or thermal ablation were included between 2009-2016.

Only three centres globally have treated a limited, 24 HEHE-patients with IRE. These patients, via their EHE-Foundations, have requested we undertake further research.

RESULTS: The first patient was treated in 2009 and had 8 IRE procedures for 11 liver tumours. The largest was 8x5x5 cms, traversed segments 4/5 and surrounded major blood vessels. The patient had no recurrence in over 10 years. The second patient was treated in 2016 and had 4 procedures for 7 tumours. There has been no recurrence of the treated lesions. In 2020, a suspicious new lesion was detected and further treatment is being considered. There were no serious complications, the first patient was treated for pain following two procedures close to the liver capsule.

Based on these findings and patient' requests, we have established an international collaborative group with radiologist in the USA and UK, EHE-Foundations (Australia,USA,UK), The Garvan Institute and the CART-wheel Registry to investigate IRE for the treatment of HEHE and IRE induced immune responses.

CONCLUSION: Two HEHE-patients treated with IRE at our institution have had favourable long-term results. An international collaborative study is required to study this rare cancer.

CARDIOVASCULAR DISEASE

16. COMBINED ANTIPLATELET/ANTICOAGULANT DRUG FOR CARDIAC ISCHEMIA/REPERFUSION INJURY

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Myocardial infarction (MI) is typically caused by rupture of atherosclerotic plaques leading to thrombotic occlusion of coronary arteries. Reperfusion of the artery results in further tissue damage, known as ischemia/reperfusion (I/R) injury, by provoking major inflammatory and microthrombotic responses, leading to loss of cardiac function. Platelets accumulate very

early in ischemic/reperfused myocardium mediating I/R injury. Current antiplatelet/anticoagulant drugs, particularly in combination, are associated with bleeding complications representing a major cause of mortality/morbidity.

Materials and Methods: We developed a single-chain antibody (scFv), which specifically binds to activated glycoprotein GPIIb/IIIa, which mediates platelet crosslinking/aggregation and thrombus formation, and genetically fused it to tick-anticoagulant-peptide (TAP), a FXa inhibitor, generating a unique dual-function antiplatelet/anticoagulant drug (Targ-TAP).

Results: Using a cardiac I/R mouse model (occlusion of the left anterior descending artery of mice for 60 min) we showed that Targ-TAP improved cardiac function 4wks post-MI (increased ejection fraction and fractional shortening, less cardiac strain) compared to non-targeted control (Mut-TAP) and PBS. This protection of cardiac function by Targ-TAP correlated with a significantly reduced infarct size in comparison with controls, as assessed by Evans Blue/triphenyltetrazolium chloride staining. Confirming that Targ-TAP does not exhibit systemic effects on hemostasis, mice treated with Targ-TAP did not display prolonged tail bleeding times or increased blood loss.

Conclusion: In summary, we describe Targ-TAP as a highly effective anti-thrombotic drug uniquely combining localized antiplatelet and targeted anticoagulant effects while preserving hemostasis for the treatment of cardiac I/R injury.

17. UNEARTHING THE EVIDENCE: POST MORTEM INTERROGATION OF CARDIAC IMPLANTABLE ELECTRONIC DEVICES

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INTRODUCTION: The diagnostic yield of post-mortem interrogation of cardiac implantable electronic devices (CIEDs) including pacemakers, defibrillators and implantable loop recorders has not been well described.

AIM: To define the feasibility and utility of post-mortem CIED interrogation.

METHODS: We reviewed all post-mortem CIED interrogations performed by the Victorian Institute of Forensic Medicine between 2005 2020 for investigation of sudden or unexplained death.

RESULTS: 260 patients (68.8% male, median age 72.8 years [IQR 62.7-82.2]) underwent post-mortem CIED interrogation (202 pacemakers. 56 defibrillators and 2 loop recorders). CIEDs were implanted for a median of 2.0 [IQR 0.75-5] years, with 19 devices requiring replacement (and 5 end of life). Post-mortem interrogation was successful in 256 (98.5%) cases. Potential CIED malfunction was identified in 21 (8.1%) cases: untreated ventricular arrhythmias (n=13), lead failures (n=3) and battery depletion (n=5). CIED interrogation directly informed cause of death in 130 (50.0%) cases, with fatal ventricular arrhythmias identified in 121 patients (46.5%). In retrospect, 72 (27.7%) patients had abnormalities recorded by their device in the 30 days preceding death: non-sustained ventricular tachycardia (n=26), rapid atrial fibrillation (n=17), longevity concerns (n=22), intrathoracic impedance alarms (n=3), lead Issues (n=3) or therapy delivered (n=1). In 6 cases where the patient was found deceased after a prolonged time, CIED interrogation accurately determined time of death. In one case, CIED interrogation was the primary method of patient Identification.

CONCLUSION: Post-mortem CIED interrogation frequently contributes important information regarding critical device malfunction, pre mortem abnormalities, cause and time of death or patient Identity. Device Interrogation should be considered for select patients with CIEDs undergoing autopsy.

18. CARDIAC REHABILITATION HAS BEEN "THROWN INTO THE 21ST CENTURY": A FOCUS GROUP STUDY EXPLORING THE IMPACT OF COVID-19 AMONG CLINICIANS IN VICTORIA

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Background: Cardiac rehabilitation (CR) education and exercise are predominantly delivered in group face-to-face settings. This delivery model was challenged during the COVID-19 pandemic in Victoria due to government stay at home orders that restricted in-person outpatient care. The experience, barriers and enablers of delivering CR during a pandemic, and identified strategies for future COVID-safe programs were explored among clinicians.

Methods: Victorian members of the Australian Cardiovascular Health and Rehabilitation Association (ACRA) were invited to attend an exploratory qualitative online focus group in November 2020. An inductive thematic analysis was undertaken before deductively applying the Non-adoption, Abandonment, Scale-up, Spread and Sustainability (NASSS) framework to identify barriers and enablers for technology adoption in CR.

Results: 30 members participated in a 106-minute focus group. 17 members who provided demographics represented multiple disciplines (nursing n=13, exercise physiology n=3, physiotherapy n=1) and geographical settings (metropolitan n=10, regional n=4, rural n=3). Four main themes were identified: Consequences of service change; Use of technology; Capacity; and Future models of care. The deductive NASSS analysis demonstrated the main challenges of continuing remotely delivered CR lie with all adopters (staff, patients, carers) and with organisations. Future CR strategies included the importance of resuming face-to-face programs but finding capacity, particularly staffing and funding, to run concurrent telehealth programs.

Conclusion: The COVID-19 pandemic forced and expedited significant changes to CR delivery models. While clinicians agreed that delivery of CR via telehealth will continue, it is now timely to review remote models of care and plan how they will integrate alongside traditional face-to-face programs long term.

19. PRONE & SUPINE 12 LEAD ELECTROCARDIOGRAPHY COMPARISONS: UTILITY OF THE PRONE EKG FOR THE DETECTION OF CARDIAC CONDITIONS IN PATIENTS REQUIRING PRONE VENTILATION WITH COVID-19

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Background: Unwell Coronavirus disease (COVID-19) patients are at risk of cardiac complications. Prone ventilation is recommended for respiratory distress but poses practical challenges to acquisition of a 12 lead electrocardiogram (EKG). The effects of prone positioning on the EKG remain unknown.

Objectives: To determine the changes in the prone EKG compared with normal supine including in cardiac conditions.

Methods: 100 patients each underwent 3 EKGs - standard supine front (SF); prone position with precordial leads attached to front (PF); and prone position with precordial leads attached to back in a mirror image to front (PB).

Results: Prone positioning was associated with QTc prolongation (PF 437+/-32ms vs SF 432+/-31ms, p <0.01; PB 436+/-34ms vs SF 432+/-31ms, p = 0.02). In leads V1-3 on PB EKG, a qR morphology was present in 90% and changes in T wave polarity in 84%. In patients with anterior ischemia, ST changes in V1-3 on supine EKG were no longer visible on PB in 100% and replaced by a R wave in V1. Bundle branch block (BBB) remained detectable in 100% on PB, with left BBB appearing as right BBB on PB in 71% and QRS narrowing with qR in V1 for RBBB. ST segment and T wave changes in limb leads, and arrhythmia detection, were largely unaffected in PB position.

Conclusion: As expected the prone back EKG is unreliable for the detection of anterior myocardial injury but remains useful for ST / T wave abnormalities in limb leads, BBB detection and rhythm monitoring. The prone EKG is a useful screening tool with diagnostic utility in COVID-19 patients who require prone ventilation.
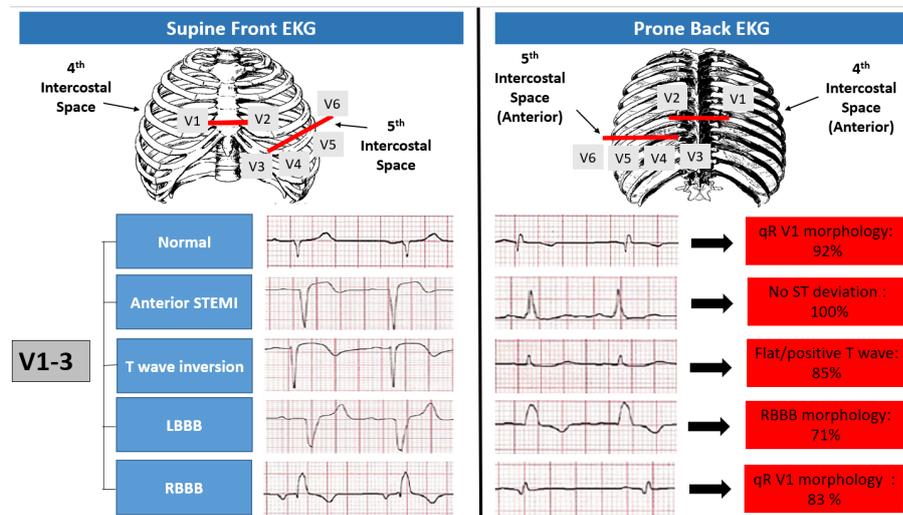
20. EFFECTS OF LIGNOCAINE VERSUS OPIOIDS ON ANTIPLATELET ACTIVITY OF TICAGRELOR: THE LOCAL TRIAL

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BACKGROUND: Procedural analgesia using opioids is routinely given to patients undergoing coronary angiography. However, opioids impair the gastrointestinal absorption of all oral $P2Y_{12}$ inhibitors, which are essential antithrombotic agents in acute coronary syndromes. Use of non-opioid procedural analgesia may provide a solution to this problem.

AIMS: We assessed the impact of intravenous fentanyl and lignocaine on the pharmacokinetics and pharmacodynamics of ticagrelor in patients with unstable angina and non-ST elevation myocardial infarction, their procedural analgesic efficacy and safety.

METHODS AND RESULTS: Seventy patients undergoing coronary angiography with ticagrelor loading were included in the pharmacokinetic and pharmacodynamic analysis of this prospective, double blind, randomised controlled trial. Plasma ticagrelor levels 2h post loading dose were significantly lower in the fentanyl compared to lignocaine treatment arm (598 vs. 1008 ng/mL, p=0.014). The area under the plasma-time curves for ticagrelor (1228 vs. 2753 ng.h/mL, p<0.001) and its active metabolite (201 vs. 447 ng.h/mL, p=0.001) were both significantly lower in the fentanyl arm. Expression of activated platelet glycoprotein IIb/IIIa receptor (2829 vs. 1426 mean fluorescence intensity, p=0.006) and P-selectin (439 vs. 211 mean fluorescence intensity, p=0.001) were significantly higher at 60 min in the fentanyl arm. High on-treatment platelet reactivity was significantly higher in the fentanyl arm at 60 min using the Multiplate Analyzer (41% vs. 9%, p=0.002) and 120 min using the VerifyNow (30% vs. 3%, p=0.003) and VASP (37% vs. 6%, p=0.002) assays. Both drugs were well tolerated with a high level of patient satisfaction (fentanyl 94% vs. lignocaine 97%, p=0.56).

CONCLUSIONS: Unlike fentanyl, lignocaine does not impair the bioavailability or delay the antiplatelet effect of ticagrelor. Both drugs were well tolerated and effective with a high level of patient satisfaction for procedural analgesia. Routine procedural analgesia during PCI should be reconsidered and if performed, lignocaine is a beneficial alternative to fentanyl.

21. COGNITIVE IMPAIRMENT IS A DETERMINANT OF PATIENT RESPONSE TO DISEASE MANAGEMENT PROGRAMS TO REDUCE READMISSION IN HEART FAILURE

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Background: Cognitive impairment (CI) is highly prevalent in heart failure (HF), and increases patients' risks of readmission.

Purpose: This study sought to determine whether the presence and degree of CI could identify patients most likely to benefit from a HF disease management program (DMP) to reduce readmissions.

Methods: 1152 consecutive Australian patients admitted with HF were prospectively followed-up for 12 months. Of these, 324 patients who received DMP (1-month duration, including post-discharge home visits, medication reconciliation, exercise guidance and early clinical review) were matched (1:2 ratio) with 648 usual care patients. Cognitive function was assessed either on the day of or one day before discharge using the Montreal Cognitive Assessment (MoCA). Outcomes included readmission or death at 1-, 3- and 12-months, and days-at-home within 12 months, from discharge.

Results: Poorer cognitive function was associated with all adverse outcomes. Compared with usual care, DMP was associated with lower odds of 30-day (OR=0.60 [0.40, 0.91]) and 90-day (OR=0.53 [0.36, 0.77]) readmission or death, and with 19 more days-at-home within 12 months, independent of HF therapy. The effect sizes of these associations were greater for patients with diminished cognition than those with normal cognition (interaction p=0.036), and might have been more pronounced among those with mild CI compared with those with more severe CI (MoCA score 17-22, OR=0.42 [0.21, 0.87] at 30-day, OR=0.31 [0.16, 0.60] at 90-day). Patients with normal cognition had fewer events, irrespective of DMP.

Conclusions: Cognitive function may determine how HF patients respond to a DMP. Cognitive screening before implementation of a DMP may allow personalized plans for patients with different levels of cognitive function.

22. OXIDATIVE STRESS PROMOTES GLUCOCORTICOID-INDUCED MINERALOCORTICOID RECEPTOR (MR) TRANSCRIPTIONAL ACTIVITY IN CARDIOMYOCYTES

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Current mineralocorticoid receptor (MR) antagonists attenuate cardiovascular inflammation, fibrosis, and progression to heart failure, even though mineralocorticoid levels (aldosterone) are not always elevated in patients with heart failure. It has been proposed that in the presence of oxidative stress, glucocorticoids (cortisol) exhibit MR agonist activity equivalent to aldosterone. However, the cellular mechanisms driving ligand-dependent MR-mediated adverse effects in stressed cells are not well understood. Recently, our laboratory demonstrated that circadian clock signalling can regulate MR transcriptional outcomes.

AIM: To determine whether enhanced ligand-dependent MR activation by oxidative stress involves cooperative circadian clock signalling.

METHODS & RESULTS: Dose-response curves for aldosterone and cortisol-induced MR-mediated transactivation of a MMTV-luciferase reporter showed the EC_{50} for aldosterone was 10-fold lower than for cortisol in rat cardiomyoblast (H9c2) cells. Addition of L-buthionine sulfoximine (LBSO) (10µM) reduced the EC_{50} concentration for each ligand by ~10-fold. In contrast, the prooxidant, hydrogen peroxide (H_2O_2) (10µM), did not modify ligand-dependent MR transactivation, suggesting that disrupting glutathione (GSH) by LBSO is important. Investigation of cellular GSH levels showed a fall in GSH with LBSO, but a modest increase (0.4 fold) in the GSH:GSSG ratio, a key cellular redox sensor; whereas H_2O_2 increased GSH:GSSG by 2-fold. Moreover, replacement of GSH or an antioxidant did not alter transactivation responses. Importantly,

LBSO+cortisol significantly upregulated mRNA levels of select MR target genes equivalent to aldosterone including glucocorticoid-induced leucine zipper (*Gilz*) and circadian genes, period homologue 1 and 2 (*Per1* and *Per2*). Pilot data suggests that co-expression of circadian transcription factors (CLOCK and Bmal) enhance LBSO+cortisol regulation of MR transcriptional outcomes.

CONCLUSION: Our data suggest circadian clock transcription factors are one mechanism whereby cortisol-MR activation induces an agonist response in stressed cardiomyocytes. A detailed understanding of MR and circadian clock signalling in cardiomyocytes may offer new opportunities for modulating the MR therapeutically in heart failure.

23. IDENTIFYING BIOMARKERS FOR PREDICTING RESPONSE TO MINERALOCORTICOID RECEPTOR ANTAGONIST TREATMENT IN HEART FAILURE

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Heart failure (HF) is a major public health burden. Mineralocorticoid receptor antagonists (MRAs) reduce hospitalisation and improve survival in patients with HF with reduced ejection fraction (HFrEF) but the widespread use of MRAs is limited by adverse effects including hyperkalaemia. The use of biomarkers to guide therapy may enable earlier treatment or minimise side effects from unnecessary therapies. We have previously described mineralocorticoid receptor responsive genes in monocytes/macrophages and hypothesised that response to MRAs can be detected in this cell population.

AIM: To identify biomarkers for predicting response to MRAs to facilitate personalised treatment of HF.

METHODS: We performed microarray-based transcriptome profiling of monocytes obtained from six patients with HFrEF, before and after three months of MRA treatment. Multidimensional scaling (MDS) was employed to visualise sample similarity followed by differential expression analysis. Top differentially expressed genes (DEGs) implicated in cardiovascular pathophysiology were validated by RT-qPCR.

RESULTS: Three patients demonstrated improvement in left ventricular ejection fraction (LVEF) after 12 months of MRA treatment (Group 1), whereas the other three patients exhibited minimal functional response to MRAs (Group 2). The MDS plot revealed distinct separation of males from females. Paired analysis of Group 1 samples (before vs after MRA treatment) identified 319 unique DEGs (estimated fold-change ≥ 2, q-value < 0.05); 1 upregulated, 318 downregulated). Group 2 had 1 unique DEG. RT-qPCR confirmed down-regulation of 12 of the top DEGs in Group 1. Additionally, cluster of differentiation (CD) encoding genes CD14, CD163 and CD68 were upregulated in Group 1 but downregulated in Group 2.

CONCLUSION: Our results show MRA treatment can significantly alter the monocyte transcriptomic profile. Further research is needed to establish the utility of these DEGs as biomarkers for early prediction of MRA treatment-response in patients with HF, and to define sex-specific differences.

24. A NOVEL ROLE FOR HEPATIC RETINOL DEHYDROGENASE 11 IN THE REGULATION OF CHOLESTEROL METABOLISM

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Dysregulation of hepatic cholesterol homeostasis contributes to elevated serum cholesterol levels, known as hypercholesterolemia, which is a significant risk factor for the development of atherosclerotic cardiovascular disease. Limitations in current cholesterol-lowering therapeutics has driven a need to identify novel targetable pathways to effectively

treat hypercholesterolemia. Here, we utilised an integrated discovery platform, combining genomic data from 107 strains of mice with untargeted liver proteomic analyses in order to identify both known and novel regulators of hepatic cholesterol metabolism. Across the 107 mice strains, we demonstrated that retinol dehydrogenase 11 (RDH11) was positively correlated with numerous cholesterol biosynthetic enzymes including Delta (14)-sterol reductase TM7SF2 (β=0.545; p=4.7e-24) and FDPS (β=0.535; p=4.7e-23). C57BL/6J mice administered the cholesterol lowering agent, simvastatin, exhibited a marked 2-fold increase in hepatic *Rdh11* mRNA expression. In contrast, mice fed a western diet exhibited a 70% reduction in *Rdh11* mRNA expression. Furthermore, we identified that transcriptional regulation of RDH11 was comparable to the sterol response element-binding protein-2 target genes, HMGCR and LDLR, and opposed that of the liver X receptor target gene, ABCA1, in response to altered cellular cholesterol conditions levels in human hepatoma (Hep3B) cells and mouse primary hepatocytes. RDH11 loss- and gain-of-function studies in Hep3B cells modulated gene markers of cholesterol metabolism (LDLR, HMGCR) cellular inflammation (NFKβ1, CHOP) and oxidative stress (GPX3, AP-1, NRF2). Lastly, mice administered an AAV8-shRNA construct targeting Rdh11, exhibited an upregulation of markers of ER and oxidative stress and reduced *Acat2* mRNA expression. Moreover, hepatic RDH11 protein expression was negatively correlated with both free and esterified cholesterol in the liver. Finally, mice receiving RDH11-shRNA exhibited a reduction in hepatic cardiolipin abundance and a concomitant reduction in the abundance of markers of the electron transport chain complexes. Consequently, these findings suggest that RDH11 plays an important role in the regulation of hepatic cholesterol metabolism.

25. HIGH POWER (40-50W) SHORT DURATION (HPSD) VERSUS LOWER POWER (25W) LONGER DURATION (LPLD) ATRIAL FIBRILLATION ABLATION: EFFECTS ON ESOPHAGEAL THERMAL INJURY AND PROCEDURAL OUTCOMES. A MULTI-CENTRE RANDOMISED CONTROLLED STUDY (HI-LO HEAT STUDY)

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Background: Lower power (25W) longer duration (LPLD) radiofrequency (RF) ablation has conventionally been used on the posterior wall during pulmonary vein isolation (PVI) for atrial fibrillation (AF), to attenuate the risk of esophageal thermal injury (ETI). High power (40-50 W) short duration (HPSD) RF ablation results in shorter procedural times with no increase in ETI. However evidence had been limited by non-randomised studies.

Aim: To compare HPSD versus LPLD ablation and the effects on esophageal thermal injury (ETI) and procedural outcomes.

Methods: 88 AF patients were randomised to HPSD or LPLD ablation using contact force sensing ablation catheters. Ablation was done using 40-50W (HPSD group) versus 25 W (LPLD group). Circa multi-sensor esophageal temperature monitoring (ETM) probe was utilized. Endoscopy was performed within 24 hours to assess for ETI. The primary outcome was incidence of ETI, with secondary outcomes including acute procedural endpoints.

Results: Mean age of the cohort was 61+/-9 years, with 31% females. PVI was achieved in 100% of patients. Significant esophageal luminal temperature rises ($\geq$ 38c) were seen in 93.2% of patients, with no difference between groups (p=0.69). First pass isolation rates were similar in both groups. HPSD group had shorter RF time (1613 vs 2303 secs, p <0.04), and fluoroscopy times (11.4 vs 13.1 mins, p=0.05). Procedural times were lower in HPSD, although not significant (133.7 vs 150.8 mins, p=0.10). Post ablation endoscopy showed 4 cases of superficial ulcer ETI (4.5%) with equal occurrence in both groups (p=1.0). All ETI were treated with PPI therapy. There was no difference in AF recurrence after a mean follow up of 6.3 months (p=0.71).

Conclusion: HPSD ablation was associated with lower RF ablation and fluoroscopy times compared to LPSD, with comparably low rates of ETI on post ablation endoscopy. HPSD ablation is a safe and efficacious approach to PVI.

26. GENERATION OF NOVEL KNOCKOUT MOUSE MODELS TO INVESTIGATE THE ROLE OF B55A IN THE HEART

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B55α is one of >20 regulatory subunits of protein phosphatase 2A (PP2A). Regulatory subunits are responsible for targeting PP2A to specific protein substrates, enabling the enzyme to carry out a range of essential cardiac functions. Despite their important function as fine-tuners of PP2A activity, the role of PP2A regulatory subunits in cardiac physiology and pathology is poorly understood. *In vitro* studies have identified B55α as a potential modulator of cardiomyocyte hypertrophy. To build on these findings and improve our overall understanding of PP2A regulatory subunit function in the heart, we generated two novel mouse models and characterised each at 10-12 weeks of age. We assessed left ventricular dimensions and function by echocardiography, and collected heart tissue for subsequent gravimetric, histological and molecular analyses. In the first model, global ablation of the gene encoding B55α (*Ppp2r2a*) resulted in embryonic lethality between day 14.5 and birth. Ventricular B55α expression was reduced by ~40% (P=0.02) and 65% (P=0.002) in adult male and female heterozygotes respectively, compared to wildtype littermates. Heterozygous mice did not display an overt cardiac phenotype (normal systolic function, no fibrosis or expression of cardiac stress markers *Nppa* or *Nppb*, P>0.05). The second mouse model employed the Cre/loxP system to achieve cardiomyocyte-specific Ppp2r2a knockout (KO). Left ventricular B55α expression was significantly (~90%) reduced in both male (P=0.0006, n=7/group) and female (P=0.004, n=6/group), mice, however we observed no increase in heart size as measured by left ventricle weight (P>0.05, n=10-14). In female cardiac-specific KO mice, we saw no indications of systolic dysfunction by echocardiography (P>0.05, n=7-13) and fibrosis was absent (P=0.99, n=4-5). These data suggest that B55α is critical for embryogenesis but does not appear to be required for postnatal cardiac development. Further *in vivo* studies are ongoing to investigate the impact of B55α deficiency in settings of cardiac stress.

27. MULTIPOLAR MAPPING WITH THE HIGH DENSITY GRID CATHETER COMPARED WITH CONVENTIONAL POINT BY POINT MAPPING TO GUIDE CATHETER ABLATION FOR FOCAL ARRHYTHMIAS

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Background: Multipolar catheters provide high density mapping which may reduce procedural duration and improve success of catheter ablation (CA) for focal arrhythmias. The high density grid (HDG) catheter is a 16 electrode mapping catheter with bipole recordings at orthogonal splines. The aim of this study is to compare the clinical and procedural features from a cohort who underwent CA for focal arrhythmias using multipolar mapping (MPM) with an age and case matched cohort using point by point (PbyP) mapping.

Methods: Consecutive patients undergoing CA for focal arrhythmias between October 2018 and January 2020 guided by MPM were compared with PbyP mapping with the ablation catheter over a similar period. Demographics, procedural features and outcomes were compared.

Results: 54 patients (27 in MPM vs 27 in PbyP mapping) underwent CA for 68 focal arrhythmias (26 atrial and 42 ventricular). In the MPM group the electrogram at the successful site was significantly earlier (39 +/- 11 ms) than in the PbyP group (33 +/- 7 ms; p =0.02). In the MPM group the mapping time (35 +/- 24 mins vs 53 +/- 31 mins in PbyP; p= 0.03) and procedural duration (126 +/- 42 mins vs 153 +/- 39 mins in PbyP, p = 0.02) were significantly shorter. There was no significant difference in radiofrequency/ fluoroscopy times, acute procedural success, and arrhythmia recurrence.

Conclusion: Multipolar mapping with the HDG catheter for focal tachycardias identified earlier activation times and was associated with shorter mapping and procedure duration with equivalent success to PbyP mapping.

DIABETES AND DIABETIC COMPLICATIONS

28. THERMALLY PROCESSED DIET-INDUCED ALBUMINURIA, COMPLEMENT ACTIVATION AND INTESTINAL PERMEABILITY ARE ATTENUATED BY RESISTANT STARCH IN EXPERIMENTAL DIABETES

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OBJECTIVE: The primary objective of this study was to ascertain whether thermally processed diets influence albuminuria and intestinal permeability via alterations in the complement cascade. A secondary objective was to see whether these pathological alterations could be ameliorated by a gut-targeted dietary intervention, resistant starch.

METHODS: Six-week-old Sprague Dawley rats were randomised to receive a control (CON; AIN93G), thermally processed diet (TPD) (AIN93G baked at 160°C for 1h) or TPD with daily gavage of either 10 mg/kg/d alagebrium chloride (ALA), an inhibitor of advanced glycation end products or daily gavage of 2mg/kg/d PMX-53, a C5a receptor inhibitor for 24 weeks. Six-week-old diabetic mice (db/db) received the CON diet or TPD with or without 12.5% resistant starch (RS) for 10 weeks. Urinary albumin, C5a and plasma MCP-1 were measured by ELISA. Plasma endotoxin was measured using a limulus amoebocyte lysate kit. Intestinal permeability was assessed *in vivo* by the clearance of FITC-labelled dextran. Transcriptomic profiling of renal cortex was determined by RNA-Sequencing.

RESULTS: The TPD increased albuminuria, plasma endotoxin and MCP-1 which were ameliorated with ALA or PMX-53. TPD increased urinary C5a, which was decreased with ALA. In db/db mice, RS supplementation of the TPD reduced albuminuria and intestinal permeability. Gene set enrichment analysis showed an upregulation in the complement cascade in TPD db/db mice, which was normalized by RS. Similarly, RS supplementation reduced urinary C5a in TPD-fed db/db mice.

CONCLUSION: These results demonstrate that thermally processed diets lead to worsening albuminuria via activation of the complement cascade. These results also indicate that resistant starch supplementation may ameliorate some of the negative effects observed with excessive intake of thermally processed diets.

GASTROENTEROLOGY

29. BALLOON OCCLUDED RETROGRADE TRANSVENOUS OBLITERATION (BRTO) OF GASTRIC VARICES USING FOAM SCLEROSANT AND A REDUCED BALLOON INFLATION TIME: FEASIBILITY AND EFFICACY

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Introduction: Balloon-occluded Retrograde Transvenous Obliteration (BRTO) is recommended for secondary prevention of gastric variceal bleeding in the American Association for the Study of Liver Disease (AASLD) guidelines, as an alternative to TIPS. However, there is significant heterogeneity in how BRTO is performed, including how and how long to occlude the outflow venous shunt amongst other variables such as variceal size, flow rate, agent used, and preparation technique.

Many centres perform BRTO with a 24-hour balloon-inflation time of the outflow shunt. Previously, we successfully reported reducing the inflation time to 2 hours which resulted in similar efficacy to published methods. However, this still results in opportunity-cost for angiography suite time and resources.

Aims: We aimed to assess the efficacy of foam sclerotherapy and reducing balloon occlusion of less than 2 hours.

Methods: Retrospective single-centre analysis of BRTO procedures between July 2015 and February 2019 for isolated gastric varices in a non-acute setting, where inflation time was 2 hours or less.

Results: 6 patients underwent BRTO with a short inflation time, with a mean age of 66 years. The median balloon inflation and thus 3% athoxysclerol foam contact time was 30 minutes (range 30-60 minutes). Mean follow-up was 27 months. 4 of the 6 patients showed complete resolution of varices, while 2 of the 6 showed a partial response. There were no patients who did not show a response to treatment and no episodes of clinically significant upper gastrointestinal bleeding.

Conclusions: This technique using a shortened balloon occlusion time resulted in complete or partial clinical and technical success in all patients, and suggests that the threshold for initiation of gastric variceal thrombosis may be below 30 minutes. This timepoint may provide a balance between adequate balloon inflation, angiography room efficiency, and hospital resource allocation with resultant procedural opportunity cost.

30. RADIOLOGICALLY INSERTED GASTROSTOMY (RIG) AT A TERTIARY CENTER: PERIPROCEDURAL SAFETY INCLUDING RATIONALIZATION OF ANTIBIOTIC PROPHYLAXIS

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Background: Long-term percutaneous enteral nutrition forms an important part of treatment for patients with an inability to meet nutrient requirements orally. Radiologically inserted gastrostomy (RIG) is an alternative to the traditionally performed percutaneous endoscopic gastrostomy technique. However, there is marked heterogeneity in the way that RIG is performed. In addition, the role for antibiotic prophylaxis during RIG insertion is not clearly established.

Aims: This study aimed to assess the safety of RIG insertion using our technique including the role of prophylactic antibiotics in RIG insertion.

Method: Retrospective study over 5 years at a tertiary teaching hospital. Periprocedural or early complications within the first 2 weeks of the procedure were collected and correlated with the use of prophylactic antibiotics.

Results: A total of 116 patients met the inclusion criteria. 18-French tube was used in 96.6%. Prophylactic 1 g cefazolin was used in 70 patients with 1 case of infection. Procedures were performed without prophylactic antibiotics in 46 patients with 3 infections, p = 0.20.

There were 12 minor complications (10.3%) including 4 cases of infection, 3 of severe pain, 1 of minor bleeding, 2 of early dislodgement, and 2 of early leak/bypass of gastric contents around the tube. There were two major complications (1.7%) consisting of right gastric artery injury requiring embolization and gastric wall injury requiring laparotomy.

Conclusion: The technique used for RIG insertion at our institution results in a low complication rate. In addition, this study shows no significant difference in early peristomal infection rate with the use of antibiotic prophylaxis.

31. COMBINATION OF TWO FIBRES WITH DIFFERENT FERMENTABILITIES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS) INITIATED ON A LOW FODMAP DIET IS WELL TOLERATED AND PROMOTES DISTAL COLONIC FERMENTATION: A DOUBLE-BLIND, RANDOMISED, CROSS-OVER, FEEDING TRIAL

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A low FODMAP diet (LFD) in patients with IBS prevents excessive fermentation in proximal colon with reduction of symptoms, but may be associated with diminished distal colonic fermentation. In experimental animals, co-supplementation of poorly- with readily fermentable fibre pushes fermentation distally with associated promotion of distal colonic health.

AIM: To determine the effects of this approach in patients with IBS initiating a LFD on symptoms and on the colonic distribution of fermentation, using the telemetric Atmo gas-sensing capsule.

METHODS: Following a 7-day baseline, patients with IBS undertook three dietary interventions: LFD (~22 g/d fibre; ~2 g/d resistant starch [RS]); LFD + poorly-fermented sugarcane bagasse (SCB) (~31 g/d fibre; ~2 g/d RS); and LFD + SCB + fermentable RS (~32 g/d fibre; 13 g/d RS). Diets were administered for 14 days with ≥21-day wash-out between. End-points included gastrointestinal symptoms (via total IBS-Severity Scoring System score), differences in markers of carbohydrate fermentation (total faecal and plasma short-chain fatty acids [SCFA] concentrations), and regional colonic hydrogen production, evaluated per-quartile colonic transit.

RESULTS: 20 patients completed the trial. The diets were well-tolerated: median IBS-SSS scores at baseline of 305 reduced by >50 (i.e., of clinical significance) with no differences across the diets (P=0.335; linear effects model). Faecal SCFA were similar across the diets (P=0.868), but plasma SCFA was ~64% higher in the SCB/RS diet compared with LFD alone (P=0.028). Regional colonic hydrogen concentrations (n=12) tended to fall distally, being a median 1.7% with LFD in quartile 4, but more than doubled with the SCB/RS diet (3.5%; P=0.037).

CONCLUSION: Supplementation of a combination of poorly-fermented and fermentable fibre in patients with IBS does not alter symptomatic benefits of a LFD, but is associated with additional fermentation distally in the colon. This study demonstrates the novel power of the gas-sensing capsule in defining colonic luminal physiology.

32. AN OPEN-LABEL PILOT STUDY OF HYPERBARIC OXYGEN THERAPY FOR PERIANAL CROHN'S DISEASE

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Treatment options for refractory perianal Crohn's disease (pCD) are limited. Small case series suggest a clinical benefit with hyperbaric oxygen therapy (HBOT) but objective measures of response are seldom assessed.

Aim: To determine the clinical and MRI-based response of patients with complex pCD to HBOT.

Methods: Patients with severe active pCD on stable doses of anti-TNF therapy were recruited to an open-label study of twenty 90-minute sessions of HBOT at 2.4 ATA over 4 weeks. MRI response was assessed at week 8, and clinical and biomarker response at weeks 8 and 16.

Results: 8 men and 1 woman (median age 26) with a median duration of pCD of 58 months were recruited; 8 completed treatment. There was an improvement in pCD activity index from a median (range) of 10 (5-19) at baseline to 7 (2-14) at week 8 and 6 (2-15) at week 16 (p=0.02 for both). There was no significant difference in the MRI response according to the van Assche or modified van Assche scores: median of 15.5 and 15 at baseline, 12.5 and 11 at week 8 (p=0.75, p=0.13 respectively). There was no difference in median CRP from baseline to week 8 or 16: 4, 4, 6 mg/L (p=0.99, p=0.87) nor median faecal calprotectin: 113.5, 190, 116 ug/g (p=0.96, p=0.93).

Conclusion: HBOT for pCD appears to be well-tolerated, with clinical improvement seen at weeks 8 and 16. A significant improvement in MRI activity was not seen, possibly due to the small sample size and short follow up, or perhaps reflecting the severity and duration of disease at study entry; as with most therapy in Crohn's disease, earlier intervention is likely to be more successful. Extending the course of HBOT may provide additional benefit but the burden of prolonged treatment might be limiting.

HEALTH SERVICES AND PATIENT SAFETY

33. A LONGITUDINAL TIME AND MOTION STUDY QUANTIFYING HOW IMPLEMENTATION OF AN ELECTRONIC MEDICAL RECORD INFLUENCES HOSPITAL NURSES' CARE DELIVERY

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AIM: Many healthcare services have or are planning to digitally transform to keep pace with increasing Electronic Medical Record (EMR) functionality. The aim of this study was to objectively measure nursing care delivery before and following introduction of an EMR.

METHODS: An extensive program of work to expand an EMR across our health service using a 'big bang' methodology was undertaken. The program incorporated digital care delivery workflows including physiological observations, clinical notes and closed loop medication management. The validated Work Observation Method by Activity Timing (WOMBAT) method was applied to undertake a direct observational time and motion study of nurses' work in a major Australian hospital immediately prior to and six months following the introduction of a full clinical EMR.

RESULTS: Time and motion results were from observing approximately one week of nursing time pre (paper) to six months post (EMR) implementation. A non-significant 6.4% increase in the proportion of time spent on direct care was observed when using the EMR with a statistically significant increase in mean time per direct care task (2.5 min vs 3.9 min, p=0.001). The proportion of time spent on medication-related activities did not significantly change although the average time per task rose from 2.0 to 2.9 minutes (p=0.008). A significant reduction in proportion of time spent in transit and indirect care tasks when using the electronic workflows was reported. No statistically significant changes to the proportions of time spent on professional communication, direct care or documentation were observed.

CONCLUSIONS: Successful EMR implementation is possible without adversely affecting allocation of nursing time. Our findings from deploying a large scale EMR across all healthcare craft groups and workflows have described for nurses that an EMR enables them to spend longer with patients per direct care episode and use their time on other activities more effectively.

34. BARIATRIC SURGERY RESOURCE CONSUMPTION AND HEALTH OUTCOMES IN PUBLIC VS PRIVATE HEALTHCARE SETTINGS: 8 YEARS OF AUSTRALIAN DATA FROM THE NATIONAL BARIATRIC SURGERY REGISTRY

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Introduction: Bariatric surgery remains largely excluded from the Australian public health care system. There are persistent perceptions of obesity as a self-inflicted disease and that outcomes are therefore inferior. It is difficult to change this perception without objective, comparative data and are no comparative data available concerning outcomes in public and private bariatric surgery.

Hypothesis: The health resource consumption and health outcomes in a matched bariatric cohort is equal in both public and private hospitals.

Aims: To evaluate the health resource consumption and patient health gains achieved from bariatric surgery in private compared with public hospital settings.

Methods: We performed a retrospective cohort study of prospectively collected data from the Australian and New Zealand Bariatric Surgery Registry of 71,917 male and females aged 18 years and over who have undergone bariatric surgery between 23/02/2012 and 31/12/2020. The main outcome measures analysed were; change in health outcomes (type 2 diabetes (T2DM) and percentage total weight loss (%TWL)) and direct crude health resource consumption (hospital bed days (LOS), hospital readmissions, reoperations and intensive care (ICU) admission).

Results: Within one year of surgery T2DM had remitted in 72.67% of private healthcare patients compared to 64.2% of public bariatric surgery patients. Medication use for diabetes declined by 59.17%% for public and 56.87% of private patients

within one year following bariatric surgery. Private healthcare patients demonstrated a greater %TWL by a mean 3.05% (CI_{95}: 2.53 – 3.57, p value <0.001) compared to public hospital patients however there was no statistically significant difference in %TWL between the two health care settings after 5years.

The prevalence of unplanned ICU admissions were identical between health settings (0.16%). However unplanned readmissions and return to theatre within 90days of surgery were slightly increased in the public hospital setting (2.53% and 3.58%) compared to private hospitals (1.54% and 1.31%) respectively.

Conclusion: Bariatric surgery performed in the public hospital system offers similar, substantial weight loss and health outcomes when compared to the private health system.

35. ASSESSING THE BURDEN OF PACKAGING AND RECYCLABILITY OF SINGLE-USE PRODUCTS IN INTERVENTIONAL RADIOLOGY

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Background: With a shift to single-use products in interventional radiology (IR) centres for sterility and cost reasons, it is prudent to consider the burden of packaging and employ efforts to assess and reduce waste, as well as promote recycling wherever possible.

Aim: This study aimed to quantify the amount of waste in IR packaging and what proportion is recyclable.

Methods: A range of IR products were weighed using mass scales. Products were assessed for total weight, overall waste, and potentially recyclable waste. Waste was defined as any packaging which was not considered vital to the product to perform its duty and thus was for packaging or shipping purposes. Products were pooled into one of the following categories: catheters and sheaths, wires, needles, devices, coils, and packs/ancillary.

Results: 72 different products were collected from 26 manufacturers to represent a range of items. The weight of all products was 12,466 g (median 51, range 2-1600), and weight of waste was 6830.7 g (median 34, range 1.1-732). The weight of recyclable waste was 5202.2 g (median 11.5, range 0-701). There were median 2 waste packages per item (range 1-5). The proportion of waste of the overall weight was 54.8% and of this, 76% of all waste was potentially recyclable.

Conclusion: There is a significant burden of waste in manufactured IR products, and while a high proportion is recyclable, we encourage manufacturers of IR products and devices to consider alternative means of transport and packaging of products which will reduce the overall waste burden.

36. IMPROVING PATIENT ACCESS TO INTERPRETERS IN ACUTE AND EMERGENCY SETTINGS THROUGH VIDEO INTERPRETING

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BACKGROUND: Despite being endorsed by best practice standards, utilisation of interpreters at Alfred Health (AH) is suboptimal with only 31% of inpatients requiring an interpreter being provided one. Failure to address language barriers restricts access to safe, equitable and high quality patient-centred care. Video interpreting is a new and innovative mode of interpreting that may address this service gap. The aim of this project is to improve access to interpreting services through on-demand video interpreting and assess whether video interpreting is a viable mode for Alfred Health.

METHODS: AH partnered with Ezispeak, Coviu and Healthdirect to develop an integrated on-demand video interpreting add-on *Ezispeakhealth*. An observational study piloted *Ezispeakhealth* in emergency and acute general medical wards between 6 April to the 30 June 2021.

RESULTS: A total of 99 video calls were completed with 89% (n= 88) being serviced. Patient access to an interpreter increased by 12% in the emergency department (31% to 43%) and by 19% in the general medicine wards (55% to 74%). The on-demand target of an interpreter joining the call in 3 minutes or less was met by 66% (n= 58) of all calls. Staff (n=71)

feedback showed 95% satisfaction, 100% found it easy to use and better than using a telephone interpreter. Patient (n=14) feedback showed 93% satisfaction, 86% ease of use and 92% found it the same or better than telephone interpreting. Cost effectiveness analysis concluded that on-demand video interpreting is half the cost of using a pre- booked video interpreter or using an external face to face interpreter.

CONCLUSION: On-demand video interpreting increased patient access to an interpreter, is an efficient and effective modality with high satisfaction and acceptability by both staff and patients. Currently the on-demand video interpreting service continues at Alfred Health with plans to expand the service further.

37. COMPARING THE ACCURACY AND COMPLICATIONS OF PERIPHERALLY INSERTED CENTRAL CATHETER (PICC) PLACEMENT USING FLUOROSCOPIC AND THE BLIND PUSHING TECHNIQUE

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Introduction: Peripherally inserted central catheters (PICCs) offer a convenient long-term intravenous access option. Different methods exist for insertion including the use of continuous fluoroscopy for guidance, or bedside insertion techniques. The blind pushing technique is a bedside approach which involves advancing a PICC through the access sheath without imaging guidance, before taking a mobile chest radiograph to confirm tip position. Obtaining optimal position is a critical aim of PICC placement as malpositioned lines have been associated with higher complications including death.

Aim: Assess the accuracy of PICC placement by comparing the tip position and complications for lines placed under fluoroscopic guidance to those placed without fluoroscopic guidance.

Methods: The Radiology Information System was used to identify 100 continuous PICC insertions in each group (fluoroscopic and blind pushing) between 1 January and 12 May 2019. Patients were excluded if there was a known history of central venous occlusion/stenosis.

Results: In the fluoroscopic-guided group, 0% of the lines were malpositioned compared with 60% of the lines placed using the blind pushing technique, $p < 0.001$.

Fluoroscopic-guided PICC insertions were in place for a total of 2446 days and demonstrated 6 complications (2.45 complications per 1000 catheter-days). This compared with blind pushing technique PICC insertions which were in place for a total of 1521 days and demonstrated 18 complications (11.83 complications per 1000 catheter-days), $p = 0.004$.

Conclusion: The use of fluoroscopy for PICC placement leads to significant improvements in tip accuracy than for PICCs placed using the blind pushing technique. While the use of these imaging resources incurs cost and time, these factors should be balanced in order to offer patients the safest and most accurate method of line insertion.

38. MORAL DISTRESS AND BURNOUT IN HEALTHCARE WORKERS DURING THE COVID-19 PANDEMIC: QUANTITATIVE RESULTS FROM A LARGE AUSTRALIAN PUBLIC HOSPITAL SURVEY

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Moral distress(MD) arises where we need to act in ways that challenge our values. It has been described amongst first responders in military conflict, emergency services and frontline healthcare workers(HCW). Validated scales exist to measure MD in HCW e.g. Moral Distress Scale – revised(MDS-R). Ongoing exposure can lead to burnout. Soon after COVID-19 was first detected in Victoria, the Alfred Health Staff Wellness Survey was conducted to determine the impact of the pandemic on staff wellbeing.

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

METHOD: An online survey collecting demographic, wellbeing (depression, anxiety, PTSD), burnout (Professional Fulfillment Index) and MD data was offered to all staff across Alfred Health. Four Covid-19-based scenarios were added to the standard MDS-R(MDS). Statistical analysis, including non-parametric tests and general linear regression modelling(GLM), was undertaken in Jamovi and R.

RESULTS: 150 staff completed the MDS. Most were female(83%), nurses(44%) and allied health(37%) with equal numbers of staff working in frontline(49%) and non-frontline settings(51%). MD was significantly higher in staff in contact with Covid-19(p=0.008) and nurses(p=0.04). MD correlated with burnout(p<0.001). Highest in nurses(p=0.01) and allied health(p=0.01). Predictors in the GLM of MD were nursing profession(p<0.001) and burnout(p=0.02).

CONCLUSION: The impact of COVID-19 on staff burnout is significant, mediated via increases in moral distress, particularly in nurses and allied health staff. Initiatives to optimize staff wellbeing may consider measures aimed at mitigating the impact of moral distress.

39. SUPPORTIVE CARE IN PANCREATIC AND OESOPHAGOGASTRIC CANCERS – A QUALITATIVE INVESTIGATION

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Aim: Pancreatic and oesophagogastric (OG) cancers have a dismal prognosis and high symptom burden, with supportive care forming an integral component of cancer management. This study aimed to explore the supportive care experiences of people living with pancreatic and OG cancers and identify opportunities for improvement.

Methods: Semi-structured interviews were conducted with people living with pancreatic and OG cancers, and their caregivers, across Victoria, Australia during 2020. Participants were recruited through site Principle Investigators based at Alfred Health, Cabrini Health and Monash Health, as well as the Upper Gastrointestinal Cancer Registry. All interviews were thematically analysed and recruitment was ceased when thematic saturation had been achieved.

Results: Thirty patients and 11 caregivers were interviewed. Themes included: (i) supportive care needs across the cancer journey, (ii) management of supportive care needs, (iii) quality of supportive care, (iv) impact of COVID-19 (v) role of the caregiver, and (vi) opportunities for improvement. Predominant supportive care needs included diet-related issues, weight loss, pain and difficulties with activities of daily living, with support provided to varying levels of satisfaction. Many patients did not access supportive care services due to COVID-19. Caregivers played a critical role in supporting patients and desired support for themselves. Greater awareness of and access to available services, availability of a cancer care coordinator and higher quality and culturally sensitive support were perceived as opportunities for improvement.

Conclusion: Unmet needs are prevalent across the pancreatic and OG cancer journey, with supportive care provided to varying levels of satisfaction. Policy-makers and health services should promote and enable access to high-quality multidisciplinary support services for patients and their caregivers.

INFECTIOUS DISEASES AND INFECTION CONTROL

40. TECHNIQUE, RADIATION SAFETY AND IMAGE QUALITY FOR CHEST X-RAY IMAGING THROUGH GLASS AND IN MOBILE SETTINGS DURING THE COVID-19 PANDEMIC

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AIMS: To develop a technique to perform mobile chest X-ray imaging through glass during the COVID-19 pandemic, allowing the X-ray unit to remain outside of the patient's room.

METHODS: The X-ray attenuation of different glass in the hospital was assessed to determine the technique parameters required to account for the glass filtration and additional source to image distance (SID) compared with a standard portable chest technique. Image quality was scored and technical parameter information collated on images acquired during the first month of implementation. Radiation measurements were undertaken in a simulated set-up to determine the appropriate position for staff to ensure occupational radiation doses were kept as low as reasonably achievable.

RESULTS: The transmission of the X-ray beam through glass was approximately 50% or equivalent to one half-value-layer at the kilovoltages used. The SID ranged from 180 to 300 cm. A sample of 30 consecutive clinical chest X-ray images for 23 patients was obtained from three locations (ED, ICU at the Alfred and ED at Sandringham Hospital) where the through glass technique was used. The majority (67%) of images were acquired at 110 kV, with an average 5.5 mAs. Image quality was found to be acceptable or borderline in 90% of the images taken through glass. The average patient dose was 0.02 millisieverts (mSv) per image (range: 0.002 to 0.07 mSv). With staff positioned at greater than 1 m from the patient and at more than 1 m laterally from the tube head outside the room to minimise scatter exposure, air kerma values did not exceed 0.5 microgray (µGy) per image.

CONCLUSIONS: The chest X-ray through glass method has been implemented safely at Alfred Health and continues to be utilised. The technique effectively reduces the cleaning time of equipment, minimises PPE use and decreases the infection risk of radiographers.

41. ULTRAVIOLET GERMICIDAL IRRADIATION (UVGI) LAUNDRY PROTOTYPE

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INTRODUCTION: At the start of the COVID-19 pandemic, there were critical shortages of N95 filtering facepiece respirators (FFRs) worldwide. The efficacy of decontamination and re-use of respirators in healthcare using ultraviolet germicidal irradiation (UVGI) had not been widely assessed. For preparedness as a crisis capacity strategy, we developed an FFR UVGI decontamination "laundry" prototype.

METHOD: UVGI inactivates microorganisms to block DNA and RNA replication. A literature review was conducted to determine 1) the UVGI dose required to inactivate a single-stranded RNA viral load, 2) penetrability and effectiveness for FFRs, and 3) treatment effects on filtration, fit and strength of the FFR. Testing was undertaken to determine the irradiance level and intensity variation in the treatment field for two different UVGI devices, the appropriateness of UV measurement meters, and the orientation for hanging FFRs to maximise coverage and throughput while not compromising safety.

RESULTS: At the time of conducting the evaluation, UVGI inactivation of COVID-19 (SARS-CoV-2) on FFRs had not been confirmed directly. The general consensus in the literature was that a UVGI dose of ≥1 J/cm^2 was required, that laundry workflow needed consideration due to remaining bio-burden, verification of the marginally acceptable dose within each treatment cycle and zone was necessary, and the maximum possible dose for multiple treatment cycles per FFR must not be exceeded due to potential integrity loss. Strict protocols were required in terms of infection control (COVID-19 contaminated masks being handled) and radiation protection (due to the UV-C hazards). It was found that 1,200 FFRs could be processed every 24 hours with a treatment zone that exhibited 60% dose variation from the edges relative to the centre.

CONCLUSION: Although never implemented, the UVGI laundry prototype was an important exercise in risk mitigation and management using new applications of technology during a crisis.

42. FEASIBILITY OF BLUETOOTH LOW ENERGY WEARABLE TAGS TO QUANTIFY HEALTHCARE WORKER PROXIMITY NETWORKS AND PATIENT CLOSE CONTACT: A PILOT STUDY

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Background: The hospital environment is characterised by a dense network of interactions between healthcare workers (HCWs) and patients. As highlighted by the coronavirus pandemic, this represents a risk for disease transmission and a challenge for contact tracing. We aimed to develop and pilot an automated system to address this challenge and describe contacts between HCWs and patients.

Methods: We developed a bespoke Bluetooth Low Energy (BLE) system for the hospital environment with anonymous tags worn by HCWs and fixed receivers at patient room doors. Proximity between wearable tags inferred contact between HCWs. Tag-receiver interactions inferred patient room entry and exit by HCWs. We performed a pilot study in four negative pressure isolation rooms from 13 April to 18 April 2021 at the Alfred Hospital. Nursing and medical staff who consented to participate were able to collect one of ten wearable BLE tags during their shift.

Results: Over the four days, when divided by shift times, 27 nursing tags and 3 medical tags were monitored. We recorded 332 nurse-nurse interactions, for a median duration of 58 seconds [interquartile range (IQR): 39-101]. We recorded 45 nursing patient room entries, for a median 7 minutes [IQR: 3-21] of patient close contact. Patient close contact was shorter in rooms on airborne precautions, compared to those not on transmission-based precautions.

Conclusion: This pilot study supported the functionality of this approach to quantify HCW proximity networks and patient close contact. With further refinements, the system could be scaled-up to support contact tracing in high-risk environments.

43. AN EVALUATION OF INTERVENTIONS TO IMPROVE OUTCOMES FOR HOSPITALISED PATIENTS IN ISOLATION: A SYSTEMATIC REVIEW

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Background: Isolation is effective in preventing transmission of infectious disease. However, preventative and protective isolation in a single room with contact restrictions has been shown to have negative effects such as increased anxiety and poor physical outcomes.

Objectives: To summarise the evidence for the effects of interventions to improve patient safety and outcomes for patients in preventative and protective isolation.

Design: Systematic review (PROSPERO protocol registration-CD CRD42020222779).

Setting: Acute hospital

Participants: Intervention studies including patients in preventative or protective isolation in a single room.

Methods: MEDLINE, Global Health, CINAHL, PsycINFO, and EMBASE were searched from 1996-October 2020 using search terms for isolation and interventions. Eligibility screening and risk of bias assessment was conducted by two independent reviewers. One reviewer extracted data and was checked by another. Main outcomes were Quality of Life and mortality.

Results: We identified 16,698 references and included six studies: 1 randomised controlled trial (RCT), 2 non-RCTs, 2 pre-post intervention trials, and 1 case control study. The studies included adults (n=4 studies), or paediatric /adolescent patients (n=2 studies) with the average age ranging from 4-71 years. Samples sizes were small (range 10-49 participants) apart from one non-RCT including >600 participants. Interventions were music therapy (n=3 studies), psychological

counseling (n=2 studies) and exercise training (n=1 study). One study reporting on Quality of Life and found no change after exercise. None of the studies reported on mortality. Details reported about the intervention were limited and all included studies were assessed as high or serious risk of bias. Due to heterogeneous results no meta-analyses were performed.

Conclusions: There is a lack of high-quality evidence for effective comprehensive interventions to manage adverse effects associated with isolation. Future studies should investigate the effect of multi-component interventions using rigorous methods to improve outcomes for hospitalized isolated patients.

44. COMBINED EFFECTS OF HOST GENETICS AND DIET ON HUMAN GUT MICROBIOTA AND INCIDENT DISEASE IN A SINGLE POPULATION COHORT

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Co-evolution between humans and the microbial communities colonizing them has resulted in an intimate assembly of thousands of microbial species mutualistically living on and in their body and impacting multiple aspects of host physiology and health. Several studies examining whether human genetic variation can affect gut microbiota suggest a complex combination of environmental and host factors. Here, we leverage a single large-scale population-based cohort of 5,959 genotyped individuals with matched gut microbial shotgun metagenomes, dietary information and health records up to 16 years post-sampling, to characterize human genetic variations associated with microbial abundances, and predict possible causal links with various diseases using Mendelian randomization (MR). Genome-wide association study (GWAS) identified 567 independent SNP-taxon associations at genome-wide significance ($p<5.0\times10^{-8}$), which included notable strong associations with LCT ($p=5.02\times10^{-35}$), ABO ($p=1.1\times10^{-12}$), and $MED13L$ ($p=1.84\times10^{-12}$). A combination of genetics and dietary habits was shown to strongly shape the abundances of certain key bacterial members of the gut microbiota, and explain their genetic association. Genetic effects from the LCT locus on $Bifidobacterium$ and three other associated taxa significantly differed according to dairy intake. Variation in mucin-degrading $Faecalicatena$ $lactaris$ abundances were associated with ABO, highlighting a preferential utilization of secreted blood antigens as energy source in the gut, irrespectively of fibre intake. $Enterococcus$ $faecalis$ levels showed a robust association with a variant in $MED13L$, with putative links to colorectal cancer. Finally, we identified putative causal relationships between gut microbes and complex diseases using MR, with a predicted effect of $Morganella$ on major depressive disorder that was consistent with observational incident disease analysis. Overall, we present striking examples of the intricate relationship between humans and their gut microbial communities, and highlight important health implications.

45. PERIOPERATIVE ADMINISTRATION OF DEXAMETHASONE AND INFECTION: THE PADDI TRIAL

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BACKGROUND: The glucocorticoid dexamethasone prevents nausea and vomiting after surgery, but there has been ongoing concern that it may increase the risk of surgical site infection. This has limited the more widespread use of this otherwise cheap and effective medication.

METHODS: In this pragmatic, international, noninferiority trial, we randomly assigned 8880 adult patients who were undergoing nonurgent, noncardiac surgery of at least 2 hours' duration, with a skin incision length longer than 5 cm and a postoperative overnight hospital stay, to receive 8 mg of intravenous dexamethasone or matching placebo while under anesthesia. Randomization was stratified according to diabetes status and trial centre. The primary outcome was surgical-site infection within 30 days after surgery. The prespecified noninferiority margin was 2.0 percentage points.

RESULTS: A total of 8,725 participants were included in the modified intention-to-treat population (4372 in the dexamethasone group and 4,353 in the placebo group), of whom 13.2% (576 in the dexamethasone group and 572 in the placebo group) had diabetes mellitus. Of the 8,678 patients included in the primary analysis, surgical site infection occurred in 8.1% (354 of 4,350 patients) assigned to dexamethasone and in 9.1% (394 of 4,328) assigned to placebo (risk difference adjusted for diabetes status, −0.9 percentage points; 95.6% CI, −2.1 to 0.3; P<0.001 for noninferiority). The results for superficial, deep, and organ-space surgical-site infections and in patients with diabetes were similar to those of the primary analysis. Postoperative nausea and vomiting in the first 24 hours after surgery occurred in 42.2% of patients in the dexamethasone group and in 53.9% in the placebo group (risk ratio, 0.78; 95% CI, 0.75 to 0.82), P<0.001. Hyperglycaemic events in patients without diabetes were rare, 22 of 3787 (0.6%) in the dexamethasone group and in 6 of 3776 (0.2%) in the placebo group.

CONCLUSION: Dexamethasone was noninferior to placebo with respect to the incidence of surgical site infection within 30 days after nonurgent, noncardiac surgery. There is no evidence that dexamethasone increases the risk of surgical site infection – it can thus be used much more broadly.

46. *TREPONEMA PALLIDUM* DETECTION IN LESION AND NON-LESION SITES IN MEN WHO HAVE SEX WITH MEN WITH EARLY SYPHILIS: A PROSPECTIVE, CROSS-SECTIONAL STUDY

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Syphilis transmission is increasing, and precisely how *Treponema pallidum* is transmitted sexually from person to person is unclear.

AIM: To determine the frequency of *T. pallidum* shedding from potentially asymptomatic sites and in different stages of syphilis infection in men who have sex with men (MSM).

METHODS: We did a prospective, cross-sectional study in MSM, aged ≥ 18 years, with laboratory-confirmed primary, secondary, or early latent syphilis. Primary and secondary syphilis lesions were swabbed and non-lesion samples were collected via oral rinse, oral cavity swab, anal canal swab, urine, and semen. Samples were tested for *T. pallidum* PCR. The primary outcome was the proportion of men with *T. pallidum* detected from potentially asymptomatic sites: namely the mouth, anus, urethra, and semen.

FINDINGS: 200 MSM were included: 54/200 (27%) had primary syphilis, 93 (47%) secondary syphilis, and 53 (27%) early latent syphilis. *T. pallidum* DNA was detected in 48/200 (24%; 95% CI 18·3–30·5) men by oral rinse or oral lesion swab, or both, 24 with no oral lesions. Oral *T. pallidum* detection was most frequent in secondary syphilis compared with other stages (41/93 [44%] of *vs* 7/107 [7%]; p<0·0001), and in men with rapid plasma reagin titres ≥1:64 compared with lower titres (37/117 [32%] *vs* 11/83 [13%]; p=0·0026). *T. pallidum* was detected by anal canal swab or anal lesion swab, or both, in 45/196 (23·0%; 95% CI 17·3–29·5) men, ten with no anal lesions. Furthermore, *T. pallidum* was detected in 12/198 (6%) of urine samples and in 6/50 (12%) of semen samples.

CONCLUSION: Unrecognised oral and anal shedding of *T. pallidum* occurs in MSM with early syphilis, most frequently in secondary syphilis, suggesting this is the most infectious stage and that earlier detection and treatment of syphilis to prevent progression to the secondary stage might improve syphilis control.

47. ANALYSING THE IMPACT OF THE COVID-19 PANDEMIC ON PEOPLE LIVING WITH HIV

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The COVID-19 pandemic has placed unprecedented demands on healthcare and social support systems in Victoria. It is unknown what impact this has had upon people living with HIV (PLHIV), a cohort that already experiences higher than population levels of substance abuse, accommodation and food insecurity, mental health issues, and stigma.

We developed an online survey in collaboration with stakeholder groups addressing the impact of the COVID-19 pandemic on PLHIV in Victoria, Australia. The survey focuses on access to HIV-specific care and anti-retroviral therapy (ART), access to care for co-morbid conditions, overall quality of life and wellbeing, employment, housing, and food. The study was approved by the Alfred Health Human Research Ethics Committee (Ref: 65769). Participants were recruited through social media advertising and the Alfred Health and Monash Health infectious diseases clinics.

Since August 26th, 108 PLHIV have completed the survey. Most respondents identified as male (75%) and 51% were aged between 30 and 50 years. Twenty-five percent answered that the pandemic has negatively impacted their life, with 46% and 29% reporting negative impacts specifically regarding personal relationships and employment respectively. The survey demonstrated that PLHIV are worried about the potential impacts of the pandemic with 71%, 72%, and 54% of respondents reporting worrying about their physical health, mental health and finances respectively.

With regards to HIV-specific care, 93% reported that they were able to access HIV providers/specialists during the pandemic with 90% reporting use of telehealth appointments. Ninety-eight percent reported they were able to access ART. Increased alcohol intake was reported by 27% and weight gain was reported by 50%.

This study has identified several domains in which PLHIV have been negatively impacted during the pandemic. We believe this analysis will assist service providers in ensuring adequate provision of care and support is maintained to PLHIV.

INTENSIVE CARE

48. A DESCRIPTIVE INVESTIGATION INTO ALARM ACTIVATION IN AN AUSTRALIAN METROPOLITAN CRITICAL CARE SETTING

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BACKGROUND: Alarm fatigue is a phenomenon referring to clinicians being desensitised to the high volume of monitoring alarms. Alarm fatigue can impact the work environment, clinical care, and patient outcomes. Explorations and understandings of alarm fatigue have yet to be a focus of attention in the Australian context.

OBJECTIVES: To describe the prevalence and type of alarms activated in intensive care and cardiac units at the Alfred Health Hospital, Victoria, Australia.

METHODS: This was a descriptive observation study of patient monitoring data gathered over a 1-month timeframe (April 2019). Data from the Philips Healthcare IntelliVue® Patient Monitoring system were extracted. After classifying alarm types (clinical or technical) and levels of urgency (lower or higher priority), further descriptive analysis were conducted to quantify the most prevalent alarms.

RESULTS: 271,414 activated alarms were identified; the majority were clinical alarms (89.1%) compared to technical alarms (10.9%). More than half of clinical alarms were classified as high priority (55.1%); the most common were heart rate (36.7%) and premature ventricular contraction (18.8%). Technical alarms were predominantly ECG lead disconnection (89%). Alarm burden was highest in the acute cardiac unit (97.7 alarms per patient per day) compared to the intensive care unit (66.6 alarms per patient per day).

CONCLUSION: This study found that the burden of alarms compared to the literature was lower in the intensive care unit and higher in the cardiac units. Further research is recommended to further explore the phenomenon of alarm fatigue in other Australian critical care settings, especially to include multiple study sites and locations, and to examine the responses required by clinicians, and whether these responses are well calibrated to detect clinical deterioration and sentinel events.

MENTAL HEALTH

49. BURNOUT AND PSYCHOLOGICAL DISTRESS AMONGST HEALTHCARE WORKERS IN AN AUSTRALIAN HOSPITAL DURING THE COVID-19 PANDEMIC

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BACKGROUND: Data from previous pandemics have identified the impact of exposure to high levels of stressful and traumatic events whilst responding to public health emergencies. Healthcare workers appear to live with higher baseline levels of psychiatric comorbidity, and to be at particular risk of psychological distress when exposed to emergencies such as pandemics.

OBJECTIVE: To examine rates of psychological distress in healthcare workers exposed to coronavirus disease 2019 (COVID-19).

METHODS: A cross-sectional survey examining demographic, employment and mental health characteristics of 320 healthcare workers in Melbourne, Australia. Data was collected between April 16th and May 13th, 2020, closing at a time that social distancing practices were being relaxed in Australia.

RESULTS: 98 participants (31%) reported that they had a prior psychiatric or substance use disorder, and 84 participants (26%) reported they had previously sought treatment for mental health reasons. Senior medical staff were significantly less likely to report a prior psychiatric diagnosis compared with other professions.

A subset of participants screened positively as having moderate or severe symptoms of depression (21%), anxiety (20%), and PTSD (29%). 23 participants (8.1%) reported suicidal ideation on several days during the 2 week reporting period. Working in a high-exposure environment (ED, ICU, respiratory or ID medicine) was associated with greater endorsement of PTSD. Resilience, burnout, pre-existing psychiatric history, and profession were associated with symptoms of psychological distress.

CONCLUSION: Even in hospital departments that were relatively well-resourced, moderate to high levels of psychological distress were reported. Continued monitoring and support for staff mental wellbeing is warranted as the COVID-19 pandemic develops and its potential health and socioeconomic impacts become apparent.

50. STIMULATING INFLAMMATION AS A NOVEL TREATMENT FOR IMPULSIVITY DISORDERS?

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Impulsivity is the tendency of an individual to rash, premature and poorly thought through decisions or actions. This behavioural trait is associated with a number of neuropsychiatric conditions including attention deficit hyperactivity disorder (ADHD) and substance use disorder. Emerging evidence suggests inflammatory markers are altered in individuals with impulsivity, however it is currently unclear whether inflammation may causally contribute to the expression of this behaviour and whether we can target this process as a potential therapeutic approach.

Aim: To examine the effect stimulating inflammation using the mild pro-inflammatory monophosphoryl lipid A (MPLA) on the expression of impulsivity in rats expressing either innately high or low levels of this behaviour.

Method: Male Wistar rats were trained on the five-choice serial reaction time task (5CSRTT) to assess baseline levels of impulsive behaviour and divided into groups based upon their expression of either high or low levels of impulsivity (n=5/group). Rats were treated with MPLA (50mg/kg, 100mg/kg, i.p.) or vehicle using a cross-over, Latin-square design, 24 hours prior to behavioural testing, to examine the effect of stimulating inflammation on the expression of impulsive behaviour.

Results: MPLA significantly reduced impulsive responding, but only in highly impulsive rats (Treatment: $F_{(2,16)}$=3.943, p=0.0405; Impulsivity: $F_{(1,8)}$=12.94, p=0.007; Impulsivity x Treatment: $F_{(2,16)}$=3.852, p=0.0431, Two-way repeated measures ANOVA). Importantly no other measures of task performance were affected.

Conclusions: The mild pro-inflammatory MPLA reduced impulsive responding on the 5CSRTT, a commonly used measure of impulsivity in rats. This treatment however was only effective in animals with inherently elevated levels of this behaviour. The results suggest that manipulating inflammation may provide a novel mechanism through which to disrupt this behaviour with potential application for the treatment of neuropsychiatric disorders characterised by maladaptive impulsivity.

NEUROSCIENCE

51. CHRONIC INTRACEREBROVENTRICULAR ADMINISTRATION OF OREXIN-A ALTERS BEHAVIOURAL OUTCOMES FOLLOWING REPETITIVE MILD TRAUMATIC BRAIN INJURY IN ADULT RATS

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Sleep is an essential process for healthy brain function, whereas sleep disturbances are a common and debilitating symptom of many neurological diseases and disorders, including traumatic brain injury (TBI). Evidence supports a bidirectional relationship between sleep and neurological disorders, wherein disturbed sleep increases the risk of neurological disorders, while the hallmark symptoms of these diseases promote sleep deprivation. The orexinergic system is known for its role in the promotion of wakefulness, but it also contributes to the progression of many neurological disorders.

AIM: To examine the effect of orexinergic manipulation on repetitive mild TBI (RmTBI) outcomes in a rat model.

METHODS: Intracerebroventricular cannulas (ICV) were implanted into the lateral ventricle of adult male Sprague Dawley rats. After a recovery period, the rats were randomly assigned to receive either RmTBIs or sham injuries spaced two days apart. The rats underwent an acute behavioural test battery, including rotarod, openfield, and elevated plus maze (EPM), to confirm RmTBI-induced impairments. Rats were then randomly assigned to undergo intermittent ICV injections of either orexin-A or vehicle at the beginning of their sleep period. This resulted in 9 Sham+Vehicle, 10 Sham+Orexin-A, 10 RmTBI+Vehicle, and 11 RmTBI+Orexin-A. A week after initiation of the ICV injections, the rats began a second behavioural test battery, which consisted of EPM, novel context mismatch (NCM), rotarod, openfield, Y-maze, and hot-cold plate.

RESULTS: Contrary to the initial hypothesis, orexin-A administration after RmTBI exhibited a potentially neuroprotective effect, as demonstrated by significant (p<.05) improvements in openfield time in centre, rotarod average speed, and NCM novelty preference.

CONCLUSION: Orexin-A's anti-inflammatory effects and the orexinergic system's influence over areas involved in learning, memory, affect, and motor control may counteract the deleterious neurological effects of RmTBI and sleep disruption. This will be investigated further using immunohistochemical techniques to examine changes in the orexinergic and neuroinflammatory systems.

52. INVESTIGATING THE DORSOLATERAL PREFRONTAL CORTEX ON THE VESTIBULAR MODULATION OF SKIN SYMPATHETIC NERVE ACTIVITY

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Functional MRI, when combined with microelectrode recordings of skin sympathetic nerve activity (SSNA), has revealed strong coupling between BOLD signal intensity in the dorsolateral prefrontal cortex (dlPFC) and insular/vestibular cortices, in evoking SSNA. We have also shown that sinusoidal galvanic vestibular stimulation (sGVS) causes robust entrainment of SSNA at low frequencies. It is unknown how the dlPFC interacts with the vestibular cortices. Therefore, we investigated the

interactions between the dlPFC and vestibular system by studying the stimulation of the dlPFC on vestibular modulation of SSNA. It was hypothesised that the combined stimulation of the dlPFC and vestibular system will show decreased entrainment of SSNA, as the dlPFC will inhibit the vestibular system. SSNA was recorded via tungsten microelectrodes inserted into the ipsilateral common peroneal nerve in 21 awake human subjects. Bipolar binaural sGVS and transcranial alternating current stimulation (tACS) (±2 mA, 100 cycles, 0.08 Hz) were applied to the mastoid processes and right dlPFC (site F4, International 10-20 system), respectively; separately and concurrently. Illusory movements were produced during sGVS but not during tACS. Moreover, when sGVS and tACS was delivered concurrently, the vestibular illusions were eliminated. Cross-correlograms revealed that modulation of SSNA during combined stimulation was not significantly different (P > 0.05) to sGVS and tACS. As illusory movements were absent and entrainment of SSNA still remained, we believe that the dlPFC shares inhibitory pathways with the vestibular system at the cortical and/or subcortical levels, whilst maintaining excitatory contributions to the SSNA output nucleus, the medullary raphe. These observations emphasise the role of the dlPFC in regulating other cortices, as well as contributing to skin sympathetic outflow. Studies show that dysfunction within the dlPFC results in the hyperactivity of the limbic/vestibular system. Considering the commonality of vertigo in mood disorders, stimulating the dlPFC can serve as a future therapeutic tool.

53. METABOLOMICS PROFILING OF THE BRAIN REVEALED POTENTIAL MECHANISMS ASSOCIATING ALZHEIMER'S DISEASE TO HIGHER SEIZURE SUSCEPTIBILITY IN MICE

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Patients with Alzheimer's disease (AD) have up to 10-fold increased risk of epilepsy, compared to healthy age-matched controls. The underlying mechanisms leading to this increased risk are unclear.

AIM: The aim of this study was to identify metabolic pathways that are altered in the early stage of amyloid precursor protein (APP) pathology to generate hypotheses regarding mechanisms associated with increased epilepsy risk in AD. The highly seizure prone Tg2576 mouse model of AD is an appropriate tool for investigating changes in the brain associated to mutant APP overexpression.

METHODS: Metabolomics data was collected from the cortex and hippocampus of 6-month-old Tg2576 mice (n=7) along with their wild-type (WT) littermate (n=7) via liquid chromatography-mass spectrometry. Univariate, multivariate and pathway enrichment analyses were performed on MetaboAnalyst and the weighted correlation network analysis was performed using R.

RESULTS: We identified 11 metabolites (adjusted p < 0.05, variable importance in projection score > 1) significantly affected by APP overexpression in the cortex. Pathway enrichment analysis yielded 4 significantly enriched metabolic pathways from the cortex and 1 from the hippocampus (adjusted p < 0.05, pathway impact > 0.2). Network analyses identified 5 pathways that were significantly correlated (adjusted p < 0.05) with AD genotype. Our analyses suggest that oxidative stress, lipid and amino acid metabolism pathways, such as glutamate, could be affected early by the APP pathology.

CONCLUSION: This study identified changes in metabolite levels and metabolic pathways that are linked to the early stage of the APP pathology in AD. These findings provide new insights into the early disruption to the metabolic processes in the CNS caused by the APP pathology, which might increase the seizure susceptibility of the brain.

54. EFFECTS OF ABC TRANSPORTER MODULATION ON OLANZAPINE ENTRY INTO THE DEVELOPING BRAIN

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Introduction. Many women with psychiatric disorders at childbearing age would have to continue medicating throughout pregnancy and lactation as cessation is potentially dangerous for both mother and child. However, information on antipsychotic drug transfer into the developing brain is limited.

Aims. i) To measure the transfer of olanzapine across placental and blood-brain barriers in rats during development following acute (single dose) or chronic (multiple doses) treatment with the drug. ii) To determine age-related effects of co-administering a known ABC transporter modulator, digoxin (Koehn et al., 2019) on olanzapine permeability.

Methods. Sprague Dawley rats were injected i.p. with 0.15mg/kg of olanzapine containing a radioactive olanzapine tracer at 3 ages (E19, P4, adult). In acute experiments, a single olanzapine dose was injected 30min before sample collection. In chronic experiments, either digoxin (30μg/kg) or olanzapine (0.15mg/kg) were given daily for 5 days. Transfer of olanzapine in the blood, brain and CSF was measured using liquid scintillation counting.

Results. An age dependent decrease in transfer into brain (from 128%±26 at E19, n=21 to 84%±26 in adult, n=4) and CSF (from 81%±9 at E19, n=20 to 13%±4 in adult, n=4) was observed after exposure to olanzapine. In pregnancy, around 40% of the drug was transferred from the maternal blood to the fetal circulation. In chronic experiments in adults, brain transfer of the drug remained at a similar level to acute treatment (around 60%). However, transfer of olanzapine into the CSF, compared to acute exposure (13%±4, n=4), significantly increased after both repeated olanzapine (45%±6, n=3) or digoxin treatments (51%±2, n=3).

Discussion. The developing brain has lower ability to restrict drug entry, resulting in their increased levels. Use of ABC transporter modulators in conjunction with antipsychotic substrate drugs may not limit drug transfer into the brain or CSF at clinical doses.

Koehn et al (2019) F1000Res 8;1372

55. MODIFIED LOW RATIO KETOGENIC THERAPY IN THE TREATMENT OF ADULTS WITH SUPER REFRACTORY STATUS EPILEPTICUS

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BACKGROUND: Induction of ketosis by manipulation of nutritional intake has been proposed as an adjunctive treatment for super refractory status epilepticus (SRSE). However, the classical 4:1 ketogenic prescription may not meet the nutrition needs, in particular adequate protein provision for critically-ill adults.

AIM: To analyse the outcomes of adults with SRSE who received ketogenic therapy using a lower ratio ketogenic prescription.

METHODS: We reviewed patients aged ≥18 years with SRSE treated with ketogenic therapy between July 2015 and December 2020 at two tertiary teaching hospitals in metropolitan Melbourne, Australia. The ketogenic prescription for all patients was 2:1, grams of fat to non-fat grams, including 20-30% of total calories provided by medium chain triglycerides. Data collected from medical records included patient demographics, medication treatment, clinical outcomes, nutrition adequacy, blood glucose concentrations and blood beta-hydroxy-butyrate concentrations and instances of ketogenic therapy-related complications.

RESULTS: There were 12 patients (female=7) treated with ketogenic therapy for SRSE. Patients received between 4 to 8 anti-seizure medications and 1 to 5 anaesthetic agents, prior to commencement of ketogenic therapy. Blood beta-hydroxy-butyrate concentrations were variable throughout ketogenic therapy (median=0.5mmol/L, range: 0.0-6.1mmol/L). SRSE resolved in 10 cases (83%) after a median of 9 days (range 2-21 days) following commencement of ketogenic therapy. Ketogenic therapy-associated complications were reported in 5 patients, leading to cessation of ketogenic therapy in 2 patients. Four patients died in hospital; the remaining 8 patients required transfer to inpatient rehabilitation facilities.

CONCLUSION: Despite the challenges in achieving and maintaining ketosis in the critical care setting, a standardised low ratio ketogenic therapy, including medium chain triglycerides can be effective for adults with SRSE. Further studies are required to determine the optimal timing, nutrition prescription and duration of ketogenic therapy for SRSE treatment.

56. FAST/SLOW KINDLING RATS: A MODEL TO EXAMINE THE RELATIONSHIP BETWEEN EPILEPSY AND ALCOHOL USE DISORDER?

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One in five people with epilepsy are also diagnosed with alcohol use disorder. It is unclear why the prevalence of this neuropsychiatric condition is increased in people with epilepsy; however, may relate to shared psychological profiles between these two disorders, including anxiety, impulsivity, and sensation-seeking. Therefore, identifying a rodent model of shared risk for both epilepsy and alcohol use disorder is necessary to examine this relationship's neurobiological and psychological underpinnings.

AIM: To determine if epilepsy prone, FAST kindling strain of rats, demonstrate differences in alcohol consumption when compared to an epilepsy-resistant strain, SLOW kindling rat, and determine if this is related to anxiety, impulsivity, and sensation-seeking behaviour phenotype.

METHOD: FAST and SLOW adult male rats (n=8/strain) were assessed for anxiety using the elevated plus-maze and the 5-choice serial reaction time task measuring impulsivity, followed by the two-bottle choice task to measure alcohol consumption. A separate cohort of rats (n=6/strain) were assessed for anxiety and novelty reactivity using the open field test.

RESULTS: FAST rats demonstrated greater anxiety-like behaviour than the SLOW rats on the elevated plus maze (time in open arm; t_{21}=4.871, p=.007), a finding confirmed by behaviour in the open field (distance travelled in the centre zone; t_{10}=2.352, p=.041). FAST rats showed lower sensation-seeking behaviour, demonstrating reduced exploratory behaviour on this task (t_{10}=3.395, p-.007). No strain differences were observed for impulsivity (t_{18}=1.730, p=.4552) or alcohol consumption (t_{21}=.7452, p=.859).

CONCLUSION: While rats prone to the development of epilepsy (FAST) showed elevated anxiety-like behaviour, no difference in voluntary alcohol consumption was observed when compared to the epilepsy resistant strain (SLOW). These strains of rats, while useful for understanding the neurobiology underlying the relationship between epilepsy and anxiety, do not appear to model shared risk for co-morbid epilepsy and alcohol use disorder.

57. ENTRY OF ANTIEPILEPTIC DRUGS, VALPROATE AND LAMOTRIGINE, INTO DEVELOPING BRAIN IN A RAT MODEL OF EPILEPSY (GAERS)

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Aims: Babies in utero and breastfed newborns may be exposed to maternally ingested antiepileptic drugs such as valproate (VPA) and lamotrigine (LTG) when such medications are required to manage seizures. Since potential deleterious effects of drugs on the highly sensitive developing brain are not well understood, this study utilised an established animal model of absence epilepsy, Genetic Absence Epilepsy Rat from Strasbourg (GAERS), to 1) determine transfer of VPA & LTG across placenta; and 2) to investigate entry of both drugs into cerebrospinal fluid (CSF) and brain of pups at different developmental stages.

Methods: GAERS at embryonic day (E) 19, postnatal day (P) 4 and 7-8 weeks (adults) were administered an intraperitoneal injection of clinically relevant doses of valproate (30 or 100 mg/kg) or lamotrigine (6 or 20 mg/kg) traced with respective [3H]-labelled drugs. 30 minutes later blood plasma, CSF and brain cortex were collected. In anaesthetised pregnant rats, samples from individual pups were serially collected along with maternal blood samples. Radioactivity in all samples was measured with liquid scintillation counting and transfer across barriers expressed as ratios of radioactivity in fetal over maternal plasma (placental barrier) or in CSF or cortex over plasma (brain barriers) (Mean±SD).

Results:

1) Placental transfer of VPA was around 44%.

2) Both antiepileptic drugs showed age-related decreased entry into the CSF and brain. CSF ratios of VPA decreased from 118.7±10.8% in E19 to 21.1±4.6% in adults and in the brain cortex from 75.6±11.6% to 21.8±3.4%. Entry of LTG was higher in E19 compared to P4 (CSF, 79.7±26.4% and 12.6±2.7%; cortex, 77.8±17.7% and 32.7±2.9% respectively).

Conclusions:

1) About half of maternal plasma concentration of VPA transferred to the fetus, indicating a significant degree of protection provided by the placenta.

2) Brain entry of both antiepileptic drugs was higher earlier in development, especially for VPA.

58. HEALTH BURDEN OF THE EPILEPSY TREATMENT GAP IN AUSTRALIA

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Though antiseizure medications help many epilepsy patients achieve seizure freedom, a "treatment gap" exists in Australia that is much higher than anticipated and inconsistent with previous systematic reviews. Assessment of its consequences can determine if narrowing this gap is worthwhile, with the potential to reshape clinical decision-making and improve healthcare resource allocation.

AIM: To assess the mortality, morbidity and healthcare utilisation of newly diagnosed epilepsy patients receiving deferred or no treatment.

METHODS: We performed linkage analysis of patients with newly diagnosed epilepsy between 1999 and 2016 with statewide healthcare databases to extract hospital admission, ambulatory psychiatric care, and mortality data from 1970 to 2019. Data were compared between patients receiving immediate, delayed and no treatment. Analyses were performed at up to 5 years post-diagnosis, adjusted for seizure type, age at onset, sex and baseline comorbidity.

RESULTS: Of 603 patients with newly diagnosed epilepsy (61% male), 181 (30%) received delayed or no treatment after a median follow-up of 6.8 years. Incidence of seizure-related healthcare utilisation in the one year post-diagnosis was higher for those immediately treated (318 per 1,000 person years) compared to those untreated (29 per 1,000 person years; p<0.001). No difference in risk of developing new comorbities was found between immediate treatment and untreated groups (IRR=0.82; p=0.63). A total of 70 (11.6%) patients died during 5 years' follow-up. There were no differences in overall mortality between immediate treatment and delayed treatment (HR=1.18; p=0.69) or untreated groups (HR=1.59; p=0.45).

CONCLUSION: Despite 30% of newly diagnosed epilepsy patients receiving deferred or no treatment in Australia, this was not associated with significantly increased morbidity or mortality versus patients treated immediately. Patients with newly diagnosed epilepsy who require immediate treatment have a high rate of seizure-related hospital admissions and further research to better understand the reasons for this is warranted.

59. PREGNANCY-RELATED RELAPSE IN NATALIZUMAB, FINGOLIMOD AND DIMETHYL FUMARATE-TREATED WOMEN WITH MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disease of the CNS and a leading cause of neurologic disability among young people. MS is typically diagnosed in women in their twenties and thirties. Pregnancy and family planning are important life events in this group, and pose special challenges for MS treatment planning.

Objective: To investigate pregnancy-related disease activity in a contemporary MS cohort.

Methods: Data were obtained from the MSBase Registry. Term/preterm pregnancies conceived from 2011-2019 were included (modern cohort). Annualised relapse rates (ARR) were calculated before, during and after pregnancy. Predictors of intrapartum and early postpartum relapse were determined by clustered logistic and Cox regression analyses, respectively.

Results: We included 1640 pregnancies from 1452 women. Disease-modifying therapy (DMT) used in the one-year preconception included natalizumab (n=219), fingolimod (n=147), dimethyl fumarate (DMF; n=57) and low-efficacy therapies (n=845). Preconception ARR by DMT class used before conception were: natalizumab, 0.29 (95% CI 0.22-0.37); fingolimod, 0.37 (0.28-0.49); DMF, 0.24 (0.13-0.41); low-efficacy, 0.29 (0.25-0.33); and none, 0.24 (0.19-0.31). Among women who used fingolimod or natalizumab, ARR increased during pregnancy. Intrapartum ARR decreased in preconception DMF, low-efficacy or no DMT groups. ARR spiked after delivery across all DMT groups. Natalizumab continuation into pregnancy reduced the odds of relapse during pregnancy (OR 0.76 per month [0.60-0.95], p=0.017). DMT re-initiation with natalizumab protected against postpartum relapse (HR 0.11 [0.04-0.32], p<0.0001). Breastfeeding women were less likely to relapse (HR 0.61 [0.41-0.91], p=0.016).

Conclusion: Women with MS prescribed natalizumab or fingolimod preconception had higher rates of intrapartum and postpartum relapse. In women considered to be at high relapse risk, use of natalizumab before pregnancy and continued up

to 32-34 weeks gestation, with early re-initiation after delivery is an effective option to minimise relapse risks. Strategies of DMT use have to be balanced against potential foetal/neonatal complications.

OBESITY

60. MECHANISM OF WEIGHT LOSS FOLLOWING SLEEVE GASTRECTOMY: ACCELERATED TRANSIT TO THE SMALL BOWEL AND CO-DEPENDENT CLEARANCE

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The mechanism of weight loss following sleeve gastrectomy (SG) is unclear, despite over 300,000 procedures being performed worldwide and >25,000 in Australia annually. Alterations in gastric emptying and transit are postulated to be associated with key outcomes.

AIM: To assess the nature of gastric emptying associated with weight loss, using scintigraphy following SG.

METHODS: Participants post-SG were categorised into optimal (n=30) and poor (n=68) weight loss cohorts. All patients underwent liquid contrast barium swallow, demonstrating normal anatomy. All participants underwent a protocolised nuclear scintigraphy designed specifically to characterise the post SG state.

RESULTS: Demographic data between SG groups are as follows; age was 47.7 vs 46.4 years (p=0.572), excess weight loss was 64.7% vs 32.0 (p=0.001), total body weight loss was 26.2% vs 14.3% (p=0.001) and duration from surgery was 11.6 months vs 58.4 months (p=0.001).Scintigraphy showed delayed gastric emptying (36.89 ± 20.16 vs 19.60 ± 4.68 minutes s, $p=0.001$), with majority of meal accumulated in the proximal stomach ($44.50 \pm 15.12\%$ vs $36.62 \pm 12.22\%$ p=0.014) on initial acquisition (10mins post prandial). A greater proportion of meal entered the small bowel ($38.40 \pm 18.13\%$ vs $27.63 \pm 12.43\%$ in poor weight loss, p=0.001). Counts observed in the small bowel at the conclusion of the scan (90-minutes) was significantly less in poor weight loss ($86.71 \pm 13.28\%$ vs $95.09 \pm 3.89\%$, p<0.001), with a greater amount of meal retained in the stomach (12.31 ± 12.87 vs $4.21 \pm 3.04\%$, p=0.001).

CONCLUSIONS: Marked differences in gastric emptying and transit were identified across a spectrum of specific variables that differentiate patients achieving satiety and weight loss following SG. Strong association of regulated gastric clearance and rapid intestinal delivery are key mechanisms of action in SG. Nuclear scintigraphy now represents a unique diagnostic tool in patients who fail to respond to SG.

OTHER

61. SURGEON ENGAGEMENT WITH PATIENT-REPORTED MEASURES IN AUSTRALIAN AND NEW ZEALAND BARIATRIC PRACTICES

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Patient-reported measures are an important metric in the reporting of patient experience, quality of life, and psychosocial well-being across multiple disease classifications and healthcare systems. Despite their relevance and importance, there remains limited uptake of these measures in bariatric clinical practice.

AIM: To determine the characteristics and distribution of patient-reported measures employed within bariatric practices across Australia and New Zealand, and to examine clinician engagement with the development of centralised measures by the bi-national Bariatric Surgery Registry.

METHODS: A comprehensive cross-sectional survey was designed for the purposes of this study. All surgeons contributing to the Bariatric Surgery Registry were invited to participate, with responses collected between May and September 2020.

RESULTS: Survey responses were received from 64 participants (36% response rate) reporting on 120 public and private bariatric practices across Australia and New Zealand. The majority of bariatric practices reported no collection of any patient-reported measure (78 of 120; 66.7%), citing insufficient staff time or resources (64 of 186; 34.4%) or being unaware of available PRMs (43 of 186; 23.1%) as primary barriers to their collection. Participants indicated the collection of patient-reported data by the Registry would be useful (47 of 57; 72.3%), highlighting the most valuable application would be a monitoring tool, facilitating increased understanding of patient health needs and quality of life, increased recognition and reporting of symptoms, and enhanced patient-physician communication.

CONCLUSIONS: Despite an overall lack of patient-reported measure use in bariatric practices across Australia and New Zealand, and evident barriers to their implementation, there is a general consensus that such data would be valuable in clinical practice. The Australian and New Zealand Bariatric Surgery Registry represents an avenue to harmonise the widespread collection of meaningful patient-reported measures, providing important patient-centred data while removing implementation barriers faced by individual surgeons and hospitals.

62. HOSPITAL-BASED OUTCOMES OF PATIENTS MANAGED IN A LUMBAR SPINE ORTHOSIS FOLLOWING TRAUMA

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INTRODUCTION: Orthoses use following lumbar spine fracture is controversial with a recent systematic review reporting that orthoses may lead increased length of stay (LOS) with no improvement in pain or function. The aim of this study is to review our patients managed with a lumbar spine orthosis in terms of function and hospital-based outcomes at discharge.

METHODS: Data including baseline demographics, discharge destination, hospital LOS, readmission, and functional outcomes were collected for patients admitted to The Alfred trauma ward managed with a lumbar spine orthosis. Patient self-reported EQ5D- 5L (5 domains) were collected on discharge.

RESULTS: 63 patients were managed in a lumbar spine orthosis on the trauma ward between November 2020 - April 2021, with 37 (59%) being male and 25 (40%) being ≥65 years. 20 (32%) were compensable and 8 (13%) were deemed frail. Median LOS was 5.7 days (IQR 3.1-9.3). 48 patients (76%) were discharged directly home including 76% ≥65 years. Living alone was not associated with being discharged directly home (p value 0.59). 3 patients (0.2%) were readmitted, all from home. In terms of EQ5D discharge outcomes, half the patients reported moderate or greater issues with self-care and pain, with anxiety and mobility issues being less prevalent (36% and 18% respectively).

CONCLUSION: Lumbar spine orthoses are commonly used to manage spinal fractures with most patients achieving discharge directly home, irrespective of age, frailty or living arrangements. Further review of data to determine fracture types and longer terms outcomes will be undertaken.

63. AUDIT OF LUNG TRANSPLANT PALLIATIVE CARE CLINIC AT ALFRED HEALTH

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Background: Lung transplant candidates experience significant symptom burden and poor quality of life, while recipients may develop graft rejection/failure complications and secondary malignancies. A specialist palliative care (PC) clinic was established at Alfred Health in 2016 to improve the quality of life of lung transplant candidates, recipients, and their family caregivers.

Aim: To characterise the patients seen in the lung transplant palliative care (LTx PC) clinic at Alfred Health

Design: Single-centre audit of hospital medical records of all patients attending the LTx PC clinic at Alfred Health between September 2016 to April 2021. The mean follow-up period was 6 months, and the average clinic attendance was 5 visits with a maximum of 13 attendances. Data were analysed using descriptive statistics on Excel, and hypothesis testing was performed using GraphPad Prism 9.

Results: 67 patients attended the LTx PC clinic during the study period. Their median age was 62 (51-67) and 49% were male. The majority (n=46, 69%) were transplant recipients. The most common primary diagnoses were chronic obstructive pulmonary disease (n=22, 67%) and chronic lung allograft dysfunction (n=19, 27.5%). Most of the patients (n=51, 76%) had died within 12 months of their first clinic appointment. Interestingly, recipients were more likely to die during clinic follow up (P=0.033). Only 10% had an advance care directive documented (n=7). Less than half (n=30, 45%) were referred to specialist community PC services.

Conclusions: Patients seen in the LTx PC clinic at Alfred Health were mostly transplant recipients and had a poor prognosis, but only a minority had documented advance care directives or were referred to specialist community palliative care services.

64. HOSPITAL STAFF WELL-BEING DURING THE FIRST WAVE OF COVID-19: STAFF PERSPECTIVES

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The highly infectious novel coronavirus spread to become a global pandemic by early 2020. Health services were required to make significant, rapid changes to service delivery in order to care appropriately for patients affected by the virus, while simultaneously protecting other patients and staff from infection.

AIM: To determine the impact of working during the early stage of the COVID-19 pandemic on the well-being of staff at one 600-bed acute hospital in metropolitan Melbourne, Australia.

METHODS: This study reports the qualitative data from an on-line survey of clinical staff working at one acute hospital between April 16th and May 13th, 2020 and captures a snapshot of clinical staff opinions before the subsequent second wave of cases. Responses to five free-text questions were analysed using inductive content analysis.

RESULTS: 321 medical, nursing, allied health, and non-clinical staff responded to the survey. Respondents reported a significant amount of anxiety, fear and uncertainty related to the pandemic, from the perspectives of work, home, family and community. They reported feeling confused by inconsistent messages received from government, hospital executive, managers and media. Seven themes were identified: 1) worrying about patient care, 2) changed working conditions, 3) working in the changed hospital environment, 4) impact of the pandemic, 5) personal isolation and uncertainty, 6) leadership and management and 7) additional support needed for staff. Despite the pandemic being comparatively well-controlled in Australia, all disciplines reported a high degree of anticipatory anxiety.

CONCLUSION: Appropriate, targeted mental health care is essential to support healthcare workers exposed to the trauma of the pandemic. Healthcare staff, including those working from home, need both practical and psychological support and regular clear communication from leaders to minimise anxiety, promote wellbeing, foster resilience, and ensure they are in a strong position to deal with the health crisis as it continues to evolve.

65. PREVALENCE OF UTERINE FUNDAL PRESSURE DURING THE SECOND STAGE OF LABOUR FOR WOMEN GIVING BIRTH IN HEALTH FACILITIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Elise Farrington[1,2], Mairead Connolly[1,2], Laura Phung[1,2], Alyce N. Wilson[1], Liz Comrie-Thomson[1], Meghan A. Bohren[3], Caroline S.E. Homer[1], Joshua P. Vogel[1,3]

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Uterine fundal pressure involves a birth attendant pushing on the woman's uterine fundus to assist vaginal birth. It is used in some clinical settings, though guidelines recommend against it.

AIM: To determine the prevalence of uterine fundal pressure during the second stage of labour for women giving birth vaginally at health facilities.

METHODS: The population of interest were women who experienced labour in a health facility and in whom vaginal birth was anticipated. The primary outcome was the use of fundal pressure during second stage of labour. MEDLINE, EMBASE, CINAHL and Global Index Medicus databases were searched for eligible studies published from 1 January 2000 onwards. Meta-analysis was conducted to determine a pooled prevalence, with subgroup analyses to explore heterogeneity.

RESULTS: Eighty data sets from 76 studies (n=898,544 women) were included, reporting data from 22 countries. The prevalence of fundal pressure ranged from 0.6% to 69.2% between studies, with a pooled prevalence of 23.2% (95% CI 19.4–27.0, I^2=99.97%). There were significant differences in prevalence between country income level (p<0.001, prevalence highest in lower-middle income countries) and method of measuring use of fundal pressure (p=0.001, prevalence highest in studies that measured fundal pressure based on women's self-report).

CONCLUSIONS: The use of uterine fundal pressure on women during vaginal birth in health facilities is widespread. Efforts to prevent this potentially unnecessary and harmful practice are needed.

66. PERCUTANEOUS HAEMATOMA DRAINAGE: 10-YEAR EXPERIENCE AT A TERTIARY INSTITUTION

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Purpose: Percutaneous haematoma drainage is a common procedure performed by radiologists. These haematomas may be secondary to trauma, post-operative or supratherapeutic anticoagulation. This retrospective study aims to evaluate the outcomes of these drainages, including rate of re-accumulation or repeat intervention required.

Methods and Materials: The study included patients who fit the inclusion criteria who had a radiologically drained haematoma over the past 10 years at our tertiary center. These were identified through a retrospective search of the Alfred Health REASON Cohort Discovery Platform. Data was collected from the picture archiving and communications system and the electronic medical record, including location, size and cause of haematoma, symptoms, method of drainage, and anticoagulation profile.

Results: 224 patients were identified, of these 130 patients were confirmed to have undergone a radiologically guided haematoma drainage. 121 of these were performed under ultrasound guidance and 9 under CT guidance. Post-operative haematomas were the most common reason for drainage, while lower limb haematomas were the most common body region.

34 patients (26.2%) had a re-accumulation of their collection, with 61.8% of these either having a repeat percutaneous drainage or other surgical intervention. There was a statistically significant difference with drainages performed via needle aspiration, with 75% of these patients not requiring a repeat intervention, compared to 69.8% of those who had a drain tube inserted (p=0.049).

There were no statistically significant differences in the platelet count, international normalized ratio (INR), or anticoagulation profiles and all patients who had a re-accumulation had their peri-procedural anticoagulation appropriately managed.

17.7% of the aspirates grew a positive culture.

Conclusion: The outcomes of percutaneous haematoma drainages are overall favorable. Careful patient selection and method of drainage improve the rate of success. Drainages also provide useful information to clinicians regarding the nature of the collection to help guide future clinical management.

67. VALIDATING A NOVEL REGULATOR OF HEPATIC LIPID METABOLISM

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Non-alcoholic fatty liver disease (NAFLD) affects one third of the Australian population and has a large genetic basis. Despite extensive efforts, findings from human genome-wide association studies (GWAS) explain only a small proportion of the estimated 30% heritability of NAFLD. An alternative approach to human GWAS is to exploit the inherent genetic diversity of a panel of inbred mice. We previously integrated genetic data with liver proteomic and liver and plasma lipidomic data from 107 genetically diverse strains of mice from the Hybrid Mouse Diversity Panel (HMDP) to interrogate hepatic lipid metabolism. Utilising a range of bioinformatic approaches, we identified several known and novel targets that regulate hepatic lipid metabolism. The abundance of one target, which we named Novel Lipid Regulator (NLR), was negatively associated with the abundance of hepatic cholesteryl esters (CE) as well as numerous triacylglycerol (TAG) species across HMDP strains. In subsequent validation studies, we characterised a novel mouse model of liver specific NLR attenuation (NLR[LKO]) in male mice fed a standard chow diet or high fat high cholesterol (western) diet for 16 weeks (n=12/group). In mice fed a chow, but not a western diet, NLR[LKO] was associated with a marked increase in hepatic TAG and CE abundance. Moreover, there was a particular enrichment in short-chain TAGs. Consistent with this, we observed an elevation in hepatic mRNA expression of *de novo* lipogenesis genes, stearoyl-CoA desaturase-1 (*Scd1*; 5.7-fold; $P<0.001$) fatty acid synthase (*Fasn*; 2.9-fold; $P<0.01$) and acetyl-CoA carboxylase 1 (*Acaca*; 2.7-fold; $P<0.01$), We also observed an increase in the protein abundance of the rate limiting enzyme in the *de novo* lipogenesis pathway, acetyl-CoA carboxylase (ACC; 1.8-fold; $P<0.0001$) and the low-density lipoprotein receptor (LDLR; 2.4-fold; $P<0.0001$). Collectively, these findings strongly implicate NLR as a novel regulator of cholesterol and TAG metabolism in a diet-dependant manner.

68. LEVELS OF PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR DURING AND AFTER HOSPITALISATION: A SYSTEMATIC REVIEW

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

Objective: To systematically review and synthesize the evidence on physical activity and sedentary behaviour during and after hospitalisation.

Data Sources: Electronic databases and reference lists of relevant articles were searched from year 2000 to April 2020

Study Selection: Studies which continuously monitored physical activity and/or sedentary behaviour in hospitalised adults across two settings (i.e. without a break in measurement between settings). Monitoring could occur from an acute to a subacute/rehabilitation hospital setting, an acute setting to home, or from a subacute/rehabilitation setting to home.

Date Extraction: Data extraction and methodological quality assessments were independently performed by two reviewers using standardised checklists.

Data Synthesis: 16 of 5564 studies were included, and comprised of heterogenous patient populations. All studies monitored patients with either an accelerometer and/or pedometer, and reported a variety of measures including steps per day, sedentary time, and activity counts. The majority of studies (13/16) showed patients engaged in 1.3 to 5.9 times more physical activity and up to 67% less daily sedentary behavior at home after discharge from acute or sub-acute settings.

Conclusions: Patients engaged in more physical activity and less sedentary behaviour at home compared to both the acute and sub-acute hospital settings. This may reflect the natural course of recovery or the impact of setting on activity levels. Enabling early discharge home through the implementation of home-hospitalisation models may result in increased patient physical activity and reduced sedentary behaviour. Further experimental studies are required investigating the impact of home-based models of care on physical activity and sedentary behaviour.

69. LEFT COMMON ILIAC VEIN COMPRESSION IN PATIENTS WITH MAY-THURNER SYNDROME: A 10-YEAR RETROSPECTIVE STUDY IN AN AUSTRALIAN COHORT

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Background: May-Thurner syndrome (MTS) is a clinical syndrome of left leg iliofemoral deep venous thrombosis (DVT) associated with an anatomic variation. It was first described by Wanke and Kiel in 1950 as an operative finding in patients with chronic thrombosis of the pelvic veins. In 1957, May and Thurner characterised compression of the left common iliac vein (LCIV) between the crossing right common iliac artery and the vertebral body of L5 in cadaveric specimens. However, LCIV compression in patients with MTS has been sparsely assessed in imaging literature, and there is conflicting evidence on what constitutes a "narrow" LCIV on computed tomography (CT).

Aims: This study aimed to assess what diameter constitutes clinically-significant LCIV compression on CT in patients with MTS.

Methods: The study covered a 10-year period from 2010 to 2020. Patients were identified through the Radiology Information System when CT scan was performed for any of the following: a diagnosis of MTS, left leg swelling due to DVT, left iliac/femoral DVT. The minimum LCIV diameter on CT in this cohort was compared to 100 asymptomatic controls, and 27 age-and-gender-matched controls.

Results: 19 patients were included. Mean LCIV diameter in the MTS group was 3.82mm (SD 1.38), control group (mean 7.17mm SD 3.19, p<0.0001) and matched control group (mean 6.86mm SD 3.03, p=0.007). Statistical threshold analysis showed that for patients with MTS, a LCIV diameter of 4.7mm or less had an 87.5% sensitivity and 72.7% specificity for the diagnosis.

Conclusions: Patients with MTS had lower mean LCIV diameter than asymptomatic matched controls. However, some minimum diameters less than 4.7mm were also seen in the control group. As such, stenosis alone does not constitute a diagnosis of MTS. The 4.7mm threshold can be used when suggesting the diagnosis of MTS on CT.

70. METFORMIN AS A POTENTIAL DISEASE-MODIFYING DRUG IN OSTEOARTHRITIS: A SYSTEMATIC REVIEW OF PRE-CLINICAL AND HUMAN STUDIES

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Objectives: Osteoarthritis causes significant pain and disability with no approved disease-modifying drugs. Metformin, an anti-hyperglycaemic drug, also has pleiotropic effects such that it has the potential to be a novel therapy for osteoarthritis. Therefore, we systematically reviewed the evidence from both pre-clinical and human studies for the potential disease-modifying effect of metformin in osteoarthritis.

Methods: Ovid Medline, Embase and CINAHL were searched between inception and June 2021 using MeSH terms and key words to identify studies examining the association between metformin use and outcome measures related to osteoarthritis. Two reviewers performed the risk of bias assessment and 3 reviewers extracted data independently. Qualitative evidence synthesis was performed. This systematic review is registered on PROSPERO (CRD42021261052 and CRD42021261060).

Results: Fifteen (10 pre-clinical and 5 human) studies were included. Most studies (10 pre-clinical and 3 human) assessed the effect of metformin using knee osteoarthritis models. In pre-clinical studies, metformin was assessed for the effect on structural outcomes (n=10); immunomodulation (n=5); pain (n=4); and main pathways of its effect in osteoarthritis (n=7). For

human studies, metformin was evaluated for the effect on structural progression (n=3); pain (n=1); and immunomodulation (n=1). Overall, pre-clinical studies consistently showed metformin having a chondroprotective, immunomodulatory and analgesic effect in osteoarthritis, predominantly mediated by adenosine monophosphate-activated protein kinase activation, with a demonstrable dose-response relationship. Evidence from human studies, although limited, it tended to support a beneficial effect of metformin in osteoarthritis.

Conclusion: We found consistent evidence across pre-clinical and human studies to support the favourable effects of metformin in chondroprotection, immunomodulation and symptomatic analgesia in osteoarthritis, specifically for knee osteoarthritis. As these effects are biologically plausible, with a demonstrable biological gradient, further randomised controlled trials in humans are needed to confirm our findings as metformin would offer a valuable novel therapeutic drug option for the treatment of osteoarthritis.

71. NON-PHARMACOLOGICAL INTERVENTIONS REDUCE DELIRIUM INCIDENCE AND DURATION IN HOSPITALISED ADULTS: A RAPID SYSTEMATIC REVIEW

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Acute delirium in hospitalised adults complicates hospital stay and is associated with poorer client outcomes.

AIM: The primary aim was to determine the effectiveness of non-pharmacological interventions compared to usual care on the incidence, severity, and duration of delirium in hospitalised adults.

METHOD: A rapid systematic review was completed. Health literature databases were searched (Medline, Embase, PsycInfo, Emcare, CINAHL, CDSR CENTRAL, and DARE) for systematic reviews and meta-analyses in July 2020, and randomised and quasi-randomised controlled trials in December 2020. Primary studies were assessed for eligibility against pre-determined eligibility criteria. Screening, data extraction, and assessment of methodological quality (PEDro) was completed independently by two authors.

RESULTS: A total of 1,880 primary studies were screened and 33 met inclusion criteria; 18 investigated multi-component interventions and the remaining 15 investigated single-component interventions. Non-pharmacological interventions when compared with the control group were associated with reduced delirium incidence (OR 0.50, 95% CI 0.38 to 0.66; Z = 4.77; P < .001; I^2 = 72%), reduced delirium duration (mean range 0.4 to 3.2 versus 0.7-12.8 days) and shorter length of stay (mean range 10.5-29.3 versus 11.4-38 days). Subgroup analysis revealed the type of non-pharmacological intervention explained the substantial statistical heterogeneity associated with delirium incidence. Evidence best supports use of multi-component (OR 0.51, 95% CI 0.37 to 0.71; P < .001) and pre-operative education interventions (OR 0.41, 95% CI 0.25 to 0.68; P < .001), as effect of specific single-component interventions (OR 0.49, 95% CI 0.16 to 1.50; P < .001) is uncertain.

CONCLUSION: Non-pharmacological interventions are effective in reducing delirium incidence, duration, and length of stay in acutely hospitalised adults. Allied Health Professionals should implement multi-component and pre-operative education interventions to reduce risk of delirium and reduce cost of care.

TRIAL REGISTRATION: International Prospective Register of Systematic Reviews (PROSPERO) registration number CRD42020201113.

72. GOALS OF CARE DISCUSSIONS OVER THE COURSE OF A PATIENT'S END OF LIFE ADMISSION: A RETROSPECTIVE STUDY

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BACKGROUND: As deaths in hospitals increase, clear discussions regarding resuscitation status and treatment limitations, referred to as goals of care (GOC), are vital. GOC may need revision as disease and patient priorities change over time. There is limited data about who is involved in GOC discussions, and how this changes as patients deteriorate in hospital.

AIMS: To review the timing and clinicians involved in GOC discussions for a cohort of patients who died in hospital.

METHODS: Retrospective observational audit of 80 consecutive end of life admissions between March 11th and April 9th, 2019.

RESULTS: Of 80 patients, 75 (93.6%) had GOC recorded during their admission, about half for ward-based non-burdensome symptom management or end-of-life care. GOC were revised in 68.0% of cases. Medical staff involved in initial versus final GOC discussions included home team junior doctor (54.7% versus 72.5%), home team consultant (37.3% versus 56.9%) and ICU doctor (16.0% versus 21.6%). For initial versus final GOC decisions, patients were involved in 34.7% versus 31.4%, and family in 53.3% versus 86.3%. Dying was documented for 92.0% of patients and this was documented to have been communicated to the family and patient in 98.6% and 19.5% of cases respectively.

CONCLUSIONS: As patients deteriorated, family and senior clinician involvement in GOC discussions increased, but patient involvement did not. Junior doctors were most heavily involved in discussions. We advocate for further GOC training and modelling to enhance junior doctors' confidence and competence in conducting and involving patients and families in GOC conversations.

73. INTRAVENOUS OXYTOCIN DOSING REGIMENS FOR POSTPARTUM HAEMORRHAGE PREVENTION FOLLOWING CAESAREAN DELIVERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND: Postpartum haemorrhage (PPH) is a leading cause of maternal mortality and morbidity. Prophylactic oxytocin is widely used to prevent PPH, however World Health Organization guidelines state there is insufficient evidence to recommend a specific oxytocin dosing regimen at Caesarean delivery (CD). We aimed to synthesise available evidence on intravenous (IV) oxytocin dosing regimens for PPH prevention at CD.

METHODS: A systematic review of randomised and non-randomised studies was undertaken. We searched seven electronic databases for studies comparing different IV oxytocin regimens for PPH prevention at CD. Outcomes included PPH ≥ 1000 mL, blood loss, and adverse maternal events. Data were analysed based on type of IV administration (bolus only, infusion only, or bolus plus infusion) and total oxytocin dose. Meta-analysis was performed using randomised trials. Non-randomised studies were reported narratively.

RESULTS: Thirty-five studies (7,333 women) were included (30 randomised trials, five non-randomised studies). Data were limited for most outcomes, and results were not conclusive. Compared with bolus plus infusion regimens, bolus only regimens probably result in slightly higher blood loss (Mean Difference, 52 mL; 95% Confidence Interval, 0.4–104 mL; moderate-certainty). Among bolus plus infusion regimens, initial bolus doses <5 IU may reduce nausea (Risk Ratio, 0.26; 95% CI, 0.11–0.63; low-certainty) vs 5–9 IU. Total oxytocin doses of 5–9 IU may increase use of additional uterotonics (RR, 13.00; 95% CI, 1.75–96.37; low-certainty) compared with 10–19 IU.

CONCLUSION: There are limited data available for comparisons of IV oxytocin regimens for PPH prevention at CD. Bolus plus infusion regimens may lead to minor reductions in blood loss, and initial bolus doses <5 IU may minimise nausea. Bolus only regimens of 10 IU may decrease use of additional uterotonics compared with 5 IU. Further comparative trials are required to understand effects on other key outcomes, particularly hypotension.

74. NURSING WORKFORCE & EDUCATION CHALLENGES TO IMPLEMENTING ECMO SERVICES IN AUSTRALIA

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BACKGROUND: The use of extracorporeal membrane oxygenation (ECMO) is increasing in the management of critical care patients. ECMO service delivery requires an organisation-supported approach to ensure appropriate resources to deliver training, equipment, capacity, staffing, and the required model of care for quality care delivery.

AIM: To explore the nursing workforce, education, and training challenges to implementing ECMO services in Australian intensive care units.

METHODS: A secondary analysis of semi-structured focus groups was conducted from 14 ECMO centres participating in the national EXCEL registry in Australia, which included 34 ICU nurses (43%), 2 (2%) ECMO nurse specialists, 2 (2%) clinical nurse consultants and 2 (2%) equipment nurses.

RESULTS: Thematic analysis identified four key nursing themes: (1) understanding the specific workforce requirements for provision of ECMO, (2) increased workload demands as a result of managing ECMO, (3) models of care and training related to implementing ECMO services. (4) ECMO provides opportunities for the creation of advanced nursing practice roles in both the ICU-led ECMO service and ICU-Perfusionist service model. There were different challenges identified for nurses in high (>30 ECMO cases per annum) and low volume ECMO centres.

CONCLUSION: There was substantial variation in the systems and models of care in hospitals that provide ECMO services across Australia. Key issues were the importance of specialist training in ECMO 'low frequency, high stakes' management. This highlights the need for workforce planning and training to meet the increasing demand for ECMO and prevention of nursing burnout. The complexity and intensity of delivering care for patients on ECMO challenges the traditional nursing workforce models. Innovative technological medical interventions provide opportunities for the creation of advanced nursing practice roles.

75. THE PAIN NURSE PRACTITIONER AND PAIN NURSE'S ROLE AND VIEW ON OPIOID MANAGEMENT IN AUSTRALIA: A NATIONAL QUESTIONNAIRE SURVEY

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Purpose: The demand for access to Australian pain management services is growing. The dual crisis of opioid abuse and chronic pain, means pain nurses and nurse practitioners (NPs) have a unique opportunity to meet clinical demands and advance their scope of practice.

Aim: To understand the profile of pain nurses and pain nurse practitioners across Australia and explore their perceptions of current opioid management.

Design: This cross-sectional study involved pain nurses or pain NPs working in Australia who are a members of a pain interest group, which are sub-groups of The Australian Pain Society (APSOC). Survey respondents were contacted via the 8 nursing Pain Interest Groups in Australia.

Methods: A UK survey tool was utilised with modifications required for application to the Australian context. Data were captured and extracted from Survey Monkey into a Microsoft Excel database.

Results: Acute pain management (92.7%) and chronic pain management (80.5%) were the primary services provided, with pain speciality nurses providing nurse education (100.0%), patient support, clinician education and policy development. Pain nurses believed there was an over-prescription of opioid analgesics in Australia (97.6%) and NPs role in opioid mitigation is primarily reducing opioid medication doses.

Conclusions: Pain nurses have a breadth of knowledge and experience, although challenges to the workforce may emerge due to an aging patient population and nursing workforce.

76. EFFECT OF ATORVASTATIN ON SKELETAL MUSCLES OF PATIENTS WITH KNEE OSTEOARTHRITIS: POST-HOC ANALYSIS OF A RANDOMISED CONTROLLED TRIAL

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Statins are often discontinued due to muscle-related side effects. The effect of statins in populations with osteoarthritis is unknown.

AIMS: To examine the effect of atorvastatin on skeletal muscle biochemistry, strength, size and symptoms in patients with symptomatic knee osteoarthritis.

METHODS: Post-hoc analysis of a multicentre randomised, double-blind, placebo-controlled trial over 2 years. Participants with knee osteoarthritis (mean age 55.7 years, 55.6% female) received atorvastatin 40mg daily (n=151) or placebo (n=153). Outcomes included levels of creatinine kinase (CK), aspartate transaminases (AST) and alanine transaminases (ALT) at baseline, 4 weeks, 6, 12 and 24 months; muscle strength measured by dynamometry at baseline, 12 and 24 months; vastus medialis cross-sectional area (CSA) on magnetic resonance imaging at baseline and 24 months; and self-reported myalgia.

RESULTS: There were no significant differences in CK and AST levels between atorvastatin and placebo groups at all follow-up timepoints. The atorvastatin group had higher ALT levels than the placebo group at 4 weeks [median 26 (interquartile range 19.5,35) vs 21 (17,29), p=0.0004) and 6 months [25 (19,34) vs 22 (15,30), p=0.007) but no between-group differences at 12 and 24 months. Muscle strength significantly increased in the atorvastatin group but not the placebo group over 24 months with no between-group differences [mean 8.5 (95% CI 2.6,14.4) vs 5.6 (-0.3,11.5), p=0.50]. Change in vastus medialis CSA over 24 months showed between-group differences favouring the atorvastatin group [+0.12 (-0.09,0.34) vs -0.24 (-0.48,0.01), p=0.03] but of uncertain clinical significance. There was a trend for more myalgia in the atorvastatin group over 2 years (8/151 vs 2/153, p=0.06), mostly occurring within 6 months (7/151 vs 1/153, p=0.04).

CONCLUSION: In those with symptomatic knee osteoarthritis, despite a trend for more myalgia, there was no objective evidence of an adverse effect of atorvastatin on skeletal muscles, including those most relevant to knee joint health.

77. YOUTH PERSPECTIVES ON LIFE AFTER LUNG TRANSPLANTATION: A QUALITATIVE STUDY

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Lung transplantation is a palliative intervention proffered to young people with end stage respiratory conditions. Average life expectancy for adolescent and young adult lung transplant recipients, is 5 years post transplant, however, premature morbidity of young people is overrepresented amongst morbidity statistics.

AIM: To explore the lived experiences of young lung transplant recipients and identify features of clinical care that were supportive and features that were lacking, in health literacy and healthcare delivery associated with lung transplantation.

METHODS: This study used an exploratory qualitative design, incorporating a consumer engagement model. A purposive sample of 16 lung transplant recipients, transplanted at the Alfred Hospital prior to 25 years of age, was identified from the National Paediatric Lung Transplant Service. Of the 16 participants, 11 were female and 5 male with an age range of 16.08

– 28.60 years at time of interview. Data collection consisted of a photo elicitation activity and one-on-one semi-structured interviews with participants. A thematic analysis was conducted using the qualitative data analysis software NVivo.

RESULTS: Themes associated with a high level of satisfaction with everyday life emerged from the 16 interviews. No participant regretted transplantation, however some described living with conditions such as Steroid Induced Diabetes and Chronic Lung Allograft Dysfunction as challenging. A need for developmentally focussed health literacy and healthcare were recurrent themes, as was the effect of clinician behaviours and language upon youth engagement in care.

CONCLUSION: Themes generated from this study reflect the voices of young people and their description of the need for: 1. Developmentally targeted education, using a multimodal approach; 2.The importance of individuated and collaborative program delivery; 3.Support to learn how to independently manage their own healthcare. In the delivery of effective healthcare, the voices of those for whom intervention is directed, are fundamental to engagement in their own care-path.

78. EXPLORING THE FEASIBILITY OF INTERROGATING CLONAL HAEMATOPOIESIS OF INDETERMINATE POTENTIAL (CHIP) IN THE ASPREE COHORT USING A TARGETED SEQUENCING APPROACH

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Clonal Haematopoiesis of Indeterminate Potential (CHIP) is development of detectable clones with somatic mutations associated with leukaemogenesis in otherwise normal, healthy people, and has been associated with increased risk of cardiovascular disease as well as blood cancers. The ASPREE (ASPirin in Reducing Events in the Elderly) trial randomised 19,114 healthy participants aged 70 years or older (or ≥65 among blacks and Hispanics in the United States) to low dose aspirin or placebo, with the primary endpoint a composite of death, dementia or persistent physical disability. Comprehensive clinical and phenotypic measures were collected throughout the trial, as well as peripheral blood samples from 12,223 participants at study entry and ~10,600 at 3 years. Participant follow-up is ongoing for endpoints, including incident cancer.

ASPREE provides a unique opportunity to investigate the incidence and progression of CHIP in an otherwise healthy elderly population, the association between CHIP and clinical outcomes and whether low dose aspirin has a modifying effect.

We have investigated the feasibility of targeted sequencing the 16 most commonly reported genes in CHIP studies in the ASPREE cohort. Given the scale of this study, costs and logistical considerations in handling and processing >20,000 samples are significant as we aspire to measure allele frequencies down to 0.5% from 40ng of genomic DNA (~11,600 genome equivalents).

We have empirically assessed IDT rhAmpSeq as a means to detect CHIP within the entire ASPREE cohort and demonstrate per sample sequencing costs of less than AUD$100 using the Illumina NovaSeq 6000 within the Genomics Facility here at the Alfred.

The challenge is now building the bioinformatic pipelines to process this data, the variant filtering logic to call CHIP in ASPREE participants. This will be demonstrated with a pilot subset of samples within the ASPREE cohort.

POPULATION HEALTH AND EPIDEMIOLOGY

79. SCOOP: STRENGTHENING COVID-19 COMMUNICATION IN PREGNANCY

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Maternity services were significantly disrupted in response to the COVID-19 pandemic. Many changes were rapidly introduced and the timely dissemination of information to pregnant people was critical.

AIM: To better understand the quality of information reaching pregnant and postpartum women regarding COVID-19 to strengthen public health communication strategies.

METHODS: This study adopted a qualitative two phased approach. Phase one included the use of data analytics tool (TIGER-C19) to collect data from social media platforms Reddit and Twitter over an 8-week period from June to July 2021. Phase two comprised of individual semi-structured online or telephone interviews with those who were or had been pregnant since March 2020. Interview data was thematically analysed, facilitated by NVivo software.

RESULTS: In total, 21 women were interviewed from June to July 2021. Participants were located in all states and territories in Australia. Preliminary results from phase 2 showed that vague or insufficient information contributed to feelings of frustration and anxiety. Women wanted further information on the risks COVID-19 posed to themselves, their pregnancies and newborns. Health providers were a trusted source of information and communication strategies that allowed participants to engage in real-time such as interactive zoom videos or live social media streams were preferred communication methods. Social media was identified as a preferred source of communication and information for many participants. When there was a perceived lack of information participants turned to informal sources, increasing the potential for exposure to misinformation.

CONCLUSION: It is vital that health services communicate with pregnant people, early and throughout the COVID-19 pandemic, especially when restrictions are (re)introduced and service delivery changes. Information and communication strategies that are clear, consistent, and readily available to pregnant and postpartum people is integral to ensuring pregnant people feel well informed and supported, thereby reducing reliance on informal and potentially inaccurate sources.

80. REMOTE PRIMARY HEALTHCARE CONSULTING IN LOW- AND MIDDLE-INCOME COUNTRIES: FEASIBILITY OF AN ONLINE TRAINING (REACH) TO SUPPORT CARE DELIVERY DURING THE COVID-19 PANDEMIC

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BACKGROUND: Despite uptake of remote consulting accelerating throughout the COVID-19 pandemic, many healthcare-professionals are practising without training. This is especially challenging in resource-poor countries, with limited telehealth experience.

OBJECTIVE: As the COVID-19 pandemic dawned, we designed a modular online training program for REmote Consulting in primary Healthcare (REaCH). We employed a train-the-trainer approach, training health workers (tier 1) to cascade the teaching to others (tier 2) in their locality. We aimed to determine if REaCH training was acceptable and feasible to health workers in rural Tanzania.

METHODS: Twelve tier 1 trainees and 63 tier 2 trainees from the Ulanga district of rural Tanzania participated between August and September 2020. A survey informed by Kirkpatrick's model of evaluation was used to capture trainee satisfaction with REaCH, knowledge gained and perceived and actual behaviour change. We analysed the survey using descriptive statistics, and the interviews of trainees and facilitators, emails, WhatsApp texts and training reports thematically.

RESULTS: We developed the REaCH training program in July 2020 and created eight modules. The program was then taught via Moodle and WhatsApp to twelve tier 1 trainees, ten of whom completed the training. Nine tier 1 trainees cascaded to 63 tier 2 trainees. All tier 1 trainees who completed the program would recommend the training to colleagues, received relevant skills, and reported applying their learning to their daily work demonstrating satisfaction, learning and perceived behaviour change. Trainees identified several barriers to implementation of their training into routine practice, including lacking technological infrastructure and support, and limited community awareness.

CONCLUSION: We successfully designed, implemented and evaluated an online-based remote consulting training program. The REaCH training program is feasible, acceptable and effective in changing trainees' behaviour. Government and organisational support are required to facilitate the expansion of the program and remote consulting in other low resource settings.

81. CO-DESIGNING *BEING YOUR BEST* PROGRAM – A HOLISTIC APPROACH TO FRAILTY IN OLDER COMMUNITY DWELLING AUSTRALIANS

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Background: Frailty is characterised by increased vulnerability and decline of physical and cognitive reserves. It mainly affects older people, leading to a cascade of repeated hospitalisations and loss of independence. Frailty and pre-frailty are modifiable with interventions including physical exercise, cognitive training, social connection and improved nutrition, especially in group settings. Uptake of referrals to services following hospital discharge is sub-optimal, indicating that a more proactive, person-centred and integrated approach is required. Co-design is premised on the people involved, such as patients, family, caregivers and healthcare professionals, being experts of their own experiences relating to health and community. Co-design is proven to help identify and shape innovative solutions and empower stakeholders to participate in the solutions that would directly impact them.

Aim: To co-design a program to help pre-frail and frail older community dwellers following hospital discharge, by increasing resilience and promoting independence.

Methods: We engaged healthcare consumers and healthcare professionals from Cabrini, The Alfred and Monash Medical Centre and a home-based nursing service in metropolitan Melbourne, Australia.

Results: From co-design sessions with 23 healthcare consumers and 17 healthcare professionals, frailty was perceived to affect physical and mental wellbeing. The co-design process resulted in the *Being Your Best* program incorporating a holistic approach, addressing four domains supported by research evidence: Moving Well, Eating Well, Thinking Well, and Connecting Well; with the aim of improving health and wellbeing and mitigating the effects of frailty through community- or home- based physical activities, nutritional support, cognitive training and social support.

Conclusions: Promoting community or home-based services for pre-frail and frail older people can raise awareness and may help in reducing the effects of frailty and improving personal wellbeing, leading to increased resilience and independence, and less re-hospitalisations.

Being Your Best is now being tested for feasibility and acceptability with recently hospitalised individuals

82. RISK FACTORS FOR OROPHARYNGEAL GONORRHOEA AMONG FEMALE SEX WORKERS ATTENDING SEXUAL HEALTH CLINICS IN MELBOURNE AND SYDNEY: A CASE-CONTROL STUDY

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BACKGROUND: The aim of this case-control study was to determine the risk factors for oropharyngeal gonorrhoea in female sex workers (FSWs).

METHODS: A case-control study involving 83 FSWs diagnosed with oropharyngeal gonorrhoea (cases) and 603 FSWs without oropharyngeal gonorrhoea (controls). Participants were recruited at two sexual health clinics in Melbourne and Sydney in November 2018-March 2020. The survey asked basic demographic questions, location of sex work, sex practices with male clients in an average working week and sex with not-at-work male partners in the last week. Nucleic acid amplified test was used for oropharyngeal gonorrhoea diagnosis. Univariable and multivariable logistic regression were performed to examine the factors associated with oropharyngeal gonorrhoea.

RESULTS: The median age of 686 FSWs was 30 (interquartile range [IQR]: 26-36). Most performed sex work exclusively in one type of venue (578; 84.3%), most commonly brothels (352;51.5%) followed by massage parlours (153;22.4%). Almost 40% were newly arrived in Australia (within 3 years). There were 417(60.8%) who tongue kissed clients and 198(28.9%) who performed condomless oral sex on clients in an average working week. There were 251(36.6%) who had not-at-work sexual partners. After adjusting for site of recruitment, age, length of time in Australia, tongue kissing clients, performing condomless oral sex with clients and having a not-at-work sexual partner, only performing condomless oral sex was associated with oropharyngeal gonorrhoea (adjusted odds ratio[aOR]: 3.5; 95%CI: 1.8-6.8; p=<0.001).

CONCLUSION: Almost 30% of FSW reported performing condomless oral sex on clients and this practice was associated with oropharyngeal gonorrhoea diagnosis. Tongue kissing with male clients was not associated with oropharyngeal gonorrhoea in FSWs.

83. VISIBLE SIGNS OF CONCUSSION AND COGNITIVE SCREENING IN COMMUNITY SPORTS

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Video surveillance and detection of players with visible signs of concussion by experienced medical staff facilitates rapid on-field screening of suspected concussion in professional sports. This method, however has not been validated in community sports where video footage is unavailable.

AIM: This study aimed to explore the utility of visible signs of concussion to identify players with decrements in performance on concussion screening measures.

METHODS: In this observational prospective cohort study, personnel with basic training observed live matches across a season (60 matches) of community male and female Australian football for signs of concussion outlined in the community-based Head Injury Assessment form (HIAf). Players identified to have positive signs of concussion (CoSign+) following an impact were compared with players without signs (CoSign-). Outcome measures, the Sport Concussion Assessment Tool (SCAT3) and Cogstate, were administered at baseline and post-match.

RESULTS: CoSign+ (n = 22) and CoSign- (n = 61) groups were similar with respect to age, sex, education, baseline mood, and medical history. CoSign+ players exhibited worse orientation, concentration, and recall, and slower reaction time in attention and working memory tasks. Comparing individual change from baseline to post-match assessment revealed 100% (95% confidence interval [CI]: 84–100%) of CoSign+ players demonstrated clinically significant deficits on SCAT3 or Cogstate tasks, compared with 59% (95% CI: 46–71%) of CoSign- players. All CoSign+ players observed to have a blank/vacant look demonstrated clinically significant decline on the Standardized Assessment of Concussion (SAC).

CONCLUSION: Detection of visible signs of concussion represents a rapid, real-time method for screening players suspected of concussion in community sports where video technology and medical personnel are rarely present. Consistent with community guidelines, it is recommended that all CoSign+ players be immediately removed from play for further concussion screening.

84. ASSOCIATION BETWEEN ARTHRITIS AND CARDIOVASCULAR RISK FACTORS IN COMMUNITY-BASED ADULTS: AN OPPORTUNITY TO TARGET CARDIOVASCULAR RISK

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BACKGROUND: Undertreated risk factors are major contributors to the burden of cardiovascular disease (CVD). Those with arthritis have an increased prevalence of CVD. CVD risk factors are often asymptomatic, which may be a barrier their treatment. Arthritis causes pain and immobility, and is a common reason for individuals to seek healthcare.

AIM: Our aims were to (i) examine the relationship between arthritis and CVD risk factors, and (ii) calculate the proportion of CVD risk factors that could be reduced if individuals with arthritis were targeted.

METHODS: An Australian National Health Survey included 13,776 participants, categorised into young, middle aged and older adults. The prevalence of arthritis, obesity, hypertension, dyslipdiaemia and diabetes was recorded. The associations between arthritis and CVD risk factors were examined using logistic regression, and the population attributable faction (PAF) of arthritis for each CVD risk factor was calculated.

RESULTS: Those with arthritis were at increased risk of obesity (1.8-2.1 fold), diabetes (1.4-4.87 fold), hypertension (1.5-2.4 fold) and dyslipidaemia (1.2-4.6 fold) compared to those without. This elevated risk remained significant even after adjusting for obesity, with the exception of diabetes in the older population. The PAF of the presence of arthritis for having at least one CVD risk factor was 30.7% in middle-aged adults and 70.4% in older adults.

CONCLUSION: Australian adults of all ages with arthritis are at increased risk of having CVD risk factors. For young and middle-aged adults, this increased risk remains significant even when adjusted for obesity. Presentation to healthcare practitioners with arthritis is an opportunity to screen for asymptomatic CVD risk factors with the potential of improving outcomes for both diseases. By adopting an approach of managing arthritis and CVD risk factors in parallel, rather than in silos, we could reduce the burden of CVD risk factors by 20 to 30%.

85. PERCEIVED DISCRIMINATION IN AUSTRALIA DURING THE COVID-19 PANDEMIC: A LONGITUDINAL STUDY

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There have been global reports of increased discrimination during the COVID-19 pandemic. This has been most commonly observed in healthcare workers and individuals of Asian descent due to the increased risk of contact with COVID-19 and the origin of the virus respsectively. As discrimination has been associated with fear in the community, the severity of COVID-related discrimination may be lower in countries with fewer number of cases such as Australia.

AIM: To observe longitudinal changes in perceived discrimination during the COVID-19 pandemic in the general population, as well as in healthcare workers and Asian sub-groups.

METHODS: A sample of 1,535 Australian adults completed the Everyday Discrimination Scale (EDS) online across a 13-month period (3rd April 2020-31st May 2021). Of these, 135 were healthcare workers and 122 were of Asian descent. Participants were asked to complete the EDS twice at the baseline assessment; first retrospectively considering discrimination experienced prior to COVID-19, and then considering experiences in the past month. Participants were then asked to repeat the survey every two months. Responses were grouped in two-month intervals.

RESULTS: In the Australian general population, EDS scores were significantly lower ($p < 0.001$) at every timepoint during the pandemic than prior to COVID-19. A similar pattern was observed in the Asian sub-group at a trend level. EDS scores were also significantly lower ($p < 0.008$) in healthcare workers for every timepoint except for a large peak in August-September 2020. This coincides with the largest peak of cases in Australia during the 13-month period and the implementation of additional restrictions such as curfews and extended lockdowns.

CONCLUSION: Our findings suggest that there is social solidarity during public health threats when there is a lesser impact on the community. When the threat to public health significantly increases, healthcare workers experience increased discriminatory behaviour and may require additional support.

86. MODELLING THE PREDICTORS OF PLATELET TRANSFUSION

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BACKGROUND: Understanding the predictors of platelet transfusion allows for better distribution of a valuable medical resource. It is not feasible to routinely stock platelets in locations where demand is not consistent. To improve access to liquid platelets and novel alternatives, there must be a comprehensive assessment of platelet demand.

AIM: To develop a predictive model to determine how many patients would have received platelets had they been available in locations without a routine supply of platelets.

METHODS: This was a retrospective analysis of the National Transfusion Dataset – a collection of electronic clinical records of adult patients who received a blood product transfusion during admission to an Australian hospital. At the time of this study, data from two Australian metropolitan hospitals for the period of 2017 to 2019 were available. To determine acute need, the model was developed based on patients with overnight stays or single day admissions resulting in death. There were 10,532 admissions from 7,813 patients analysed.

The dataset was partitioned 80/20 for model training and testing. Univariate analysis was conducted on the variables, with additional selection undertaken using backwards stepwise and elastic net methods. The final model was based on agreement of all methods, accounting for clinical and biological plausibility.

RESULTS: Twenty-seven variables were selected by all methods and included in the final model. These were transfusion of fresh frozen plasma, cryoprecipitate or clotting factors; a diagnosis of haematological cancer, anaemia or renal impairment;

aspirin use; procedures including chemotherapy, neurosurgery, bypass, sedation and low risk cardiac surgery; and laboratory values including platelet count, INR, haemoglobin level, creatinine level and pH.

CONCLUSION: Significant variables included in the model were fresh frozen plasma transfusion, platelet count, cryoprecipitate transfusion and chemotherapy. Prediction of platelet transfusion using this model could assist in improving access to platelet transfusions in regional and remote hospitals.

87. COMMUNITY PERSPECTIVES AND EXPERIENCES ON QUALITY MATERNAL AND NEWBORN CARE IN EAST NEW BRITAIN, PAPUA NEW GUINEA

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Quality maternal and newborn care is essential for improving the health of mothers and babies. Low- and middle-income countries, such as Papua New Guinea (PNG), face many barriers to achieving quality care for all. Efforts to improve the quality of maternal and newborn care must involve community in the design, implementation and evaluation of initiatives to ensure that interventions are appropriate and relevant for the target community.

AIM: To describe community members' perspectives and experiences of maternal and newborn care and their ideas for improvement in one province, East New Britain, in PNG.

METHODS: We undertook a qualitative descriptive study in partnership with and alongside five local health facilities, health care workers and community members, using a Partnership Defined Quality Approach. We conducted ten focus group discussions with 68 community members in East New Britain PNG to explore perspectives and experiences of maternal and newborn care, identify enablers and barriers to quality care and to identify interventions to improve care. Discussions were transcribed verbatim. A mixed inductive and deductive analysis was used including application of the World Health Organisation (WHO) Quality Maternal and Newborn Care framework.

RESULTS: Using the WHO framework we present the findings in accordance with the five experience of care domains. We found that the community reported multiple challenges in accessing care and facilities were described as under-staffed and under resourced. Community members emphasized the importance of good communication and competent, caring and respectful healthcare workers. Both women and men expressed a strong desire for companionship during labor and birth. Several changes were identified by the community that could immediately improve the quality of care.

CONCLUSION: Community perspectives and experiences are critical for informing effective and sustainable interventions to improve the quality of maternal and newborn care and increasing facility-based births in Papua New Guinea. A greater understanding of the care experience as a key component of quality care is needed and any quality improvement initiatives must include the user experience as a key outcome measure.

88. THE EFFECTIVENESS OF PRECONCEPTION CARE INTERVENTIONS IN PRIMARY CARE SETTINGS: A SYSTEMATIC REVIEW

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BACKGROUND: Pregnancy outcomes can be adversely affected by a range of modifiable risk factors including alcohol consumption, smoking, obesity and poor nutrition during the preconception period. Preconception care (PCC) involves

interventions that identify and seek to change behavioural, biomedical and social risks present in women and men of reproductive age. Primary care is well situated to offer PCC interventions, but the effectiveness of such interventions in primary care has not been established.

AIM: To investigate the effectiveness of PCC interventions delivered in primary care settings on reducing high-risk behaviours in men and women and improving pregnancy outcomes.

METHODS: OVID Medline, Cochrane Central Register of Controlled Trials, EMBASE, Web of Science, Scopus and CINAHL databases were searched for English language randomized controlled trials (RCTs) from 2000 onwards. For inclusion, PCC interventions must be provided in primary care settings to women and/or men of reproductive age. No geographical limits were applied. All stages of screening and data extraction involved dual review. PROSPERO registration: CRD42021235499.

PRELIMINARY RESULTS: Thirty articles were eligible (24 RCTs).The main interventions were: provision of a special diet (n=4), folic acid (n=3) and/or education (n=21). Following the provision of a special diet, a significant improvement in pregnancy outcomes was reported; provision of folic acid supplementation reported a statistically significant improvement in self-reported folate/folic supplement intake and women were more likely to consume foods rich in folate; after educational interventions, enhanced knowledge of risk factors, reduced alcohol and tobacco consumption and higher self-efficacy towards healthy life-style behaviours was reported.

CONCLUSION: Only studies providing a special diet or folic acid investigated pregnancy outcomes. However, most studies used an educational intervention but did not investigate the impact on pregnancy outcomes. Therefore, more research is required to establish the effectiveness of preconception care interventions on pregnancy outcomes in primary care settings.

RENAL MEDICINE

89. HOME BEFORE HOSPITAL: A WHOLE SYSTEM RE-DESIGN PROJECT TO IMPROVE RATES OF HOME-BASED DIALYSIS THERAPY: EXPERIENCE AND OUTCOMES OVER 8 YEARS

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Despite evidence that clinical outcomes for patients treated with peritoneal dialysis (PD) or home haemodialysis are better than for patients treated with hospital-based haemodialysis, rates of home-based dialysis therapies world-wide remain low. Home-based dialysis care is cost-effective and indeed the favoured dialysis option for many patients.

METHODS AND OBJECTIVES: Using a lean-thinking framework and established change management methodology, a project embracing a system-wide approach at making a change where a 'Home before Hospital' philosophy underpinned all approaches to dialysis care was undertaken. Three multidisciplinary working groups (pathway, outreach and hybrid) were established for re-design and implementation. The primary aim was to improve home-based dialysis therapy prevalence rates from a baseline of 14.8% by ≥2.5%/year to meet a target of 35%, whilst not only maintaining but improving the quality of care provided to patients requiring maintenance dialysis. A 'future' state pathway was developed after review of the 'current' state and formed the basis on which a nurse-led outreach service was established. With multidisciplinary team support, the outreach service model focussed on early, consistent, and frequent education, patient support in decision-making, and clinician engagement.

RESULTS: A target prevalence of >30% for home-based therapies (mainly achieved with PD) was achieved within 2 years. This prevalence rate reached 35% within 3 years and was maintained at 8 years. In addition, selected patients already on maintenance satellite-based haemodialysis (Hybrid Working Group) were educated to achieve high levels of proficiencies in self-care.

CONCLUSION: Having the system-wide approach to a Quality Improvement Process and using established principles and change management processes, the successful implementation of a new sustainable model of care focussed on home-

based dialysis therapy was achieved. A key feature of the model (through outreach) was early nurse-led education and support of patients in decision-making and ongoing support through multidisciplinary care.

RESPIRATORY MEDICINE AND LUNG TRANSPLANT

90. WHO SUCCEEDS AT HOME? IDENTIFYING RESPONDERS TO HOME-BASED PULMONARY REHABILITATION

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INTRODUCTION: In our health service, home based pulmonary rehabilitation (HBPR) is offered as an alternative to traditional centre-based PR. Participants in HBPR are expected to complete unsupervised exercise and are given the opportunity to progress exercise goals during weekly phone calls. However, some people who start HBPR do not complete the program or achieve clinical improvements.

AIMS: To identify reasons for selecting HBPR, and to identify baseline factors associated with program completion and clinical improvement.

METHODS: This study included individuals who attended a baseline HBPR assessment. Baseline and end-rehabilitation assessments for the eight-week program include exercise capacity (6-minute walk distance [6MWD]), health-related quality of life (Chronic Respiratory Disease Questionnaire [CRQ], COPD Assessment tool [CAT]), and emotional functioning (Hospital Anxiety and Depression scale). Program completion was defined as participation in 70% of phone calls. Minimum important differences (MID) were defined for dyspnoea (score ≥2.5 CRQ dyspnoea domain) and exercise capacity (6MWD ≥30metres).

RESULTS: 71 people attended baseline HBPR assessments over 2.5 years (43 female, mean age 71 [SD 12] years, FEV_1 57 [22] % predicted, 6MWD 361 [SD 155] metres). The most common diagnoses included chronic obstructive pulmonary disease (n=49), asthma (n=8) and bronchiectasis (n=7). Reasons for choosing HBPR included symptom limitation (n=32), work commitments (n=24), and transportation (n=15). Of these, 53(75%) people completed the program, 23 (55%) achieved MID in dyspnoea and 16 (40%) achieved MID in 6MWD. There were no baseline factors associated with program completion. Lower baseline CAT scores were associated with achieving MID in 6MWD (p = 0.034). Higher CAT scores at baseline were associated with achieving MID in dyspnoea (p=0.086).

CONCLUSION: Baseline demographic and clinical characteristics are not related to completion in HBPR. Baseline CAT score is associated with clinical improvement in exercise capacity and dyspnoea.

91. WHOLE-LUNG LAVAGE FOR PULMONARY ALVEOLAR PROTEINOSIS IN AUSTRALIA – SAFETY AND EFFICACY AT A SINGLE CENTRE

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Pulmonary Alveolar Proteinosis (PAP) is caused by alveolar macrophage dysfunction and accumulation of lipoproteinaceous material within alveoli.[1] Whole lung lavage (WLL) is an established treatment for patients with moderate to severe respiratory impairment. We report safety and efficacy of WLL for PAP at an Australian centre performing WLL of each lung on sequential days in the intensive care unit between 2003-2021.

METHODS: Data was extracted from medical records. Change in arterial-alveolar oxygen gradient (A-a) and arterial pO_2/fraction inspired oxygen (P/F) ratio were calculated from arterial blood gases prior to WLL and discharge home.[2] Change in DLCO and FVC used the temporally closest measures peri-procedure.

PATIENTS: 7 patients underwent WLL and 10 cycles were completed (1 patient 2 cycles, 1 patient 3 cycles). Mean patient age was 40.1 years (SD 14.3), 5 were men. Two patients were anti-GMCSF antibody positive (5 unknown). The mean volume lavaged was 16.5L (SD 6.7).

SAFETY: Peripheral saturation of oxygen (Sp02) <88% occurred in 10 of 20 WLLs despite maximal inspired oxygen. The mean nadir SpO2 was 84% (SD 9.6%). The mean retained volume of fluid was 0.9L (SD 6.15). Mean days to extubation was one day (SD 1.1).

EFFICACY: There was significant improvement in FVC of 4.88% predicted (SD 3.11, p=0.03) and P/F ratio of 113.38mmHg (SD 143.72, p=0.04) but no significant change in DLCO of 3.36% (SD 8.93, p=0.49) and A-a of -121.02mmHg (SD 167.62, p=0.06).

SUMMARY: WLL for PAP is an invasive intervention with frequent hypoxia despite appropriate preparation. We are developing an assessment strategy including symptomatic, functional, radiological and physiological measures to understand the impact of WLL on patient outcomes.

[1] Kumar A, Abdelmalak B, Inoue Y, Culver DA. Pulmonary alveolar proteinosis in adults: pathophysiology and clinical approach. The Lancet Respiratory Medicine. 2018 Jul 1;6(7):554-65.
[2] Helmholz HF. The abbreviated alveolar air equation. Chest. 1979 Jun 1;75(6):748.

92. TELEREHABILITATION COMPARED TO CENTRE-BASED PULMONARY REHABILITATION: A RANDOMISED CONTROLLED EQUIVALENCE TRIAL

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INTRODUCTION/AIM: Pulmonary rehabilitation is an effective treatment for people with chronic respiratory disease but is delivered to fewer than 5% of eligible individuals. The aim of this study was to investigate whether home-based telerehabilitation was equivalent to centre-based pulmonary rehabilitation in people with chronic respiratory disease.

METHODS: We undertook a multi-centre randomised controlled trial with assessor blinding, powered for equivalence. Individuals with a chronic respiratory disease referred to pulmonary rehabilitation at one of four participating sites (including one rural site) were eligible and randomized using concealed allocation to pulmonary rehabilitation or telerehabilitation. Both programs were twice weekly for eight weeks. The primary outcome was change in chronic respiratory disease questionnaire dyspnoea domain at end rehabilitation, with a pre-specified equivalence margin of 2.5 points. Follow-up was at 12 months. Secondary outcomes included exercise capacity, health-related quality of life, symptoms, self-efficacy and psychological well-being.

RESULTS: We randomised 142 participants to pulmonary rehabilitation (n=72) or telerehabilitation (n=72). The intention to treat analysis included 96% and 97% of participants respectively. There were no significant differences between groups for any outcome at either time-point. We were unable to confirm equivalence of telerehabilitation for the primary outcome of change in chronic respiratory disease questionnaire dyspnoea domain at end rehabilitation (mean difference (95%CI) -1point (-3 to 1)), and inferiority of telerehabilitation could not be excluded at either time-point. At end-rehabilitation, telerehabilitation demonstrated equivalence for 6-minute walk distance (MD -6m, 95%CI -26 to 15) with possibly superiority of telerehabilitation at 12-months (MD 14m, 95%CI -10 to 38). Both groups achieved meaningful improvement in dyspnoea and exercise capacity at end rehabilitation.

CONCLUSION: Telerehabilitation may not be equivalent to centre-based pulmonary rehabilitation for all outcomes, but is safe and achieves clinically meaningful benefits. When centre-based pulmonary rehabilitation is not available, telerehabilitation may provide an alternative program model.

93. PULMONARY REHABILITATION FOR INTERSTITIAL LUNG DISEASE: EVIDENCE INTO PRACTICE?

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Introduction: Pulmonary Rehabilitation (PR) is an important component in the treatment of people with interstitial lung disease (ILD) and improves functional capacity and dyspnea.

Aim: To investigate the proportion of patients with ILD referred to PR and to understand their experiences and reasons for non-participation or non-completion.

Methods: Patients in the Alfred Health ILD registry between 2015 and 2019 were eligible for inclusion. Demographic information and data regarding referral and attendance to PR were collected. Patients with a PR referral were invited to participate in a semi-structured interview conducted over the phone. Open-ended questions were developed to investigate participant's experience with PR. Data was analysed using deductive thematic analysis.

Results: Of 336 patients with ILD, 136 (40%) had been referred to PR during the study period. Patients referred to PR were similar in age to those who were not (mean (SD) 67(12) vs 66(12), p=0.73) but had worse respiratory function (FVC 71(22) vs 80(20), p=0.001). Participants interviewed (n=21) had mean age 71(6) years and FVC 72(22). Major themes related participant's experiences were (1) Value components of PR (2) Knowledge about PR and (3) Barriers. Social aspects, individualisation of the PR program and educational sessions were most appreciated topics mentioned. Poor accessibility, lack of perceived benefits and fear of exercise were some of the identified barriers to PR.

Conclusions: Referral to PR is common for patients with ILD particularly in those with lower respiratory function. Overcoming barriers to PR attendance may require alternative program models to improve accessibility and enhance understanding of its potential benefits.

94. THE EFFECT OF DONOR TOBACCO SMOKING HISTORY ON RECIPIENT'S LONG-TERM SURVIVAL POST LUNG TRANSPLANTATION

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Lung transplantation is a widely accepted form of treatment for patients with end-stage lung disease. However, the use of lungs from a donor with a significant tobacco smoking history remains controversial as implications of donor smoking in early post-operative outcomes for recipients have been established.

AIM: To investigate the effect of donor smoking on long term survival in lung transplant recipient (Oto et al., 2004).

METHOD: The long term survival of 163 heart-and-lung transplant (HLTx) and bilateral lung transplant (BLTx) recipients between 1995-2002 were retrospectively reviewed. Eighty-three (53.5%) donors had no smoking history whilst 72 (46.5%) had a smoking history. Kaplan-Meir Regression models were used to assess 10 year mortality rates (all-cause death). To test the cumulative dose effect of donor pack years, recipients with a donor smoking history were divided into two groups: smoking history of 1-15 pack years (n=30) and 16+ pack years (n=42). Hazard ratios were compared between groups.

RESULTS: There was no significant difference in 10 year survival between lung transplant recipients with and without donor smoking history (p=0.51). There were no between group differences for smoking history (p=0.79) (Figure 1). There was no statistical difference in hazard ratios between never smokers (p=0.439), donor smoking history of 1-15 pack years (p=0.615) and 16+ pack years (p=0.721).
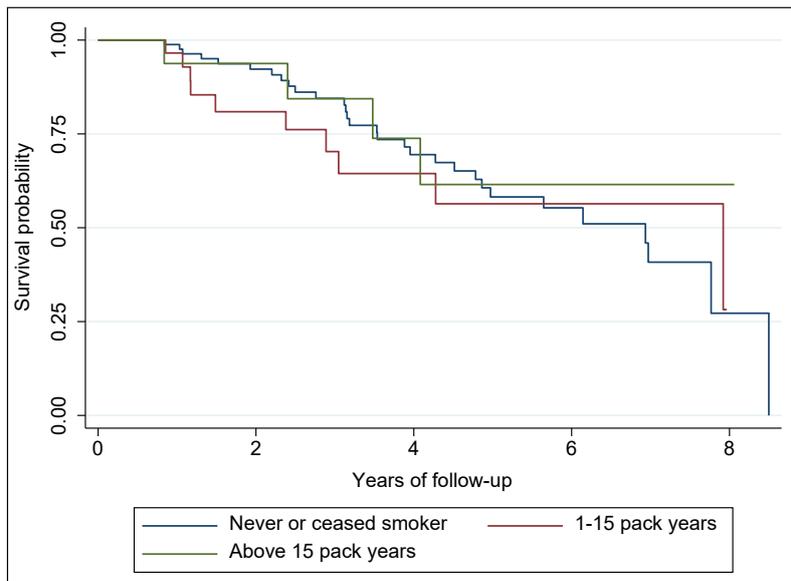
Figure 1. Kaplan-Meier curve, dose effect

CONCLUSION: A smoking history, no matter the cumulative amount, in lung transplant donors does not affect the long term survival of the lung transplant recipient in this retrospective cohort. This finding may have implications for expanding the donor criteria and enabling lung transplant opportunities for a greater number of patients with end-stage lung disease.

95. DEVELOPMENT OF A SELF-MANAGEMENT PACKAGE FOR PULMONARY FIBROSIS: AN INTERNATIONAL DELPHI STUDY

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Self-management is a critical part of disease management for people with pulmonary fibrosis (PF) but there is a lack of consensus regarding what components should be included.

AIM: To attain consensus from PF experts and people with PF on the essential components and optimal format of a self-management package for PF.

METHODS: A 2-round Delphi process was conducted between February and June 2021. In each round, a panel of international health professionals with an expertise in PF completed an online survey to rate a range of components, and statements regarding the format and delivery of a self-management package in PF. Consensus was defined a priori. An online focus group of people with PF was conducted following each survey round to include patient perspectives and validate the items selected.

RESULTS: Forty-five PF experts participated in round 1 and 51 in round 2. Participants included respiratory physicians, nurses, physiotherapists, exercise physiologists, psychologists, and clinical researchers. Both focus groups included six patients with IPF and non-IPF diagnoses (median forced vital capacity: 57 (ranged 8-94)% predicted). A total of 12 components were considered essential for self-management in PF: 1) understanding treatment options for PF; 2) understanding and accessing clinical trials; 3) managing medications and side effects; 4) role of oxygen therapy; 5) role and importance of pulmonary rehabilitation and regular physical activity; 6) managing shortness of breath; 7) managing fatigue; 8) managing mood; 9) managing co-existing medical conditions; 10) smoking cessation advice and support; 11) accessing community support; and 12) how to communicate with others when living with PF. Both groups agreed that the components should be individualised, and that effective self-management in PF required goal setting and feedback.

CONCLUSION: This study identified essential components of self-management in PF and provided a basis for the development of a self-management package for PF.

96. IMPROVING THE PREDICABILITY OF TIME TO DEATH IN CONTROLLED DONATION AFTER CIRCULATORY DEATH LUNG DONORS

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Although the use of donation-after-circulatory-death (DCD) donors has significantly increased lung transplant (LTx) rates, 25-40% of intended DCD do not convert to actual donors due to non-progression to asystole in the required time frame after withdrawal of cardio-respiratory support (WCRS). Predicting which intended DCD patient will progress remains problematic, and no studies have focused specifically on DCD lung donor progression.

Aim: A retrospective review of intended DCD lung donors to develop a prediction model of the likelihood of progression to death.

Methods: All intended DCD lung donors referred to the Alfred Lung Transplant Service were reviewed. Donor demographics & relevant medical history, reason for WCRS, ICU hemodynamic/ventilation/admission data were collated, with significant variables analysed using logistic regression and construction of a classification and regression tree (CART) model.

Results: Between 2014 and 2018, 159 of 334 referred DCD donors were accepted with 100 (63%) progressing to LTx donation, while 59 (37%) did not progress. Comparing progressed and non-progressed DCD, in logistic regression the significant factors related with progression to actual donation were length of ICU stay ≤5 days, severe infra-tentorial brain damage on imaging and the use of vasopressin. CART modelling of the likelihood of death with-in 90 minutes post WCRS provided prediction with a sensitivity of 1.00 and a positive predictive value of 0.56 (Figure 1). Of the 59 who did not progress, 26 patients (44%) died within the subsequent 6 hours.

Conclusion: DCD lung donor referrals received early after ICU admission, with non-spontaneous ventilatory mode, deep coma and severe infratentorial damage were relevant predictors of progression to death. This CART prediction model is useful to exclude DCD donor candidates with low probability of progression, and is now assisting the LTx team to make decisions on lung donor retrievals and better resource allocation.
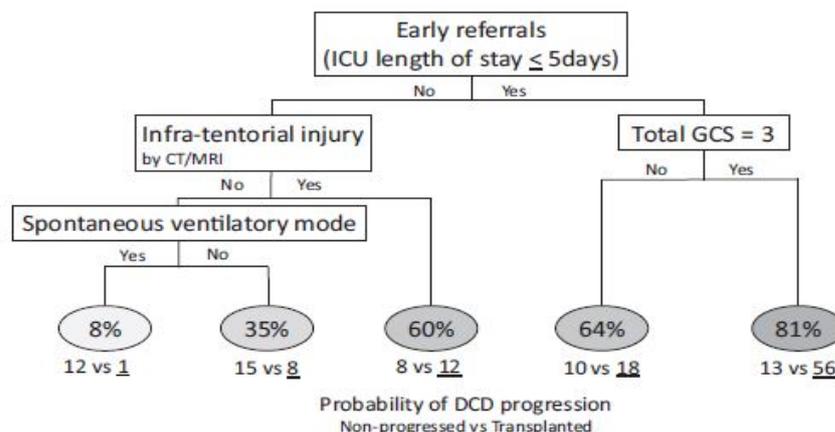
Figure 1: CART model

97. CHILDREN'S AND ADOLESCENT'S PERCEPTION OF ENGAGEMENT IN EVERYDAY ACTIVITIES AFTER LUNG TRANSPLANTATION

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Following lung transplantation, it is unknown how children/adolescents self-assess their performance in everyday activities, how important these activities are for them, and whether resumption of everyday activities influences self-reported quality of life.

AIM: To examine the effect of lung transplantation on children's and adolescent's perception of engagement in everyday activities, over the first 18 months post-transplant.

Method: A single case study pre-post design was conducted at a National Paediatric Lung Transplant Service. All eligible patients (aged between 6 and 18 years, at least 3-months post first single lung transplant) and their parent were invited to participate. Outcomes were collected at 3-months and 18-months post-transplant. Outcomes included self-reported quality of life (Paediatric Quality of Life Inventory (PedsQL), including the Transplant Module)) and self-reported engagement in meaningful life roles, (Child Occupational Self-Assessment (COSA) Scale)). Analysis included paired between-time differences and descriptive analysis.

RESULTS: Seven participants were recruited to the trial with a mean age of 13 (SD 4) years (range 6 to 17 years) and a diagnosis of cystic fibrosis. Self-reported quality of life remained stable between 3-months and 18-months for both children and parents. Children's self-reported quality of life significantly decreased (-13.68, 95% CI -25.75 to -1.59; p=0.03) as measured using the Transplant Module from 3-months to 18 months, however parent's ratings remained stable. Big problems with self-care tasks, family engagement, and coping with worries were reported at 3-months. At 18-months, the problem activities had shifted to community engagement and independence.

CONCLUSION: Time is a factor in self-reported quality of life and engagement in meaningful life roles for children/adolescents and their parents 3 months to 18 months post lung transplant. Findings highlight the importance of focusing on occupational roles and occupational performance of children and adolescents when designing post-transplant interventions, suggesting a key role for occupational therapy after transplantation.

98. TOP 10 RESEARCH PRIORITIES FOR PULMONARY FIBROSIS: WHAT MATTERS MOST TO PEOPLE LIVING WITH THE DISEASE, THEIR CAREGIVERS, HEALTHCARE PROFESSIONALS AND RESEARCHERS?

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People with pulmonary fibrosis (PF) experience a high symptom burden, reduced quality of life and a shortened lifespan. Treatment options are limited and little is known about what patients, caregivers and healthcare professionals (HCPs)/researchers consider as being the most important research priorities.

AIM: This study aimed to identify the top 10 research priorities for PF across all stakeholders.

METHODS: Participants included people with PF, caregivers and HCPs/researchers involved with PF. The research priority setting exercise involved three stages: (1) identifying priorities using an open-ended questionnaire and thematic analysis, (2) development of specific research questions at a face-to-face workshop and (3) online ranking of research questions to identify the top 10 research priorities.

RESULTS: 196 participants completed stage 1 generating 560 questions from which 14 research themes were identified. Stage 2 involved 32 participants and generated 53 research questions from which 39 unique questions were used for the final ranking. Stage 3 was completed by 270 participants. Across all stakeholders, the top ranked priorities focused on medications to reverse scarring in the lungs (ranked 1st), approaches to improving lung function (ranked 2nd and 8th), interventions aimed at alleviating symptoms including shortness of breath and cough (ranked 5th 6th and 7th), prevention of PF (ranked 3rd and 4th) and the best exercise programme for PF (ranked 10th). There was good consensus among people with PF/carers and HCPs/researchers on the top 10 priorities, however, causes of acute exacerbations and early diagnosis for improving survival, was ranked higher by HCPs/researchers.

CONCLUSION: This is the first research setting exercise for pulmonary fibrosis. Identification of priority areas related to reversing lung scarring, improving lung function, alleviating symptoms and effective exercise programs will allow researchers, funders and policymakers to ensure that future research efforts are well aligned with stakeholder priorities.

99. COMPARISON OF WORK OF BREATHING: HEART FAILURE VS INTERSITIAL LUNG DISEASE

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BACKGROUND: Heart failure with central sleep apnoea and Cheyne Stokes respiration (HF-CSA-CSR) and interstitial lung disease (ILD) are characterised by tachypnoea, reflecting an increased work of breathing (WOB). Whilst tachypnoea is continuous in ILD, it is periodic in HF-CSA-CSF. Our hypothesis is that the periodicity reflects adaptive efficiency.

METHODS: We assessed polysomnograms of male patients attending for either heart transplant or ILD assessment. WOB during non-REM sleep was estimated by the breath to breath interval (BBI), from which respiratory rate (RR) was calculated. An age matched control group with snoring, AHI<5 and neither HF or ILD was included.

RESULTS: 523 sleep studies over a 3 year period were reviewed. Four patients were identified in each group. They were matched for age and BMI. During the hyperpneic phase of the HF-CSA-CSR and ILD group, as compared with the normal group there was a shorter BBI: HF-CSA-CSR (mean±sd) 3.4 ±0.1, ILD: 3.5 ±0.3, control: 4.4 ±0.4, P=0.003. There was no difference in BBI between the HF-CSA-CSR and ILD group. There was no difference in FVC or awake $PaCO_2$ between the HF-CSA-CSR and ILD groups. Respiratory rate during slow wave sleep (SWS) was different between groups: ILD (mean±sd): 18.2 ±2.3, control: 14.3 ±1.0, HF-CSA-CSR: 10.3 ±0.8, P =0.0002. RR was significantly lower in the HF-CSA-CSR group in SWS when compared to ILD and control groups.

CONCLUSION: This data would suggest that both HF-CSA-CSR and ILD have similar severities of tachypnoea (aka work of breathing) compared with controls, however the RR in SWS is significantly lower in the HF-CSA-CSR group compared with ILD, despite similar PaCO2. This would indicate HF-CSA-CSR has similar WOB, yet greater efficiency, than ILD. RR may serve as a marker of WOB for patients undergoing workup for ILD or heart transplant assessment.

TRAUMA AND EMERGENCY MEDICINE

100. FACTORS ASSOCIATED WITH OUTCOMES IN A CHEST TRAUMA COHORT

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Background: Chest trauma is associated with significant morbidity and mortality, and accounts for over 15% of all trauma admissions worldwide.

Aims: To describe characteristics and hospital outcomes for patients with chest trauma (isolated or in combination with other injuries).

Methods: Demographic data for patients admitted to the Alfred trauma ward were collected, including the STUMBL score which predicts risk of complications for patients with chest trauma. Outcome measures including hospital length of stay

(LOS), intensive care unit (ICU) readmission, frailty, mortality, and discharge disposition were also collected, and their association with chest trauma described.

Results: From November 2020 to April 2021, 1037 patients were admitted to the trauma ward and 30% of these had chest trauma (n=307). Of the 65% with a STUMBL score >15 (deemed high risk for complications), 56% required an ICU admission compared with 24% in the low risk group (p<0.001). When taking into account gender, ICU stay and fund, there is no association between higher or lower risk STUMBL scores, and total LOS (p=0.71) or ward LOS (p=0.16). Having an ICU stay was the only factor associated with total and ward LOS (<0.001. No difference in ICU readmission related to high risk chest injury (p=0.54) or in regards to discharge destination or mortality (p=0.48) were seen.

Conclusion: High risk chest trauma is associated with ICU stay, but not with hospital outcomes such as discharge destination or LOS. The effect of increased physiotherapy intensity in this group will be further discussed.

101. SPLENIC SALVAGE AND COMPLICATIONS AFTER SPLENIC ARTERY EMBOLIZATION FOR BLUNT ABDOMINAL TRAUMA: THE SPLEEN-IN STUDY

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Background: As an adjunct to non-operative management, splenic artery embolization (SAE) has been increasingly utilized throughout the world and is now the standard of care for hemodynamically stable patients.

Aim: Assess the rate of splenic salvage and complications after SAE for blunt trauma and further sub-stratify the role of angiography in AAST grade III injuries with significant hemoperitoneum.

Methods: All patients between 1 January 2009 and 1 January 2019 who underwent blunt trauma and proceeded to embolization were included. Technical success was defined as successful angiographic occlusion of the target artery at the conclusion of embolization. Clinical success was defined as splenic salvage at discharge. Vascular lesions were characterized including those with active bleeding, pseudoaneurysm, and arterio-venous fistula.

Results: Two hundred thirty-two patients were included in the study. Treatments were performed at a median of 0 days (range 0–28 days) and the median AAST grade was IV (range III-V). Technical success was achieved in all patients. There were 13 complications (5.6%) consisting of re-bleed (9, 3.9%), infarction (3, 1.3%), and access site haematoma (1, 0.43%). Clinical success was achieved in 97% of patients with 7 patients requiring splenectomy after SAE (3.0%) at a median time of 4 days (range 0–17 days). Angiography in patients with grade III injuries identified 18 occult vascular injuries not identified at initial CT (p<0.0001).

Conclusion: The SPLEEN-IN study shows that treatment of intermediate-high grade blunt force traumatic splenic injuries using SAE resulted in a low rate of complication and splenic salvage in 97% of patients, providing a safe and effective treatment in stable patients. In addition, angiography of grade III injuries identified occult vascular lesions and may warrant treatment of select patients in this cohort.

102. ASSOCIATION BETWEEN TYPE 2 DIABETES AND LONG-TERM OUTCOMES IN MIDDLE-AGED AND OLDER TRAUMA PATIENTS

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BACKGROUND: Diabetes is associated with increased hospital complications and mortality following trauma. However, there is limited research on the longer-term recovery of trauma patients with diabetes. The aim of this study was to explore the association between type 2 diabetes (T2D) and in-hospital and 24-month outcomes in major trauma patients.

METHODS: In this cohort study using the Victorian State Trauma Registry, middle-aged and older adults (≥ 45 years) with major trauma were followed up at 24-months post injury. Logistic regression (univariable and multivariable) analyses were used to determine the association between diabetes status and 24-month patient-reported outcomes. In-hospital outcomes were compared between groups using chi-square tests.

RESULTS: Of the 11,490 participants who survived to hospital discharge, 8,493 survived to 24-months post-injury and were followed-up at that time point: 953 people (11%) with and 7540 (89%) without T2D. People with T2D had a higher in-hospital death rate (19%) compared to people without T2D (16%), p<0.001. After adjusting for confounders, people with T2D had poorer outcomes 24-months post injury than people without T2D, with respect to functional recovery (Extended Glasgow Outcome Scale) (adjusted odds ratio [AOR] [95% CI]: 0.57 [0.48, 0.68]) and return to work/study (AOR [95% CI]: 0.51 [0.37, 0.71]). People with T2D experienced higher odds of problems with mobility (AOR [95% CI]: 1.91 [1.59, 2.29]), self-care (AOR [95% CI]: 1.94 [1.64, 2.29]), usual activities (AOR [95% CI]: 1.50 [1.26, 1.79]), pain and discomfort (AOR [95% CI]: 1.76 [1.49, 2.08]), anxiety and depression (AOR [95% CI]: 1.46 [1.24, 1.71]), and self-reported disability (AOR [95% CI]: 1.51 [1.28, 1.79]) than people without T2D.

CONCLUSION: Major trauma patients with T2D have a poorer prognosis than patients without T2D, both during their hospital admission and 24-months post-injury. Patients with T2D may need additional health care and support following trauma to reach their recovery potential.

103. ARTIFICIAL INTELLIGENCE ASSISTANCE IN DIAGNOSING INCIDENTAL PULMONARY EMBOLISM

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Pulmonary embolism (PE) is the third most common cause of cardiovascular death worldwide. Although computed tomography pulmonary angiography (CTPA) has become the gold standard in confirming the diagnosis of PE, incidental PE is often detected in other routine CT scans that image the chest with a prevalence between 1.1-3.6%.

There has been substantial progress made in deep learning algorithms that can learn feature representations from large datasets and do not require prior explicit definitions. Integration of these algorithms within the imaging workflow can increase triaging efficiency, reduce interpreting errors, and minimise the radiologists' workload and fatigue.

The aim of this study is to evaluate the performance of an FDA-approved, deep convolutional neural network based AI tool for the detection of incidental PE in routine contrast-enhanced CT (CECT) studies of the chest in our institution for a period prior to its implementation. A total of 612 CECT examinations including the thorax were performed between November and December 2019: 119 CTPAs and 493 CT Chest.

Upon the reviewing radiologist's second read, 22 of the 612 exams were PE-positive and 590 were PE-negative. The prevalence of PE in the sample was 3.6%. Fifteen PE were identified on CTPA exams and 7 were identified on other CECT exams (incidental PE). The algorithm flagged 36 studies as PE-positive and 576 as PE-negative with 14 false positive (FP) cases, had a specificity of 97%, a sensitivity of 82%, a PPV of 50%, and a NPV of 99%. It also detected 6 of the 7 incidental PE, 4 of which were not documented in the radiology report; however, 63% of the flagging in those non-dedicated CTPA studies were FPs compared to only 20% on dedicated CTPAs.

In the last decades, there have been concerns regarding the overdiagnosis of pulmonary embolism while mortality rates remain unchanged. Overdiagnosis refers mostly to cases of small peripheral embolisms, for which, if no treatment is offered, are unlikely to cause more harm than if anticoagulation therapy is started. Added to that, on the hands of an inexperienced radiologist, flagged false positives scans can contribute toward this trend.

The implementation of a sensitive screening AI tool increases the accuracy of radiology reports and impacts on patients' clinical management. Although this invariably leads to overdiagnosis, the long term clinical implication is still to be determined.

104. PROXIMAL SPLENIC EMBOLISATION VERSUS DISTAL SPLENIC EMBOLISATION FOR MANAGEMENT OF FOCAL DISTAL ARTERIAL INJURIES OF THE SPLEEN

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Introduction: To compare the outcomes of proximal (pSAE) versus distal (dSAE) splenic artery embolisation for management of focal distal arterial splenic injuries secondary to blunt splenic trauma.

Method: Ethical approval was granted by the hospital research and ethics committee, Project 389/19. All patients who underwent splenic artery embolisation secondary to blunt abdominal trauma from 1 January 2009 to 1 January 2019 were reviewed. Patients with a tandem embolisation (both proximal and distal embolisations) or those with no acute vascular injury on angiography were excluded. Patient demographics, injury type/ AAST grade (2018 classification), technique of embolisation and outcomes were collected. Complications and splenectomy rates up to 30 days were recorded.

Results: 136 out of 232 patients had an embolisation performed for a distal vascular injury including active arterial bleeding, pseudoaneurysm or arteriovenous fistula. Mean age was 41 (range 16–84). Mean AAST grade was 4 (range 3–5). Mean Injury Severity Score was 22. pSAE was performed in 79.4% ($n = 108$) and dSAE in 20.6% ($n = 28$). Major complications occurred in 12 patients (pSAE $n = 12$, 11.1%; dSAE $n = 0$, $P > 0.05$); 6 pSAE required splenectomy ($n = 6$, 5.6%). There was no significant difference in outcomes between the two groups or when based on AAST grading.

Conclusion: No significant difference was observed between proximal and distal embolisation techniques for blunt trauma patients with a distal vascular injury in terms of technical and clinical success.

105. UTILITY OF COMPUTED TOMOGRAPHY ANGIOGRAPHY IN TRAUMATIC LOWER LIMB INJURY: REVIEW OF CLINICAL IMPACT IN LEVEL 1 TRAUMA CENTRE

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Introduction: CT angiography (CTA) is efficient and accurate in detecting lower limb vascular injury in the setting of trauma. However, its use should be limited to diagnosis in limited settings where there are hard or soft signs of traumatic vascular injury.

Aims: This study aimed to correlate the use of CTA in our level 1 trauma centre, and the clinical impact of the CTA findings.

Materials and methods: All CT leg angiography acquired from January 2016 through April 2019 were reviewed via retrospective search. Studies not acquired for trauma were excluded. Imaging and reports were reviewed to assess for vascular injury. Electronic medical records were reviewed to assess the presence or absence of classical 'hard' or 'soft' signs of vascular injury and whether vascular intervention was undertaken.

Results: A total of 347 lower limb injuries were identified in 273 men and 74 women. Mean age was 41.5 years ranging from 15-95 years. 268 cases were fractures with 177 open injuries. 301 of injuries were secondary to blunt trauma, 31 penetrating injury occurred and 15 cases were ascribed to blast/gunshot injury. 74 (21.3%) studies were deemed to have a positive finding of vascular injury, 249 (71.8%) were reported as negative and 24 (6.9%) were indeterminate. Of the cases with positive findings, 26 underwent intervention (7.4% of all patients undergoing CTA). No patients with negative CTA required intervention, while three (3, 0.8% of total) with indeterminate findings required intervention. Where there were no clinical signs (absence of any hard or soft signs) 249 CTA's were performed and none required any form of intervention.

Conclusion: In the absence of clinical signs of vessel injury, CT angiography is unlikely to demonstrate occult vascular injury requiring intervention in the setting of lower limb trauma.

106. NEW ALLIED HEALTH MODEL OF CARE: EARLY AND INTENSIVE THERAPY FOR ACUTE HOSPITAL TRAUMA INPATIENTS

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Introduction: Evidence suggests that early and intensive allied health (AH) therapy may allow for improved outcomes following hospitalisation. Whether this is applicable for trauma patients is unknown.

Methods: In 2018, the Transport Accident Commission and Alfred Health partnered to establish a new 7-day model of AH care for acute hospital trauma patients. The team consisted of physiotherapists, occupational therapists, orthotists, speech pathologists, dietitians, social workers, neuropsychologists, clinical psychologists and allied health assistants. The team was led by a multi-professional Allied Health Team Leader.

Underpinning the model of care was a quality management system and improvement science methodology to integrate, embed and sustain this new workforce. Outcomes include discharge destination, length of stay (LOS), discharge day/time, hospital acquired complications and readmission rates as compared to a similar patient cohort in 2019.

Results: The 12-month project commenced in January 2020, paused for 6 months due to COVID, recommencing in November 2020. Reporting, education, governance structure and learnings from the establishment of the team will be described. Six month outcomes showed a decrease in ward LOS of 0.25 days (Median 3.2 days) with no increase in hospital readmission rate (9%). The 2020 cohort were found to have a 52% increase in the odds of being discharged home rather than to another inpatient bed (acute or rehabilitation) and there was a decrease in ICU readmissions of 1.3%.

Conclusion: Providing early, intensive AH therapy with a team based approach to patient care can lead to improved patient and hospital outcomes, and reduce health service utilisation.

107. LONG TERM IMMUNE FUNCTION FOLLOWING SPLENIC ARTERY EMBOLISATION FOR BLUNT ABDOMINAL TRAUMA

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The spleen is commonly injured in blunt trauma and a common cause of intra-abdominal bleeding and splenic artery embolisation has become the preferred method of treatment over recent decades.

AIM: To quantify long-term splenic immune function post splenic artery embolisation for blunt trauma.

METHODS: Quantitative splenic immune function was assessed in a previous study at this institution at a median of 6.5 months after embolisation. These patients were invited for longer-term follow-up at a median of 102 months (8.5 years) after embolisation. The median splenic injury grade was American Association for the Surgery of Trauma (AAST) 4. IgM memory B cell levels (percentage of lymphocytes and percentage of B cells) and splenic volume were assessed.

RESULTS: Of the 49 patients who were evaluated previously, 9 patients agreed to return for long-term follow-up. One patient was excluded due to unrelated chronic immune disease. Seven cases were proximal embolisation, with one distal embolisation. IgM memory B cell levels were normal for all patients at long-term follow-up, with significant increases in proportions of IgM memory B Cells compared to previous early follow-up; p=0.02. One patient with low IgM memory B cell levels at short-term had normalised levels at long-term follow up. Splenic volume trended downwards over time (p=0.05), however splenic volume does not correlate with function.

CONCLUSION: This study quantitatively demonstrated preserved long-term splenic immune function following splenic artery embolisation for blunt abdominal trauma, and a significant increase in the long-term splenic immune function when compared to short-term. Therefore, splenic artery embolisation should not be dissuaded by concerns about longer-term immune function, as patients in our cohort quantitatively remained or returned to normal. This data will help guide clinical decision making and rationalise future use of antibiotic prophylaxis and vaccination in patients post embolisation.

108. EARLY PHARMACOLOGIC VENOUS THROMBOEMBOLISM (VTE) PROPHYLAXIS AFTER SPLENIC ARTERY EMBOLISATION IS NOT ASSOCIATED WITH AN INCREASED RISK OF RE-BLEED

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Background: Prevention of venous thromboembolism (VTE) after major trauma is a challenge. A landmark study from Geerts et al. showed that 58% of major trauma patients experienced VTE during their admission. Currently, no direct evidence exists concerning the interplay between high-grade splenic injury treated with splenic artery embolisation (SAE), and appropriate timing for pharmacologic VTE prophylaxis.

Aim: This study aimed to assess the timing of VTE prophylaxis after SAE for blunt trauma and the relationship between initiation of pharmacologic prophylaxis and splenic re-bleed requiring splenectomy.

Methods: Retrospective study over a 10-year period from 1 January 2009 to 1 January 2019. All adult patients where SAE was employed after blunt trauma were included.

Results: 232 patients were treated with SAE. 181 patients received VTE prophylaxis for median splenic injury grade of AAST IV (IQR 1), of mean age 41 years (SD 19), and median ISS 24 (IQR 18). 51 patients were categorised as low-risk and thus did not received VTE prophylaxis. Their median injury grade was AAST IV (IQR 1, p=0.144), age 36 years (SD 17, p=0.074), and median ISS 17 (IQR 10, p=0.268).

In the VTE prophylaxis group, the median time to beginning VTE prophylaxis was 59.5 hours (IQR 46 hours) and there were 6 patients (3.5%) who required subsequent splenectomy. There were no splenectomies in the group without VTE prophylaxis.

Multivariate analysis showed that the incidence of re-bleed after SAE has no association with starting prophylactic anticoagulation within the first 24 hours after SAE (OR 0.3, p=0.441, 95%CI 0.014-6.505), within hours 24-48 after SAE (OR 0.2, p=0.268, 95%CI 0.007-4.382), or within hours 48-72 (OR 0.1, p=0.167, 95%CI 0.005-2.501).

Conclusion: When a patient is deemed to be at high risk of VTE after SAE, the odds of splenectomy is not significantly different when beginning LMWH <24 hours after embolization.

109. PARAMEDIC STREAMING UPON ARRIVAL IN EMERGENCY DEPARTMENT: A PROSPECTIVE STUDY

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OBJECTIVE: The role of paramedics in hospital triage or streaming models has not been adequately explored and is potentially a missed opportunity for enhanced patient flow. The aim of the present study was to assess the concordance between a streaming decision by paramedics with the decision by nurses after arrival to the ED.

METHODS: A prospective observational study was conducted. Paramedics were met at the entrance to the hospital and asked which destination they thought was appropriate (the index test). The ED nurse streaming decision was the reference standard. Cases of discordance were reviewed and assessed for clinical risk by an independent expert panel that was blinded.

RESULTS: We collected data from 500 cases that were transported by ambulance consisting of 55% males with a median age of 57 years (interquartile range 38–75). The overall concordance between paramedics' and streaming decision was 86.4% (95% confidence interval 83.1–89.1). The concordance was highest among patients streamed to resuscitation and

general cubicles. Among discordant cases (n = 68), 39 were streamed to a more acute destination than the paramedic suggested. Of the 68 discordant cases, 56 were deemed to be of no clinical risk.

CONCLUSION: Despite limited knowledge of patient load within the ED, paramedics can allocate a streaming destination with high accuracy and this appears to be associated with low clinical risks. Early pre-hospital notification of streaming destination with proactive allocation of ED destination presents a real opportunity to minimise off-load times and improve patient flow.

110. OUTCOMES FOR EMERGENCY DEPARTMENT PATIENTS WITH SUSPECTED AND CONFIRMED COVID-19: AN ANALYSIS OF THE AUSTRALIAN EXPERIENCE IN 2020

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AIM: The aim of this study was to describe the characteristics and outcomes of patients presenting to Australian emergency departments (EDs) with suspected and confirmed COVID-19 during 2020, and to determine the predictors of in-hospital death for SARS-CoV-2 positive patients.

METHODS: This analysis from the COVED Project presents data from twelve sites across four Australian states for the period from 1 April to 30 November 2020. All adult patients who met local criteria for suspected COVID-19 and underwent testing for SARS-CoV-2 in the ED were eligible for inclusion. Study outcomes were mechanical ventilation and in-hospital mortality.

RESULTS: Among 24,405 eligible ED presentations over the whole study period, 423 tested positive for SARS-CoV-2. During the "second wave" from 1 July to 30 September 2020, 26 (6%) of 406 SARS-CoV-2 patients received invasive mechanical ventilation, compared to 175 (2%) of the 9,024 SARS-CoV-2 negative patients (OR 3.5; 95% CI: 2.3-5.2, p<0.001), and 41 (10%) SARS-CoV-2 positive patients died in hospital compared to 312 (3%) SARS-CoV-2 negative patients (OR 3.2; 95% CI: 2.2-4.4, p=0.001). For SARS-CoV-2 positive patients, the strongest independent predictors of hospital death were age (OR 1.1; 95% CI: 1.1-1.1, p<0.001), higher triage category (OR 3.5; 95% CI 1.3-9.4, p=0.012), obesity (OR 4.2; 95% CI: 1.2-14.3, p=0.024) and receiving immunosuppressive treatment (OR 8.2; 95% CI: 1.8-36.7, p=0.006).

CONCLUSION: ED patients who tested positive for SARS-CoV-2 had higher odds of mechanical ventilation and death in hospital. The strongest predictors of death were age, a higher triage category, obesity and receiving immunosuppressive treatment.

111. LONGITUDINAL ANALYSIS OF NEUTROPHIL TO LYPHOCYTE RATIO OVER TIME IN TRAUMA PATIENTS

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BACKGROUND: The neutrophil to lymphocyte ratio (NLR) has been proposed as a marker of systemic inflammation in major trauma patients that is associated with in-hospital mortality.

OBJECTIVES: The aim of this study is to determine the discriminative ability of the NLR profile over 48 hours as a predictor of in-hospital mortality following major trauma.

METHODS: This was a case-control study involving all major trauma patients meeting criteria for inclusion into the Alfred Health Trauma Registry who presented directly from the scene of injury over a 24-month period. Patients were then divided into two groups, cases being major trauma patients who died at hospital discharge and controls being patients who survived. We extracted data for 0, 24 and 48 hour NLR values for each patient. Primary outcome was mortality at hospital discharge.

RESULTS: Data were extracted for 1,689 major trauma patients, of which 72% were male, median age was 49 years (IQR 31-68) and most (90%) patients presented after a blunt mechanism of injury. There were 165 cases who were compared to 1,524 controls Significant differences were observed for age ($p<0.001$), Injury Severity Score ($p<0.001$) and NLR values across all three time-points. Analysis of response profiles demonstrated a significant difference between the trajectories of NLR between 24 and 48 hours (chi2 test characteristic for parallelism 89.8, $p<0.001$).

CONCLUSIONS: NLR trajectory over 48 hours from admission demonstrated promise as a prognostic tool after trauma and warrants further investigation.

112. REGIONAL ANAESTHESIA FOR RIB FRACTURES: A PILOT STUDY OF SERRATUS ANTERIOR PLANE BLOCK

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OBJECTIVE: Rib fractures are not only painful but are associated with morbidity and mortality, especially in older patients. The Serratus Anterior plane block (SAPB) is a plane block distant from major neurovascular bundles and may provide anaesthesia to a substantial area of the hemithorax. This pilot study was designed to assess if the SAPB can be safely and efficiently incorporated to the trauma reception workflow of an adult, level-1 trauma centre.

METHODS: A convenience sample of 20 adult patients with at least two or more unilateral rib fractures received an SAPB performed by an Emergency Physician in addition to their standard analgesic regime. Time to perform the procedure, the number of attempts and complications were recorded as feasibility measures. Secondary outcome was safety of the block. Numerical pain scores at pre-determined time points over 4 hours, the diagnosis of hospital acquired pneumonia, hospital Length of Stay (LOS) and mortality at hospital discharge were collected to provide pilot data on effectiveness.

RESULTS: The median time to perform the procedure was 5.5 (IQR: 4.6-10) mins with a range of 2-10.5 mins. Most (16; 80%) SAPBs were completed in a single attempt. There were no documented complications. Median pain scores reduced from 6.5 (6-8) and were maintained at 3 (2-5) at 4 hours after the SAPB.

CONCLUSIONS: This study demonstrated feasibility of ultrasound guided SAPB among patients with multiple rib fractures in the Emergency Department. No complications were observed. Further prospective evaluation of analgesic effects in a larger cohort is indicated.

113. THE COST TO PERFORM SPLENIC ARTERY EMBOLISATION FOLLOWING BLUNT TRAUMA: ANALYSIS FROM A LEVEL 1 AUSTRALIAN TRAUMA CENTRE

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Introduction: Splenic artery embolisation (SAE) has been shown to be an effective treatment for haemodynamically stable patients with high-grade blunt splenic injury. However, there are no Australian estimates of how much treatment costs.

Aims: The purpose of this study was to evaluate the cost of providing SAE to patients in the setting of blunt abdominal trauma at an Australian level 1 trauma centre.

Methods: This was a single-centre retrospective review of 10 patients who underwent splenic embolisation from December 2017 to December 2018 for the treatment of isolated blunt splenic injury, including cost of procedure and the entire admission. Costs included angiography costs such as equipment, machine, staff, and post-procedural costs including pharmacy, general ward costs, orderlies, ward nursing, allied health, and further imaging.

Results: During the study period, patients remained an inpatient for a mean of 4.8 days and the rate of splenic salvage was 100%. The mean total cost of splenic embolisation at our centre was AUD$10523 and median cost AUD$9959.6 (range of $4826-$16836). The use of a plug as embolic material was associated with increased cost than for coils. Overall cost of patients requiring ICU was mean AUD$11894 and median AUD$11435.8. Overall cost for those not requiring ICU was mean AUD$7325 and median AUD$8309.8.

Conclusion: Splenic embolisation is a low-cost procedure for management of blunt splenic injury. The cost to provide SAE at our centre was much lower than previously modelled data from international studies. From a cost perspective, the use of ICU for monitoring after the procedure significantly increased cost and necessity may be considered on a case-by-case basis. Further research is advised to directly compare the cost of SAE and splenectomy in an Australian setting.

114. IS FRAILTY ASSOCIATED WITH POOR HOSPITAL BASED OUTCOMES?

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Introduction: Frailty has a huge impact on outcomes following trauma, with it better reflecting outcomes than age itself. Frailty also leads to prolonged hospitalisation and increased burden on the hospital system. The aim of this study is to review the prevalence of frailty in our trauma cohort and the association of frailty with hospital based outcomes.

Methods: Patient demographics, discharge destination, hospital length of stay (LOS), and mortality were reviewed. Frailty was assessed using the Clinical Frailty Scale (score <4 non frailty, 4 vulnerable, ≥5 frail). Factors associated with frailty and outcomes including discharge destination (home or inpatient care) and LOS (p value <0.2) were included in multivariate models.

Results: 1019 patients were admitted to the trauma ward between November 2020-April 2021 with 176 (17%) being frail and 116 (11%) being vulnerable. In the group over 65 years, 38% were frail. Taking into account age, gender, injury type, residence (home/aged care facility), and in-hospital delirium, frailty was associated with an increased LOS (p<0.001). When taking in account the same factors, being frail was associated with discharge to further inpatient care (AOR3.44 95%CI 1.97-6.02 p value <0.001) whilst being vulnerable was not. All 7 deaths in our cohort were frail.

Conclusion: After taking into account confounding factors, frailty is associated with an increased LOS and over three times the odds of a discharge to further inpatient care, thus further increasing the hospital costs. Identifying frailty on admission will help prioritise resources to limit burden on hospital systems and improve patient outcomes.

115. RISK STRATIFICATION OF EMERGENCY DEPARTMENT PATIENTS WITH ACUTE PULMONARY THROMBOEMBOLISM: IS CHEST PAIN A REASON TO INVESTIGATE?

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Background: Presentation to the emergency department with chest pain is common and is a diagnostic challenge in differentiating the broad spectrum of potential diagnoses. In addition, the diagnosis of acute pulmonary thromboembolism (PE) is also common and is also a challenge given the symptoms and signs can be non-specific. Whilst chest pain has been suggested to increase risk of PE, in the experience of the authors it is commonly seen as an indication for ordering computed tomography pulmonary angiography (CTPA) scans which are negative.

Aims: This study aimed to risk-stratify chest pain as a presenting symptom in patients with a diagnosis of PE to assess for any association. In addition, assess traditionally acknowledged PE risk factors in an Australian population.

Methods: Retrospective single-centre cohort study from 1 January 2019 to 1 January 2020. 730 patients presenting to emergency department and who went on to CTPA examination were included.

Results: The rate of CTPA being positive in this study was 11.6% (85/730). Chest pain was associated with a non-significant reduction in the odds of PE (OR 0.774, p=0.327). Univariate analysis showed significantly increased odds of a diagnosis of PE with presentation for leg pain/swelling (OR 6.670, p<0.001). Multivariate analysis showed increasing age (OR 1.018, 95%CI 1.002-1.034, p=0.024), clinical signs of a DVT (OR 3.194, 95%CI 1.803-5.657, p<0.001), and positive D-dimer (OR 1.762, 95%CI 1.011-3.071, p=0.046) were associated with increased odds of PE.

Conclusion: Emergency Department presentation with chest pain, whilst the most common reason to perform a CTPA, resulted in a weak protective effect with regards to the diagnosis of pulmonary thromboembolism. The use of CTPA in this setting may be rationalised according to other factors such as localised leg pain as a symptom, signs of DVT, increasing age, or positive D-dimer.

116. DEMOGRAPHICS AND HOSPITAL OUTCOMES FOR TRAUMA PATIENTS FOLLOWING AN ICU ADMISSION

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Introduction: Mortality following trauma has decreased since the implementation of the Victorian State Trauma System, resulting in an increased focus on patient reported outcomes. More severely injured patients often require an intensive care unit (ICU) stay.

Aim: To compare the demographics and hospital outcomes of patients admitted ward 5W with and without an ICU stay.

Methods: Data including patient demographics, discharge destination, hospital/ICU length of stay (LOS), readmission, and mortality were reviewed. Patient self-reported EQ5D- 5L (5 domains) were collected on discharge.

Results: 1037 patients were admitted to the trauma ward between November 2020-April 2021 and 332 (32%) had an ICU admission. There was no difference in age (median ICU 56 years vs 60, p = 0.45) with more patients requiring ICU being male (75% vs 65%, p value 0.008). Median ICU LOS was 3.8 days (IQR 1.88-7.58 days). Only 8 patients (0.2%) were readmitted to ICU. In terms of patient-related outcomes, only the EQ5D domain of "usual activities" showed a between group difference, with the ICU group reporting worse outcomes (p value 0.037). 82% of non-ICU patients were discharged home compared to 70% of ICU patients (p value <0.001). There was no difference in mortality (ICU 3 pts: non-ICU 4 p value 0.26).

Conclusion: Almost one third of patients had an ICU admission. Self-reported function on discharge between those patients with and without an ICU stay was not different for mobility, self-care, anxiety or pain EQ5D domains though fewer patients were discharged directly home in the ICU group.

117. CLINICAL USE OF AIDOC "ALWAYS-ON AI": DOES IT HELP INCREASE RADIOLOGISTS' EFFICIENCY AND IMPROVE PATIENT CARE?

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Rapid detection of IntraCranial Hemorrhage (ICH) is crucial for assessing patients with neurological symptoms. Prioritising these urgent scans for reporting presents a challenge for radiologists. At our institution, CT exam requests have increased by 35% since 2015, whereas the incidence of ICH and the number of radiologists have remained the same. Artificial intelligence (AI) offers a solution to enable radiologists to triage urgent scans and potentially reduce reporting errors.

AIM: The purpose of this study was to evaluate the accuracy of an ICH-detection AI solution.

METHODS: The FDA-approved ICH-detection AI solution, based on a convolutional neural network, analysed all technically adequate CT brain exams performed at our institution between November - October 2019. An independent radiologist retrospectively second-read all the CT scans and reports and then reviewed the output of the AI solution for True/False Positives/Negatives.

RESULTS: 1269 CT brain scans were analysed by the AI solution. The independent radiologist confirmed that 184 were ICH-positive and 1085 were ICH-negative. One case that was flagged by the AI solution was initially reported as ICH-negative; however, the independent radiologist confirmed this case was ICH-positive. The sensitivity and specificity of the AI solution were 90.8% (n=167 TP) and 97.2% (n=1055 TN), respectively. The PPV and NPV were 84.8% and 98.4%, respectively. False Positive studies (n=30) were due calcification (falx n=2, dural n=1, meningioma n=1, other n=1), artefacts (n=5), hyperdense lesions (n=5), falx (n=4), dural thickening (n=4), vessels (n=2), C1-2 pannus (n=1), DVA (n=1), tentorium (n=1), choroid plexus (n=1), and colloid cyst (n=1).

CONCLUSION: The sensitivity and specificity of the AI solution was tested on a sample of real-world data from a high-volume centre and shows comparable results to that reported in literature The high PPV makes the prioritisation efficient and reliable, with only 1-2 cases in 10 incorrectly prioritised. The one case that was overlooked by the reporting radiologist indicates the value of enhanced detection when using AI in time-critical indications such as ICH, and can serve as a QA second-read system. Currently, our institution's reporting system has relatively short reporting times, measured from end of the exam to finalisation of the report. Further research into the changes in reporting time pre- and post-AI implementation is required to assess the triaging capabilities and impact of the AI solution. Any improvements, as a result of AI implementation, would provide further evidence to support the use of AI technology in Radiology to increase radiologists' efficiency and improve patient care.

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