AlfredHealth

ABSTRACT BOOK

ALFRED HEALTH WEEK RESEARCH POSTER DISPLAY

The Alfred

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CONTENTS

CATERGORY **PAGE**

ALLERGY ASTHMA AND IMMUNITY

1. THE USE OF DUAL ENERGY CT IN the DIAGNOSIS OF GOUT: A RETROSPECTIVE ANALYSIS

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Gout is the most common form of inflammatory arthritis in men and women. Despite this, the diagnosis of gout remains challenging for clinicians as the 'gold standard' synovial fluid aspiration is often not feasible. Dual Energy Computed Tomography (DECT) is a recent diagnostic development that has been used to assist gout classification.

AIM: To retrospectively analyse the use and effectiveness of DECT in the diagnosis of gout as a part of the The American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) algorithm.

METHODS: 166 adults (127 male, 39 female) underwent a total of 214 DECT examinations for suspected crystal arthropathy. All examinations were performed on a General Electric dual energy CT scanner. Examinations were reported from post-processed images on the Gemstone Spectral Imaging (GSI) software that colour-codes urate at greater than 1200mg/cm^3. Each examination was reported by a specialist musculoskeletal radiologist. The DECT report findings, subject clinical history, laboratory results and other relevant imaging pertaining to the ACR-EULAR gout criterion were retrospectively collected and analysed from the patient e-Medical record.

RESULTS: 55 examinations were 'gout positive' (25.7%), 7 were 'pseudogout positive' (3.3%) and 14 were 'equivocal' (6.5%). The remaining 138 examinations were negative (64.5%). DECT assisted in classifying gout in an extra 30 examinations that would not have met the criteria for gout without the technology. Based on the ACR-EULAR classification of gout, there were 20 cases where a DECT examination could have been avoided as the criteria for gout had already been met prior to the examination.

CONCLUSION: DECT is a valuable tool in the diagnosis and exclusion of crystal arthropathies for referring physicians in the correct clinical setting. The use of DECT as a limited hospital resource can be improved by referring doctors using and adhering to the criteria proposed by the ACR-EULAR in the classification of gout.

2. FLOW CYTOMETRIC ANALYSIS FOR THE IDENTIFICATION OF IMMUNOPHENOTYPIC DIFFERENCES BETWEEN PAD WITH AND WITHOUT NON-INFECTIOUS COMPLICATIONS

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BACKGROUND: Patients with predominantly antibody deficiency (PAD) suffer from severe and recurrent infections due to defects in B-cell antibody responses. Disease incidence is estimated to be 1:25,000 in Australia, and patients require lifelong immunoglobulin replacement and prophylactic antibody treatment. Notably up to 68% patients develop non-infectious complications (NIC) including autoimmunity, which are difficult to treat causing high morbidity and early mortality in PAD patients. Currently, the aetiology of NIC is unknown and there are no diagnostic and prognostic markers to identify patients at risk.

AIM: To identify immunological differences that associate with NIC in PAD patients.

METHODS: We developed a standardised 11-colour flowcytometry panel that was utilised for in-depth analysis of B- and T-lymphocytes in 62 adult PAD patients and 62 age-matched controls.

RESULTS: 27 PAD patients had B-cells and 24 had T-cells below the normal range. Clinical examination of patients identified 47% PAD+NIC, with autoimmunity being the most prevalent. PAD+NIC exhibited marked reductions in B-cells, particularly transitional and IgM+-memory B-cells, with severe decreases in class-switched B-cells identified in both PAD cohorts.

Naïve CD4+ and CD8+ T-cell numbers were dramatically reduced in both cohorts, with memory cell numbers unaffected. As a proportion of CD4+ or CD8+ T-cell memory skewing is observed. Absolute numbers of Th17, Tregs and Tfh17 cells are reduced in PAD+NIC, with Tfh numbers unaffected, although relatively they comprise upto 30% CD4+ T-cells.

CONCLUSION: Class-switched memory B-cells, naïve CD4+ and CD8+ T-cells are severely reduced in both PAD cohorts . In addition, PAD+NIC have severe reductions in B-cell, Th17, Treg and Tfh17 numbers. These key differences can be utilised as biomarkers for disease pathogenesis. Our data demonstrates that it is critical to measure absolute cell numbers in order to identify phenotypic defects which will guide genomic analysis of patients, enabling definitive diagnosis and predictive information for disease prognosis.

3. SAFETY AND TOLERABILITY OF A NOVEL PEPTIDE-BASED IMMUNOTHERAPY FOR PEANUT ALLERGY

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RATIONALE: Peanut allergy is a life-threatening condition for which there is currently no cure. Immunotherapy using whole peanut preparations is hindered by risk of causing severe allergic reactions during treatment. PVX108 is a peptide-based immunotherapy being developed to treat peanut allergy without triggering allergic reactions during treatment.

METHODS: PVX108 comprises a mixture of short, synthetic peptides derived from sequences of major peanut allergens, formulated for intradermal injection. Basophil reactivity to PVX108 was assessed using blood samples from peanut allergic donors. Safety and tolerability of PVX108 was assessed in a randomized, double-blind, placebo-controlled phase I trial in peanut-allergic adults. Cohorts were randomized 2:1 to receive PVX or placebo. The first eight cohorts received a single injection. The dose was escalated for each successive cohort upon safe completion of the prior cohort. The ninth cohort received six injections at the highest dose (150nmol) over 16 weeks.

RESULTS: Basophil assays confirmed lack of basophil reactivity to PVX108 in contrast to peanut extract in 146 peanut-allergic donors. The phase I trial enrolled a total of 66 subjects. There were no serious adverse events. Adverse events considered possibly or probably related to treatment were graded mild or moderate, with the majority being transient injection site reactions. None was deemed of clinical concern by the study Safety Review Committee. There was no relationship between dose level and frequency or severity of adverse events.

CONCLUSION: Basophil reactivity and phase I data demonstrate that PVX108 has a highly favourable safety profile for treatment of peanut allergic individuals, including those with severe allergy.

4. REDUCING PERIOPERATIVE HYPOTENSION THROUGH TEMPORARY PERIOPERATIVE DISCONTINUATION OF RENIN-ANGIOTENSIN ANTAGONISTS: AN OBSERVATIONAL STUDY OF ORTHOPAEDIC ARTHROPLASTY PATIENTS

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Perioperative hypotension is a common surgical complication with prolonged perioperative hypotension independently associated with adverse postoperative vascular events and increased mortality in patients undergoing non-cardiac surgery.

AIM: To determine in adult patients chronically prescribed renin-angiotensin antagonists (RAAs) and undergoing orthopaedic arthroplasty if temporary discontinuation of regular angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers across the perioperative period reduces the incidence of clinically significant postoperative hypotension within the first 72 hours.

METHODS: This retrospective study was undertaken across Alfred and Sandringham hospitals to evaluate patients before and after implementation of a guideline recommending temporary discontinuation of RAAs perioperatively. The primary outcome was incidence of significant hypotension, SBP≤100mmHg within 72-hours post-operatively. Secondary outcomes included incidence of MET calls for hypotension, acute kidney injury (AKI), hypertension, and major adverse events. In addition to outcome data, demographics and potential confounders collected included surgery length, intravenous fluids received, other antihypertensive medications, elective status, anaesthesia, blood loss, non-steroidal anti-inflammatory drug and vasopressor use, and American Society of Anesthesiologists score.

RESULTS: In total, 233 participants taking renin-angiotensin antagonists prior to orthopaedic arthroplasty were recruited; pre cohort included 119 patients (November 2016 to July 2017) and 114 patients in the post cohort (November 2017 to July 2018). The post cohort demonstrated a statistically significant reduction in incidence of clinically significant hypotension within the first 72-hours postoperatively, with 41% of patients experiencing SBP≤100mmHg, compared to 56% in the pre cohort (p=0.026). There were no significant differences in incidence of hypertension or major adverse events between cohorts; a lower rate of AKI was observed in the post cohort (10% vs 18%, p=0.088).

CONCLUSION: In patients chronically prescribed renin-angiotensin antagonists and undergoing orthopaedic arthroplasty, temporary discontinuation in the perioperative period resulted in a statistically significant reduction in clinically significant postoperative hypotension.

CANCER RESEARCH

5. DIRECT TARGETS OF JAK-STAT SIGNALLING WHICH UNDERPIN HUMAN MYELOPROLIFERATIVE NEOPLASMS

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Myeloproliferative neoplasms (MPNs) are characterised by excess production of mature blood cells accompanied by an increased risk of thrombosis and progression to marrow fibrosis and AML. Most are driven by a mutation (V617F) in the pseudo-kinase domain of JAK2, which leads to unrestrained cell proliferation. To find direct targets of JAK2-STAT signalling in MPNs, we undertook ChIP-Seq for pSTAT5 and pSTAT3 in cell lines, HEL and SET2. HEL cells have 13-16 copies of JAK2-V617F as determined by FISH and SNP arrays. They have high levels of pSTAT5 and pSTAT3 by phosphoflow and Western blotting. SET-2 cells were derived from a patient with JAK2-V617F^{+} ET; they also have high levels of pSTATs.

We found ~690 pSTAT5-occupied sites and >10,000 pSTAT3-occupied sites in HEL cells. The majority resides in distal enhancers. We found new enhancers in well-known target genes such as *BCL2L1*, which encodes the pro-survival protein, BCL-X. The human enhancer is in a similar relative position to the recently described mouse EPO-dependent enhancer. We also found new direct target genes that encode for proteins with interesting predicted functions. SET-2 cells have similar pSTAT5 and pSTAT3-bound sites suggesting commonality of functions. We show pSTAT3 and pSTAT5 bind as dimers in vivo to typical GAS elements, but with slightly different site preferences. This has implications for differential target gene regulation. We undertook expression profiling using SLAM-seq following treatment with ruxolitinib and validated novel target genes by qRT-PCR. In short, we have discovered hundreds of direct JAK-STAT target genes involved in cell survival, proliferation, down regulation of cytokine signalling, and novel functions. The genes provide new insights into the biology of MPNs, and a source of potential new biomarkers and drug targets. We have validated some in primary MPN samples.

6. A NOVEL THERAPEUTIC APPROACH IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

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BACKGROUND: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide with 300,0000 deaths and 550,0000 new cases reported every year. Poor survival rate (50%) is a reflective of the lack of targeted treatments in the cancer. Our lab has previously elucidated a novel GRHL3/GSK3B/c-Myc signalling axis contributing to carcinogenesis in HNSCC. I-BET 151 is small molecule inhibitor that inhibits c-Myc transcription by preventing bromodomain recruitment to chromatin.

AIM: To evaluate therapeutic potential of I-BET 151 in preclinical models of HNSCC.

METHOD: Efficacy of I-BET 151 was analysed in diverse HNSCC preclinical models including human HNSCC cell lines (SCC-25, SCC-47, SCC-22B, Detroit, FaDu) and mice models. Carcinogen (4-NQO) treated genotypic (Grhl3 knock-out) mice models as well as orthotopic xenograft mice models engrafted with human HNSCC cell lines were employed in the experiments. Effect of the drug in the experimental models were analysed by means of appropriate cell assays (cell proliferation assay, clonogenic assay), histological methods (H&E staining, IHC) and molecular techniques (Western blot, qPCR, ChIP assay).

RESULT: I-BET 151 perturbed proliferation and clonogenic capacity of the cell lines in-vitro. Reduced tumour growth and improved overall survival were observed in drug treated orthotopic xenograft mice models. In carcinogen treated models, treatment with IBET-151 significantly reduced tumour burden and increased tumour free survival in wild type mice whereas the response to treatment was not significant in Grhl3 knockout mice.

CONCLUSION: Overall, the study indicates that I-BET 151 is effective in treating HNSCC in the preclinical models. Also, extend of GRHL3 inhibition correlated with the drug effectiveness *in vivo* and this strategy could be applied in patient stratification. Although targeting the GRHL3/GSK3B/c-Myc axis holds promise in HNSCC, pathway cross-talk and functional compensation from inhibiting single pathway members must be investigated prior to incorporating such therapeutic agents in to routine clinical care.

7. TREATING PROSTATE CANCER WITH LOW DOSE-RATE SEED BRACHYTHERAPY AT THE ALFRED FOR 20 YEARS

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We have used low dose-rate radioactive-seed implant brachytherapy ("LDR brachy") to treat prostate cancer (PCa) at the Alfred for >20 years.

AIM: To describe the long-term disease control and patient-reported outcome measures after LDR brachytherapy.

METHODS: Review of prospective quality-registry of patient disease, treatment, disease-control and self-reported quality-of-life for all men treated 1998-2013. Endpoints were PSA-control using standard ("Phoenix") definitions, prostate-cancer-specific- and overall-survival, and standard regular surveys of adverse-effects.

RESULTS: We implanted 900 men: 555 with "NCCN low-risk" PCa, and 345 intermediate risk (186 NCCN "favourable" group and 159 "unfavourable"). Median age was 62 (IQR: 57-67). The median presenting PSA was 5.4 ng/L (IQR: 4.0-7.2). After a median followup of 9.4 years, there were 16 PCa deaths, and 89 deaths from other causes. The PSA-control rate was 5-, 10-, and 15-years was 95%, 89%, and 85% respectively, for the whole group. The was no difference associated with patient age, year of implant, or implanting clinicians. There was a difference depending on risk factors: at ten years the PSA-control in the low-, the favourable intermediate-, and the unfavourable intermediate-risk groups was 92%, 85% and 78%. The PCa-specifc survival probabilities were 99.6%, 99%, and 96% at 5, 10, and 15 years. After 10 years followup, more than 60% of men had "no" or a "very small problem" with sexual function; major urinary and bowel problems were uncommon.

CONCLUSION: In a large prospectively-monitored group treated with LDR brachytherapy at the Alfred, over a 20-year period the disease-control rates are equivalent too that seen in the surgical arms of randomised trials of radical prostatectomy with similar low rates of side-effects as seen in large series. These effects appear sustained over long follow-up.

8. HIGH DOSE-RATE BRACHYTHERAPY (HDR) AT THE ALFRED CURES MORE PROSTATE CANCER

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INTRODUCTION: Escalating (”boosting”) radiation dose to prostate cancer (PCa) by adding HDR to external beam radiotherapy (EBRT) is a standard treatment for PCa, with theoretical advantages for patients. Previous randomised controlled trials have demonstrated improved biochemical-control by dose-escalation with HDR (HDR+EBRT) compared with EBRT only, but no decrease in disease-specific mortality. We have used HDR+EBRT for PCa at the Alfred for 20 years, and we wanted to determine if HDR+EBRT in our patient cohort improved survival.

METHODS: Consecutive patients with localised PCa treated with HDR+EBRT between 1998 and 2004 were followed in a prospective registry, and compared with all men treated contemporaneously for PCa with EBRT alone. Endpoints were biochemical recurrence, freedom from PCa-death, overall survival, and quality-of-life in HDR patients evaluated by regular patient-reported outcome measure survey forms. Survival outcomes were assessed (Stata 15) using log-rank tests and Kaplan-Meier survival plots, and multivariable analysis performed using Cox regression.

RESULTS: 215 out of 654 patients received HDR+EBRT for PCa. Median follow-up was nearly ten years. There was superior overall survival ($p<0.01$) at 15 years in this group (67%) versus the EBRT-only group (53%).The survival benefit was most pronounced in patients with high-risk PCa. The cumulative incidence of grade 3+ gastrointestinal toxicity was 3% at 10 years, but the prevalence rate at any time was <1%. Erectile dysfunction peaked 6 months post treatment, but then improved until year 3 when almost 75% of men with function prior to treatment had erectile function. There was a decline beyond this time.

CONCLUSIONS: In our cohort, overall- and disease-specific-survival was better in the men treated with the addition of HDR to EBRT and this was most obvious in men with high-risk disease. Our results are consistent with a survival benefit of HDR+EBRT and we think more suitable men should be treated with this technique.

9. MYOSTEATOSIS PREDICTS HIGHER COMPLICATIONS AND REDUCED LONG-TERM SURVIVAL FOLLOWING RADICAL OESOPHAGOGASTRIC CANCER SURGERY

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BACKGROUND: Oesophagogastic cancer surgery is associated with high morbidity but lacks clinically effective physiological staging tools. Evidence suggests low muscularity (myopenia) may increase surgical risk but has not proven a powerful predictor of outcomes. There is limited data on the impact of low muscle attenuation (myosteatosis), however, mechanistically this could represent a more likely potent of adverse outcomes.

AIM: To determine whether myosteatosis is associated with increased risk of postoperative complications, including anastomotic leak, is an independent predictor of overall and severe complications, and significantly reduces long-term mortality and disease-free survival following radical oesophagogastric cancer surgery.

METHODS: Muscle attenuation was assessed using preoperative abdominal CT images and body composition analysis software. Myosteatosis was defined using published cut offs and assessed against anthropometric, oncological, surgical and survival data.

RESULTS: One hundred and eight patients were included, 75% (*n*=81) male, mean age 66 years (±9.9). Median BMI was 24.4kg/m^2 (IQR 6.2), 56% (*n*=61) had myosteatosis. The myosteatosis group were older (69 years vs 63 years non-myosteatosis, *p*=0.001) and greater proportion of females had myosteatosis (78% vs 49% male, *p*=0.019). There were no differences in anthropometric, clinical or oncological characteristics. Patients with myosteatosis had higher overall complication rates (64% vs 38%, *p*=0.001), severe complications (26% vs 9%, *p*=0.013) and a higher proportion of anastomotic leaks (15% vs 2%, *p*=0.041). Myosteatosis was an independent predictor of overall complications (OR 2.65, 95% CI 1.10-6.38, *p*=0.03) and severe complications (OR 3.79, 95% CI 1.05-13.7, *p*=0.042). Patients with myosteatosis had reduced overall (37.5 months vs 50.5, *p*=0.004) and disease-free (34.5 months vs 48.8, *p*=0.007) survival compared to patients with normal muscle attenuation.

CONCLUSION: Myosteatosis is associated with a significantly increased risk of overall and severe complications including anastomotic leak as well as substantially reduced long-term survival. Assessment of muscle attenuation is a potentially valuable physiological staging tool.

10. THE IMPACT OF SPECIFIC ANATOMICAL LOCATION ON MELANOMA SURVIVAL: INDEPENDENT HIGH AND LOW RISK SITES

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BACKGROUND: Anatomical location of melanoma has been demonstrated to independently influence melanoma specific survival (MSS), however previous findings have been conflicting or have been unable to fully adjust for potential confounders

AIM: We aimed to compare the MSS of specific anatomical subsites in greater detail than previously undertaken

Methods: A prospective cohort study was performed of primary invasive cutaneous melanomas with known thickness and location reviewed at a tertiary referral centre over 21 years.

RESULTS: 3570 primary cutaneous invasive melanoma cases were included. After adjustment for clinicopathological variables (including thickness, ulceration, mitotic rate, sex, age and subtype), patients with posterior scalp melanoma were associated with worse MSS (hazard ratio, HR, 2.46; 95% confidence interval, CI, 1.38 to 4.40) compared to the upper back, whereas melanoma on the thighs, forearms/hands and anterior upper arms had better MSS. Intermittent (HR 0.56; 95% CI 0.41 to 0.76) and chronically sun-exposed sites (HR 0.70; 95% CI 0.51-0.96) had improved survival compared to rarely exposed sites on multivariate analysis.

CONCLUSION: Altered MSS for patients with melanoma of the posterior scalp, thighs, forearms and hands, anterior upper arms appears independent of clinicopathologic factors. Results were similar for both sexes and age groups. Several subsites had reduced univariate but not multivariate survival (anterior scalp, temporal and periauricular scalp and plantar feet) indicating greater efforts for earlier diagnosis may improve MSS. The posterior scalp should be considered a poor prognosis site and may require heightened surveillance of recurrence.

11. CLINICAL UTILITY OF ANTI-THYROID ANTIBODIES AND TSH AS DIAGNOSTIC OR PROGNOSTIC ADJUNCTS IN PATIENTS WITH INDETERMINATE THYROID NODULE CYTOLOGY

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BACKGROUND AND AIMS: Indeterminate fine needle aspiration cytology (FNAC) imposes challenges in the management of thyroid nodules. This study aimed to examine whether preoperative anti-thyroid antibodies (Abs) and TSH are indicators of thyroid malignancy and aggressive behaviour in patients with indeterminate FNAC.

METHODS: This was a retrospective study of patients undergoing thyroidectomy from 2008 to 2016. We analysed demographic data, Abs and TSH levels, FNAC results and histopathology. Serum marker levels were categorised as 'Undetectable', 'In-range' if detectable but within normal range, and 'Elevated' if above upper limit of normal. 'Detectable' levels referred to 'In-range' and 'Elevated' combined.

RESULTS: There were 531 patients included. Of 402 patients with preoperative FNAC, 104 (25.9%) had indeterminate cytology (Bethesda III-V) with 39 (37.5%) malignant and 65 (62.5%) benign cases on histopathology. In the setting of indeterminate FNAC, an increased risk of malignancy was associated with 'Elevated' thyroglobulin antibodies (TgAb) (OR 7.25, 95%CI 1.13-77.15, P=0.01) and 'Elevated' thyroid peroxidase antibodies (OR 6.79, 95%CI 1.23-45.88, P=0.008). Similarly, while still 'In-range', TSH>1mIU/L was associated with an increased risk of malignancy (OR 3.23, 95%CI 1.14-9.33, P=0.01). The risk of malignancy increased as the number of markers increased from none, to one ('Elevated' Abs or TSH>1), to two ('Elevated' Abs and TSH>1), with the risk of 21%, 33%, 75% respectively (P=0.03). In all patients with malignancy, the mean tumour size was 7.79 mm larger in those with TSH>1 (P=0.03); furthermore, in PTC patients, 'Detectable' TgAb conferred a 4x risk of lymph node metastasis (95%CI 1.03-13.77, P=0.02).

CONCLUSION: In this cohort, in patients with indeterminate FNAC, Abs and TSH were independently and synergistically associated with an increased risk of malignancy. Additionally, TgAb and TSH were potential markers of aggressive biology. As such, they may be diagnostic and prognostic adjuncts, aiding decision-making for the extent of thyroid surgery.

12. INFLUENCE OF THE TIME INTERVAL FROM DIAGNOSIS TO TREATMENT ON SURVIVAL FOR EARLY-STAGE NON–SMALL-CELL LUNG CANCER: DATA FROM THE VICTORIAN LUNG CANCER REGISTRY

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INTRODUCTION: There is significant variation in survival time among patients with early-stage lung cancer who are treated with curative intent. Guidelines suggest that treatment should be initiated rapidly after diagnosis, but the effect of these policies on survival is not well understood.

AIM: To investigate the effect of variation in the time interval between diagnosis and treatment initiation on survival in early-stage lung cancer.

METHODS: Patients with Stage I and II non-small-cell lung cancer were identified from the Victorian Lung Cancer Registry (VLCR). The interval between the dates of clinical diagnosis and first treatment with curative intent were calculated, and patients were categorised into four interval groups (<14 days, 14-28 days, 28–56 days and >56 days). Clinical variables including age, sex, performance status, smoking status, tumour morphology, socioeconomic status, hospital location and hospital type were inspected. An estimate of patient survival time was presented using the Kaplan-Meier method, with patients stratified into stage I and stage II groupings. Survival groups were compared using the log rank test. A Cox proportional hazards model was then used to control for and estimate the effect of these variables on overall survival.

RESULTS: There were 1,324 eligible patients identified from 30 hospitals. After an average follow-up period of 28 months (SD 21), 14.8% of patients were deceased. There was a statistically significant stepwise worsening in survival rates over the four diagnosis-treatment interval groups when stage I and II patients were analysed together and stage I patients were analysed alone (both $p<0.001$, chi^2).

CONCLUSION: Our data appear to demonstrate a relationship between the diagnosis-to-treatment interval and overall survival in patients with early stage non-small-cell lung cancer. These findings may provide support for policies aimed at reducing patients' waiting periods between diagnosis and initiation of treatment.

13. DEVELOPMENT AND EXTERNAL VALIDATION OF A PREDICTIVE MODEL OF URETHRA TOXICITY FOR PATIENTS TREATED WITH HDR BRACHYTHERAPY BOOST INCLUDING THE EFFECT OF NEO-ADJUVANT ANDROGEN DEPRIVATION

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For prostate cancer, comparable or superior biochemical control has been reported using High-Dose-Rate brachytherapy (HDRB), combined with external-beam-radiotherapy (EBRT), compared to dose-escalation with EBRT alone. HDRB could allow further beneficial prostate dose-escalation, but this increase is limited by normal-tissue toxicity, especially to the urethra.

AIM: To establish guidelines for the urethra doses in HDRB-boost, fitting a regression model of urethra-stricture data collected at the Alfred, and validating the model with an external cohort, looking at the effect of using Androgen-Deprivation (AD).

METHODS: We employed a widely-used radiobiological model (the Lyman-Kutcher-Burman or "LKB" model) to fit (MATLAB) clinical and dosimetric data of 258 patients, treated at the Alfred (cohort1) as a sigmoid function of Equivalent Uniform Dose (EUD). We used an external cohort of 187 patients (cohort2) treated in the TROG03.04 RADAR trial to validate the Alfred model. We assessed goodness-of-fit with calibration plots.

RESULTS: The Alfred cohort had HDRB prescription doses of 17-19 Gy in 2-3 fractions and an EBRT dose 46Gy in 23 fractions. The urethra stricture rate was 12.8%, The LKB parameters TD50 (Gy), m and n obtained are in Table1(a). Calibration showed agreement between the observed- and modelled-toxicity (slope=0.924, R^2=0.71). Bootstrapping confirmed the results (Table1(b)). In the external validation cohort, the HDRB dose was 19.5Gy in 3 fractions, EBRT 46/23, and the toxicity rate 8.7%. Calibration confirmed the observed toxicity obtained with cohort2 was well represented by the Alfred model (slope=0.85, R^2=0.94). When cohort1 was stratified by the use or not of Androgen-Deprivation, TD50 decreased when AD was not present (Table1(d)).

Table 1: NTCP parameters

HDRB + EXBRT	**TD50 (Gy)**	**m**	**n**
a: cohort 1	116.7	0.23	0.3
b: cohort 1--bootstrapping	116.5 (CI:114.8-118.3)	0.23 (CI:0.22-0.23)	0.3
c: cohort 1--With AD	118.2	0.23	0.3
d: cohort 1--without AD	104.9	0.23	0.3

CONCLUSION: We established a model for urethra stricture risk, and validated with an independent cohort. This allows guidelines for our radiation dose prescription to minimise urethral risk with HDRB dose-escalation, and so improve patient-outcomes, and also raised a question as to whether AD is protective.

CARDIOVASCULAR DISEASE

14. PREVALENCE, OUTCOMES AND COST IMPLICATIONS OF PATIENTS UNDERGOING SAME DAY DISCHARGE AFTER ELECTIVE PERCUTANEOUS CORONARY INTERVENTION IN AUSTRALIA

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The rates of elective percutaneous intervention (PCI) have increased significantly in Australia with half of procedures performed in stable coronary artery disease. Despite international growth in the use of same day PCI, there remains little data on the impact of same day PCI in the Australian setting.

AIM: To determine the prevalence, clinical outcomes and cost implications of same day discharge (SDD) amongst Australian patients undergoing elective (PCI).

METHODS: Retrospective observational cohort study of patients who underwent elective PCI in Victoria between January 2014 to December 2017, obtained from the Victorian Cardiac Outcomes Registry (VCOR). The primary outcome measured was the incidence of 30-day major cardiac events (MACE) and secondary outcomes included in-hospital complications and 30-day readmissions. These were compared between patients who were discharged on the same day post PCI and those observed as inpatients overnight (ON). Propensity score matching for patient age, gender, presence of at least stage 3 chronic kidney disease and complex lesions were used to compare both groups.

RESULTS: 18,106 patients- mean age of 68±11years and 13938 (77%) males were included. The rate of SDD was 3.3% while 96.7% patients stayed in hospital overnight. At 30 days, unplanned cardiac re-hospitalization occurred in 9.8% amongst SDD and 11.7%, amongst ON patients (p=0.173). Propensity matching highlighted SDD to be non-inferior to overnight, with no significant difference in 30-day MACE (0.5%, 95% CI: 0.34, 1.35) but SDD was associated with reduced average length of stay by 2.06 days (95% CI: 1.94, 2.19). We observed substantial hospital variation for SDD from 0% to 16.6% of elective PCI procedures.

CONCLUSIONS: SDD appears to be safe and feasible with no increase short-term adverse outcomes or rehospitalisation. Given significant benefits in reducing cost and bed utilisation, a more consistent use of SDD could markedly improve the value of PCI care in Australia.

15. ASSOCIATION OF PERI-PROCEDURAL INTRAVENOUS MORPHINE USE ON CLINICAL OUTCOMES IN ST-ELEVATION MYOCARDIAL INFARCTION (STEMI) TREATED BY PRIMARY PERCUTANEOUS CORONARY INTERVENTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND: Morphine analgesia may affect the absorption of co-prescribed P2Y12 antagonists, attenuating platelet inhibition. The impact of peri-procedural intravenous (IV) morphine administration on clinical outcomes in patients undergoing primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI) is not well-defined.

METHODS: Analysis of the electronic databases MEDLINE, EMBASE, CENTRAL, Scopus, Web of Science and ClinicalTrials.gov for the association of peri-PCI IV morphine use with myocardial infarction (MI) and mortality.

RESULTS: Eleven studies (1 randomised controlled trial; 10 cohort studies) were included for systematic review. Five studies, including 3,748 patients were included in meta-analysis of the primary outcome. Of 3,748 patients, 2,239 were treated concurrently with ticagrelor, 1,256 treated with clopidogrel and 253 with prasugrel. There was a trend towards increased risk of in-hospital or 30-day myocardial infarction with IV morphine (odds ratio 1.88; 95% CI 0.87-4.09, I^2 0%). Across seven studies and 6,585 patients, no increased risk of mortality at the same time points was evident (odds ratio 0.70, 95% CI 0.40-1.23, I^2 19%).

CONCLUSION: Peri-PCI IV morphine administration during STEMI was associated with a greater risk of in-hospital or 30-day recurrent MI. While not reaching statistical significance, this signal of increased risk warrants further randomised trial data.

16. SURVIVAL AND FUNCTIONAL OUTCOME AFTER IHCA: A MULTI-CENTRE PROSPECTIVE COHORT STUDY

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BACKGROUND: In Australia and New Zealand the estimated incidence of in-hospital cardiac arrests (IHCA) is 1.3 - 6.0 per 1000 hospital admissions. Functional outcome after IHCA is not well described in the literature.

AIM: To evaluate survival and functional outcome at hospital discharge following IHCA.

METHODS: Emergency calls were screened and data collected for IHCAs. Patients were included if aged ≥18yrs, unresponsive with no respiratory effort and cardiac compressions commenced. Patients were excluded if a pre-existing NFR order was in place or if the emergency call did not fit the criteria for IHCA. Data collected included patient demographics, clinical and cardiac arrest characteristics, medical management, survival and functional outcome at hospital discharge using the modified Rankin Scale (mRS) and Katz-ADL.

RESULTS: Between July 2017 and August 2018, 152 patients suffered 159 IHCAs (male 66.4%; median age 71.5yrs (61.6 - 81.3)). Sixty patients (39.5%) survived, of whom 43 (71.7%) had a good neurological outcome (mRS 0-3) and 38 (63.3%) were independent with activities of daily living (ADLs) at hospital discharge (Katz-ADL=6).

Seventeen survivors (28.3%) had decreased function at hospital discharge compared to admission. At hospital discharge 7 patients were partially dependent (Katz-ADL 3-5) and 10 were fully dependent (Katz-ADL ≤ 2).

Factors associated with a good neurological outcome at hospital discharge included younger age (p=0.011), working prior to admission (p<0.001), cardiovascular-related admission (p=0.002), shorter hospital length of stay (LOS) prior to arrest (p=0.002), shockable rhythm (p=0.001), witnessed arrest (p=0.001) and shorter duration of CPR (p<0.001).

CONCLUSION: The majority of IHCA survivors had a good neurological outcome and two-thirds of patients were independent with ADLs at hospital discharge. Factors associated with good neurological outcome could be identified.

17. A PROJECTED COST ANALYSIS OF ENDOVASCULAR TREATMENTS FOR PERIPHERAL VASCULAR DISEASE OF THE SFA

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Peripheral arterial disease (PAD) carries a significant disease burden, affecting 15% of the Australian population. While percutaneous transluminal angioplasty (PTA) and bare metal stenting (BMS) have been mainstay treatments there is increasing evidence for the use of drug coated balloons (DCB) and drug eluting stents (DES) to improve the longevity of endovascular treatment.

AIM: To estimate the cost effectiveness of these interventions when adjusted for clinically driven target lesion revascularisation rates in an Australian hospital setting.

METHODS**:** A systematic review was undertaken of level 1b (randomised control trials) data and re-intervention rates were extracted or extrapolated. Re-intervention rates were taken to be the weighted mean across published studies identified by systematic review. The mean device cost of DCB and DES were $AU1000 and $AU1775 respectively; cost projections to 24 months were calculated for PTA, BMS, DCB and DES therapies. Previously published hospital costing data from FY 2013-2015 was utilised as a baseline for extrapolation.

RESULTS**:** The mean cost of admission for PTA and PTA with BMS was $8107 and $13966 respectively. The projected admission costs for DCB and DES were $9107 and $15741 respectively. When adjusted for 2 years of follow up and pooled re-intervention rates, the mean projected 2 year costs were $12,677 for PTA, $19,317 for BMS, $11,676 for DCBs, and $18,020 for DES.

CONCLUSION**:** Our results suggest that in an Australian climate DCBs offer a lower 2 year re-intervention rate without extra cost; and both BMS & DES are less cost effective interventions.

18. ROLE OF HISTONE METHYLTRANSFERASE SET7 IN MITOCHONDRIAL GENE REGULATION AND CARDIAC FUNCTION

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Set7 is a protein lysine methyltransferase that regulates transcriptional networks by methylation of histone and non-histone proteins. Recent studies have shown that Set7 is involved in various cellular responses such as metabolic memory and muscle cell differentiation, however the physiological role of this enzyme in the heart remains unclear. In this study, we characterise the Set7 knockout (Set7 KO) mouse assessing its specific role in cardiac function. We observed histological abnormality and reduced contractility in the left ventricle (LV) of Set7 KO mouse. RNA-sequencing shows significant down-regulation of mitochondrial function pathways consistent with abnormal mitochondria morphology, reduction of oxidative phosphorylation activity and mitochondrial DNA copy number. In Set7 KO animals, gene network analysis and chromatin immunoprecipitation assays identify mitochondrial genes are subject to reduced mono-methylation of histone 3 lysine 4. These findings define a novel role for Set7 regulation linking mitochondrial integrity with abnormal cardiac function.

19. USING THE SIX-MINUTE WALK TEST TO PREDICT DISABILITY-FREE SURVIVAL FOLLOWING MAJOR SURGERY

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BACKGROUND: The six-minute walk test (6MWT) is a common means of functional assessment. Its relationship to disability-free survival (DFS) is uncertain.

METHODS: This sub-study of the Measurement of Exercise Tolerance for Surgery study had co-primary outcome measures: correlation of the preoperative 6MWT distance with 30-day quality of recovery (QoR-15) and 12-month World Health Organisation Disability Assessment Schedule (WHODAS) scores. The prognostic utility of the 6MWT and other risk assessment tools for 12-month DFS was assessed with logistic regression and receiver operating characteristic (ROC) curve analysis.

RESULTS: Of 574 patients recruited, 567 (99%) completed the 6MWT. Twelve months after surgery, 16 (2.9%) patients had died and 444 (77%) had DFS. The 6MWT correlated weakly with 30-day QoR-15 (rho = 0.14, P=0.001) and 12-month WHODAS (rho = -0.23, P<0.0005) scores. When the cohort was split into 6MWT distance tertiles, the adjusted odds ratio of low versus high tertile for DFS was 3.13 (95%CI 1.54 – 6.35). The only independent variable predictive of DFS was the Duke Activity Status Index (DASI) score (adjusted OR 1.06, P<0.0005). Area under the ROC curve for DFS was 0.63 (95% CI 0.57 – 0.70) for the 6MWT, 0.60 (95% CI 0.53 – 0.67) for CPET-derived VO2peak and 0.70 (95% CI 0.64 – 0.76) for the DASI score.

CONCLUSIONS: Of the risk assessment tools analysed, the DASI was most predictive of DFS. The 6MWT was safe and comparable to CPET testing for all predictive assessments. Future research should aim to determine optimal 6MWT distance thresholds for risk prediction.

20. RETINOL DEHYDROGENASE 11 IDENTIFIED AS A POTENTIAL NOVEL REGULATOR OF HEPATIC CHOLESTEROL METABOLISM

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BACKGROUND AND AIM: Disruptions to hepatic cholesterol homeostasis can promote the onset of hypercholesterolemia, a major risk factor for cardiovascular disease. Limitations in current therapeutics have driven the need to identify novel targetable pathways to address the increasing incidence of individuals with hypercholesterolemia. In order to interrogate hepatic cholesterol metabolism, we developed an integrated systems-biology discovery platform, consisting of 107 inbred mouse strains and performed proteomic and lipidomic analyses on the livers of these mice.

METHOD AND RESULTS: We assessed protein:protein and protein:lipid associations in order to identify novel proteins/pathways not previously associated with cholesterol metabolism. Retinol dehydrogenase 11 (RDH11) was identified to correlate β=0.3 ($p<0.00001$) with Lanosterol 14α-demethylase a known cholesterol synthesis enzyme. In order to validate the role of RDH11 *in vivo* two mice studies assessed. Mice gavaged with a statin for 2 weeks had marked increase (~2 fold increase, $p=0.0507$) in RDH11 gene expression. In contrast, mice feed a western diet (high fat, high cholesterol) for 16 weeks had significant reduction (70% reduction, $p<0.05$) in RDH11 gene expression. To further elucidate this association a panel of *in vitro* cells studies were perform that modulated intracellular cholesterol levels. RDH11 transcriptional regulation was highly correlated with known markers of cholesterol synthesis (HMGCR), uptake (LDLR) and efflux (ABCA1) in these panels. Furthermore, the promoter region of RDH11 was demonstrated, in Hep3B cells, to be responsive to cholesterol depletion, similar to that of other putative cholesterol metabolism genes. Lastly, knockdown of RDH11 in Hep3B cells via siRNAs resulted in modulation of markers of cholesterol metabolism and cellular inflammation, suggesting that RDH11 drives changes in intracellular cholesterol metabolism.

CONCULSION: These findings provide evidence for a novel association between RDH11 and cholesterol metabolism as well as offering greater understanding of intracellular cholesterol regulation by RDH11. Retinol Dehydrogenase 11 identified as a potential novel regulator of hepatic cholesterol metabolism.

21. UNSUPERVISED MACHINE LEARNING IDENTIFIES TREATMENT RESPONSE TO SPIRONOLACTONE IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

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BACKGROUND: Heart Failure with Preserved Ejection Fraction (HFpEF) is a heterogenous condition with several subgroups. Spironolactone has been postulated as beneficial therapy in certain patients, i.e. lower ejection fractions or lower natriuretic peptide levels. We aimed to determine whether machine learning (ML) methods could identify treatment responders.

METHODS: TOPCAT was a large international randomised trial of spironolactone in patients with HFpEF. We utilised data from 654 patients from the Americas echocardiographic arm. Dimensionality reduction was applied using t-stochastic neighbour embedding, followed by hierarchical cluster analysis, then long term outcomes were stratified by treatment.

RESULTS: Three clusters were identified. Long term outcomes were similar between groups. Cluster 2 (n=146) patients demonstrated a significant response with spironolactone treatment ($p=0.002$) whereas those in clusters 1 and 3 (n=401 and n=107) had no significant difference in long term outcome. Compared with the other clusters, Cluster 2 patients were younger, more obese, more hypertensive, and had relatively preserved renal function.

CONCLUSION: Unsupervised ML methods may be able to identify a homogenous subgroup of patients with HFpEF who may respond more favourably to treatment with spironolactone.

22. GUT MICROBIOME AND ATHEROSCLEROTIC PLAQUE INSTABILITY: DOES CHOLINE CONSUMPTION IN RED MEAT INFLUENCE PLAQUE STABILITY?

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BACKGROUND: Myocardial infarction is the major cause of deaths worldwide. Gut bacteria can process choline as abundant in red meat and subsequently converted by flavin-containing monooxygenase in the liver to trimethylamin-N-oxide (TMAO), which is strongly associated with cardiovascular events.

AIM: To investigate the gut microbiome and its association with atherosclerotic plaque instability.

METHODS: Forty-eight Apolipoprotein E deficient mice were randomly divided into two groups and two time points, fed with a high fat diet (containing either 0.44% choline or 3% choline) at 12 weeks of age, for 7 or 14 weeks. All mice underwent Tandem Stenosis (TS) surgery to induce the development of unstable plaques. Stool samples were collected directly from the colon. Measurements of gut microbes were performed by AGRF diversity profiling. After bacterial genomic DNA isolation, 16S rRNA were sequenced by targeting 27F-519R (V1-V3) and 341F-806R (V3-V4) on the Illumina MiSeq platform. Vessel segments of TS were histologically processed and plaque composition of lipid, collagen, and intraplaque haemorrhage (marker of unstable plaques) were performed by a series of chemical staining and immunohistochemistry.

RESULTS: Monocytes and granulocytes in mouse blood were significantly increased in the high choline group ($p<0.05$, unpaired *t*-test) after 7 weeks of high fat diet (21% fat, 0.15% Cholesterol, 3% Choline). Profiling of gut microbiota showed that *Firmicutes* were down regulated in the high choline group ($p<0.05$, unpaired t-test). Within Phylum *Firmicutes*, only *Clostridia* (class) *Clostridiales* (order) were significantly downregulated. Plasma TMAO were significant higher in both time points in the high choline group ($p<0.01$). Interestingly, histological analysis of TS segments showed that TER-119 (intraplaque haemorrhage marker) and CD42c (platelet marker) were significantly increased in the high choline group, indicating atherosclerotic plaques are more unstable and prone to rupture ($p<0.05$, unpaired t-test). Nevertheless, CD68 (Foam cells) in plaques, and total atherosclerotic plaque burden in the aortic sinus and aortic arch were not affected by the elevated levels of choline consumption or circulating TMAO.

CONCLUSION: Choline intake increases circulating monocytes, granulocyte numbers and plasma TMAO. Nevertheless, the total plaque burden is not changed by an increased choline intake. The association of *Firmicutes, Clostridia* and *Clostridiales* seems to contribute to atherosclerotic plaque instability.

DIABETES AND DIABETIC COMPLICATIONS

23. EFFECTS OF DIFFERENT LEVELS OF HYPERGLYCEMIA ON MITOCHONDRIAL BIOENERGETICS IN DIABETIC KIDNEY DISEASE

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AIMS: Effective energy generating pathways are central to maintaining normal renal function. Changes in mitochondrial homeostasis, including defective respiratory chain function and quality control are suggested to be central to the development of diabetic kidney disease (DKD), however, whether this response is explicitly driven by systemic glucose concentrations is not yet known. Here, we investigated the effects of titrating blood glucose concentrations in a model of streptozotocin-induced diabetes on aspects of mitochondrial function including mitochondrial turnover and signaling.

METHODS: Diabetic rats received an intensive insulin therapy protocol or a conventional insulin therapy protocol for eight weeks duration, resulting in blood glucose levels of ~20mmol/l or 30mmol/l, respectively. Analyses of renal function and histology and mitochondrial bioenergetics in the kidney were determined and compared to control (~5mmol/l glucose).

RESULTS: Intensive insulin therapy led to improved long-term glucose control. Both insulin treatment protocols led to the hallmarks of diabetic kidney disease- albuminuria and glomerulosclerosis, however, intensive insulin therapy afforded significantly better renoprotection including dampening pathways of fibrosis and prevention of tubular injury. Mitochondrial energy generation pathways were altered in diabetes, with a decline in complex I activity. Quantitative proteomics of mitochondria revealed clear differences in the abundances of proteins between groups. 760 mitochondrial proteins were identified in the 3 groups; pathways that were upregulated following standard insulin therapy (and to a lesser extent following intensive insulin therapy) include fatty acid and ketone body metabolism and oxidation-reduction processes; downregulated pathways include mitochondrial transmembrane transport (e.g., carrier proteins supporting OXPHOS, and protein translation processes.

CONCLUSIONS: Taken together, these data demonstrate that changes in blood glucose directly impact mitochondrial bioenergetics and turnover, which correlate with the severity of the renal lesion in diabetes. This study clearly indicates that hyperglycemia is a key determinant of mitochondrial homeostasis in DKD.

24. RESISTANT STARCH AMELIORATES ADVANCED GLYCATION ENDPRODUCT-INDUCED ALBUMINURIA IN A MOUSE MODEL OF TYPE 2 DIABETES

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INTRODUCTION AND AIM: Heat treating foods leads to the formation of advanced glycation endproducts (AGEs) which contribute to chronic renal injury. Recent research implicates gut dysbiosis in the progression of diabetic nephropathy. This study investigates whether excess consumption of dietary AGEs causes gut dysbiosis, exacerbating renal injury in a type 2 diabetes mouse model.

METHODS: Six week old diabetic (db/db) and non-diabetic (db/h) mice were randomised (n=12/group) to receive a low AGE (LAGE, unbaked rodent chow) or a high AGE diet (HAGE, baked at 160°C for 1 hour), with or without resistant starch (RS) for 10 weeks. 24-hour urine was collected and albuminuria was measured. Intestinal permeability was assessed *in vivo* by the clearance of FITC-labelled dextran (500mg/kg body weight). Statistical differences were assessed by one-way ANOVA.

RESULTS: The high AGE diet exacerbated albuminuria in db/db mice (874.4±154.8 vs 536.2±96.5µg/24h, P<0.05, db/db HAGE vs db/db LAGE), and RS attenuated this AGE-induced increase (874.4±154.8 vs 515.5±71.9µg/24h, P<0.05, db/db HAGE vs db/db HAGE+RS). Db/db mice had greater gut permeability compared to db/h mice (2.38±0.32 vs 1.05±0.11µg/ml, P<0.01, db/db LAGE vs db/h LAGE). Db/db-HAGE-fed mice trended towards increased gut permeability (3.43±0.43 vs 2.38±0.32µg/ml, P=0.06, db/db HAGE vs db/db LAGE), an effect not observed in RS-fed db/db mice.

CONCLUSION: Heat-treated diets led to increased intestinal permeability and worsening albuminuria in db/db mice. RS was protective against high AGE-induced albuminuria in db/db mice. These preliminary studies support the notion that dietary AGEs contribute to renal disease via alterations in gut homeostasis.

25. RISK SCORING SYSTEM FOR MACRO- AND MICRO-VASCULAR COMPLICATIONS RELATED TO TYPE 2 DIABETES IN SAUDI ARABIA

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BACKGROUND**:** The high prevalence of diabetes related complications in Saudi Arabia warrants the use of a risk prediction tool to predict these complications. This tool will help in patient counselling and early intervention to prevent complications. Due to the variation in lifestyle, genetic, and environmental factors between Saudi Arabian and other populations, a population specific risk prediction tool is preferred.

AIM**:** To develop risk prediction models for diabetes related complications for adults with type 2 diabetes in Saudi Arabia.

METHOD**:** Data from a survey conducted among 1121 adults with type 2 diabetes in Saudi Arabia was used. Missing data was imputed and bootstrap-receiver-operation characteristic method was applied for developing models for major diabetes complications of coronary artery disease, diabetic foot, stroke, neuropathy, kidney disease and retinopathy. Models were validated using decile-decile plot and bootstrapping methods.

RESULTS**:** Age ≥60 years, gender, low education level, body mass index ≥30 kg/m², physical inactivity, longer sitting time, smoking, longer duration of diabetes, insulin use, low adherence to treatment, family history of diabetes, glycated Haemoglobin ≥9%, hypertension and dyslipidaemia appeared as predictors in one or more of the models. The area under receiver operating characteristic curves ranged from 71.2% to 80.5%, and slope calibration ranged from 93.7% to 99.3%.

CONCLUSION**:** The developed risk prediction models require readily available information from routine clinical practice and the models have high discrimination and calibration power. Therefore, we recommend the use of these models in the clinical assessment of major complications for people with type 2 diabetes in Saudi Arabia.

26. BLOCKADE OF THE MITOCHONDRIAL PERMEABILITY TRANSITION PORE IN DIABETIC KIDNEY DISEASE

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Diabetes Mellitus is one of the most important global health issues of the 21st century. Approximately 30% of patients will develop diabetic kidney disease (DKD). Few effective therapies are available to slow the clinical progression of DKD to End Stage Renal Disease. Much of the underlying aetiology of DKD remains unknown, however mitochondrial dysfunction is co-associated with the disease. Studies from our laboratory, and others, have previously demonstrated an increased propensity for the formation of the mitochondrial permeability transition (mPT) pore alongside DKD associated mitochondrial decline.

AIM: to examine the impact of reduced mPT pore capacity on the development of DKD in male mice by targeting Cyclophilin D to directly interrupt pore function.

METHODS: In Study 1, we used a Cyclophilin D genetic knockout model *(Ppif -/-*). Wild type and *Ppif -/-* mice (n=15/group) were rendered diabetic using streptozotocin (55mg/kg/day), or Citrate Control (non diabetic), and followed for 20 weeks.

In Study 2, we used the db/db mouse model and their db/h littermate controls. Mice were randomized to receive a pharmacological Cyclophilin D inhibitor, the non-immunosuppressive Cyclosporin A analogue – Alisporovir, by daily oral gavage for 16 weeks (10mg/kg/day) from 6 weeks of age.

RESULTS: Diabetic animals in both studies sustained hyperglycemia with no observed difference associated with reduced mPT capacity. Complete loss of Cyclophilin D exacerbated renal injury in Study 1 as observed by an increase in Glomerular Sclerosis Index (Score: Ppif+/+ 1.28(SD 0.13); Ppif-/- 1.47(SD 0.19)), however with no change in mean 24hr Albuminuria (Ppif+/+ 137.2µg/24hrs (SD 36.63); Ppif-/- 134.1µg/24hrs (SD 48.22)). Partial inhibition by Alisporivir in Study 2 had no significant effect on either marker of renal injury in db/db animals.

CONCLUSION: This study underpins the complex role of the mPT in renal function, and reveals that reducing mPT pore opening events will not ameliorate DKD. *Funding provided by Diabetes Australia*

HAEMATOLOGY AND MALIGNANT HAEMATOLOGY

27. INHIBITION OF COMPLEMENT C5A RECEPTOR AMELIORATES TISSUE PLASMINOGEN ACTIVATOR MEDIATED INCREASE IN BLOOD BRAIN BARRIER (BBB) PERMEABILITY

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BACKGROUND: Tissue plasminogen activator (t-PA), an important activator of fibrinolysis, can increase BBB permeability and trigger the infiltration of immune cells into the central nervous system. Few plasmin-dependent and -independent pathways participate in this phenomenon, for example, activation of Rho-Kinase 2 and platelet derived growth factor C, respectively. Since plasmin also possesses pro-inflammatory properties, including C3 and C5 convertase activity, we hypothesized that complement activation plays an additional role in this process.

AIM: To evaluate the effect of complement inhibition on t-PA- and plasminogen (plg)-mediated opening of the BBB using an established *in vitro* model with C5 and C5a-receptor 1 (C5aR1) inhibitors.

METHODS: An *in vitro* model of the BBB was assembled on porous membranes of Transwell inserts as a co-culture system of human brain endothelial cells on the luminal surface and human immortalized astrocytes on the abluminal surface. The luminal compartment was stimulated with t-PA and plasminogen in the presence of drugs, PMX205 (non-competitive inhibitor of C5aR1), Avacopan (C5aR1 antagonist) or Eculizumab (humanised monoclonal inhibitor of human C5). BBB permeability was assessed at either 5hr or 24hr post-stimulation by evaluation of fluorescent albumin passage from the luminal to the abluminal chambers over 1hr. Permeability changes were calculated relative to non-treated controls.

RESULTS: PMX205 decreased t-PA mediated increase in BBB permeability by 24%, at 4hr ($p<0.05$) and 20% at 24hr ($p<0.05$). Avacopan also showed a 17% reduction in this increased permeability at 24hr ($p=0.1$). Interestingly, eculizumab was without any significant effect at both time points.

CONCLUSION: t-PA- and plasmin-mediated increase in BBB permeability is partly driven by C5a receptor activation. Inhibition of C5 or C5aR1 may have therapeutic implications in traumatic brain injury and stroke thrombolysis, where either endogenous or administered t-PA can compromise the BBB, leading to secondary insults.

28. HEALTH-RELATED QUALITY OF LIFE (EQ-5D-5L) AT DIAGNOSIS IN PATIENTS WITH MULTIPLE MYELOMA IN THE MYELOMA AND RELATED DISEASES REGISTRY

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AIM: Multiple myeloma (MM) is an incurable disease associated with high disease burden and health-related quality of life (HRQOL) assessment can help to optimise patient care.

METHOD: HRQOL was assessed using the EQ-5D-5L questionnaire at diagnosis in MM patients in the MRDR (Jan 2013 - Apr 2018). Stata version 15.1 was used.

RESULTS: 413 patients on the MRDR had completed all 5 EQ5D domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and the EQ VAS score (self-rated health status from the worst [0] to the best [100] health imaginable). Median age was 67y (60-74) and 65% were male. Characteristics did not differ substantially between patients who completed the EQ5D (n=413) and those who did not (n=848).

In self-care (washing or dressing), 69% of pts reported no problems at diagnosis, while only 22% were pain-free. Problems with mobility were reported in 55%, anxiety/depression in 56%, and problems with usual activities in 68% of patients at diagnosis.

41% of patients reported moderate to extreme problems in usual activities and 39% in pain/discomfort. With increasing age, more patients had problems with mobility, self-care and usual activities ($p \leq 0.009$), and a lower EQ VAS score ($p=0.04$). As disease stage (ISS) increased, limitations in mobility and usual activities were more frequent ($p \leq 0.01$), and EQ VAS score reduced (0.005). Problems in all 5 health domains were more frequent in patients with ECOG≥2 and EQ VAS score was lower (53±21 v 74±18) compared to ECOG<2 ($p<0.001$).

Problems with mobility, usual activities, and EQ VAS score were associated with a higher risk for early mortality (12m post diagnosis, $p<0.05$) in univariate analyses.

CONCLUSION: Pain/discomfort was the most frequently reported health issue in MM, and self-care related problems the least, compared to the other health domains. Also, more health problems were reported with increasing age, ECOG≥2 and increasing disease stage (ISS).

29. IMPLEMENTATION OF A MULTIDISCIPLINARY SURVEILLANCE TEAM TO IMPROVE INFERIOR VENA CAVA FILTER RETRIEVAL

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Prolonged indwelling time of inferior vena cava (IVC) filters is associated with complications. Observational studies demonstrate 35% retrieval rates, with significant loss-to-follow-up.

AIM: To evaluate the impact of a multidisciplinary surveillance program on timely retrieval of IVC filters and patient follow-up.

METHODS: Prospective study of IVC filters inserted at The Alfred Hospital from July 2017-March 2018. Consecutive IVC filters placed for confirmed venous thromboembolism (VTE) or primary VTE prophylaxis with contraindication to anticoagulation were identified via a central repository. The database developed was overseen by a multidisciplinary team of haematologists, Anticoagulation Stewardship pharmacist and nurse coordinators. The team reviewed patient records and intervened where necessary to facilitate IVC filter removal. Primary outcomes were retrieval rate and documented retrieval plan.

RESULTS: A total of 146 patients underwent IVC filter insertion (11.2 p/month). 77 (53%) had a prophylactic indication for insertion and 69 were for confirmed VTE. 22 patients (15%) died during follow-up from causes unrelated to the IVC filter, and were excluded.

Over a median follow-up of 155 days, 71% (88/124) of IVC filters were retrieved. Average indwelling time was 145 days (range 5-402), with 2% retrieved before day 30, 21% before day 90 and 74% before day 180. Retrieval rates were 63% (41/65) in the prophylactic group versus 80% (47/59) in the therapeutic group (p=0.05).

Active engagement by the multidisciplinary team occurred in 48% (42/88) of successful filter retrievals. Of 36 patients with IVC filters remaining in-situ, plan for removal with ongoing review was in place for 32 (89%). Overall, 97% of the cohort had IVC filter retrieved or a documented plan.

CONCLUSION: Implementation of a multidisciplinary surveillance program has derived a favourable IVC filter retrieval rate over a short period. This quality improvement strategy, which included active intervention, resulted in almost complete patient follow-up. Further enhancements to ensure more timely filter retrieval are proposed.

30. A WEIGHT-ADJUSTED CONTRAST DOSE AND INCREASED ADMINISTRATION RATE COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAM (CTPA) PROTOCOL FOR THE DIAGNOSIS OF PULMONARY EMBOLUS (PE): AN EVALUATION OF PULMONARY TRUNK ENHANCEMENT AND DIAGNOSTIC CONFIDENCE

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The use of CTPA examinations for the detection of PE is becoming more common due to the ease of access and quicker diagnosis times. In 2015, a new imaging protocol was introduced to improve the diagnostic quality of CTPA examinations using a weight-based contrast dose and increased administration rate technique.

AIM: To compare the diagnostic quality of the new protocol, protocol-B, to the previous standard protocol, protocol-A; to determine if there is a reduction in the number of repeat scans and to assess the impact on patient outcomes.

METHODS: A total of 2398 consecutive examinations were selected for this retrospective study. Protocol A (n=1133) involved the intravenous administration of 60ml non-ionic iodinated contrast at a rate of 4ml/s through a 20-gauge cannula. Protocol B (n=1265) used a weight-adjusted contrast dose model of 1ml of IV contrast per kilogram (capped at 75ml), administered at 5ml/s through an 18-gauge cannula. Mean attenuation in the pulmonary arteries (PA) were analysed on a Barco Nio Colour LED display monitor. Images were graded as Cat-1 (high quality, >304 hu), Cat-2 (diagnostic quality, 211-304 hu), Cat-3 (sub-optimal, non-diagnostic study, low-diagnostic-confidence <211 hu).

RESULTS: Univariant analysis was performed. Protocol B was associated with a 9.22% increase in PA enhancement, no significant impact on positive pulmonary emboli (PE) findings (14.56% Protocol A, 15.81% Protocol B), a significant decrease in indeterminate findings (12.36% Protocol A, 7.04% Protocol B). With Protocol B there was a significant increase in the number of CAT-1 scans ($p<0.0001$) and Cat-2 scans ($p<0.0001$) and reduction in the number of repeat scans due to poor diagnostic quality.

CONCLUSIONS: A weight-adjusted contrast dose and increased administration rate CTPA can lead to a significant increase in high quality diagnostic examinations, resulting in fewer indeterminate examinations.

31. EXTENDED THROMBOPROPHYLAXIS IN HIGH-RISK SURGERY: A REVIEW OF CURRENT PRACTICE

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BACKGROUND: The significant risk of post-operative venous thromboembolism (VTE) is dependent on both patient- and procedure-related risk factors. Post-operative enhanced recovery and trends towards earlier discharge may necessitate extended thromboprophylaxis, when a patient's VTE risk persists after leaving hospital. Therefore, instead of abrupt cessation of inpatient VTE prophylaxis, some guidelines recommend extended thromboprophylaxis be continued in certain high-risk patients after discharge.

AIM: To investigate current thromboprophylaxis prescribing for patients undergoing high-risk surgery and discharged early from hospital.

METHODS: This single-centre retrospective cohort study used ICD-10-AM procedure codes to identify patients undergoing surgeries associated with high VTE risk from July-September 2017. Data was collected from electronic medical records. The primary outcome was the proportion of patients discharged early (<7 days post-operatively) following high-risk surgery who received extended pharmacological thromboprophylaxis (after discharge). Descriptive statistics were evaluated using Fisher's exact tests, with two-sided p-value≤0.05 considered statistically significant.

RESULTS: A total of 220 patients were identified, two patients were omitted due to in-hospital death (non-vte related). The median age was 54 years [iqr 39, 67]. Of the 218 included patients, 35 (16.1%) were discharged on an anticoagulant, of which 26 (11.9%) were prescribed extended pharmacological vte prophylaxis, with a median prescribed duration of 30 days. Of the 183 patients not discharged on extended thromboprophylaxis, 168 (92.3%) were compliant with institutional guidelines. Management of the remaining 14 (7.7%) patients was deemed inappropriate due to lack or insufficient duration of extended thromboprophylaxis indicated by institutional guidelines.

CONCLUSION: A low proportion of our patient cohort was discharged on extended pharmacological thromboprophylaxis after high-risk surgery. However, practice was mostly compliant with institutional guidelines. Further investigation, with a larger sample size, is needed to ascertain true compliance and properly identify whether more comprehensive guideline recommendations are required to reduce risk of postoperative VTE.

32. THE SAFETY OF CONTINUING THERAPEUTIC ANTICOAGULATION DURING INFERIOR VENA CAVA FILTER RETRIEVAL: A 6-YEAR RETROSPECTIVE REVIEW FROM A TERTIARY CENTRE.

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PURPOSE: Assess the safety of IVC filter retrieval in patients taking anticoagulation, compared to a non-anticoagulated cohort.

METHODS: Single centre retrospective analysis of patients who underwent IVC filter retrieval between January 2012 and February 2018. Information about patient demographics, anticoagulation, tilt, major and minor complications were collected. Major complications were defined as: IVC intussusception, IVC injury without haemorrhage, IVC injury with haemorrhage, retained fragment of filter, filter fracture and filter embolisation. Minor complications were defined as: neck haematoma and puncture site infection.

RESULTS: A total of 357 patients (age 18-95, Male: 231 patients, Female: 126 patients) underwent IVC filter retrieval. Of these 182 patients were on anticoagulation and 175 patients were not on anticoagulation. IVC filter retrieval was technically successful in 349 patients. 5 major complications (1.4% of retrievals) were recorded and no minor complications (0% of retrievals). In the anticoagulation cohort there were 2 major complications (1.1% of retrievals) both related to IVC injury with haemorrhage. In the non-anticoagulated cohort there were 3 major complications (1.7% of retrievals) relating to filter embolisation, IVC injury without haemorrhage, and filter fracture.

CONCLUSION: IVC filter retrieval is a safe procedure with a low complication rate. Being on anticoagulation does not increase the risk of a major complication or change the management of major complication compared with a non-anticoagulated cohort. IVC filter retrieval is safe to perform in patients currently taking prophylactic or therapeutic anticoagulation based on our cohort.

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33. THE IMPACT OF OCCUPATIONAL THERAPY IN A TARGETED THERAPY ACUTE REHABILITATION PROGRAM (TTARP)

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TtARP is a multidisciplinary rehabilitation program, staffed by a full-time occupational therapist, physiotherapist and allied health assistant. It provides increased intervention to patients waitlisted for sub-acute rehabilitation with the aim to facilitate discharge directly home and reduce length of hospital stay. The aim of this study was to

AIM: This paper outlines the occupational therapy role, scope of practice and TtARP program outcomes.

METHOD: A multi-method service evaluation was conducted over a 5 month period in 2018. Data was collected on admission and discharge to the TtARP program, and included patient demographics, discharge destination and patient functional status. The Functional Autonomy Measurement System (SMAF) was used to measure functional outcomes. The type of TtARP occupational therapy intervention was recorded for each patient and coded against the domains of the SMAF. Staff satisfaction was collected from occupational therapy staff at the end of the program via a survey, where staff rated the program on a 5-point Likert Scale.

RESULTS: 384 patients were referred to the TtARP program of which 206 (54%) were female with a mean age of 71 (SD 17) years and mean acute length of stay of 13 [SD 17] days. 269 (70%) patients were discharged home. Admission and discharge SMAF scores were available for analysis from n=165 participants. SMAF data showed improvements in functional ability from admission to discharge, mapped to the same areas of occupational therapy intervention, suggesting that TtARP therapy improved patient independence levels. 10 staff (50%) complete the survey. Overall results were positive with staff agreeing TtARP occupational therapy intervention assisted facilitating discharge (4.3 mean response where 1 is 'strongly disagree' and 5 is 'strongly agree') and targeted agreed upon goals (4.2 mean response, where 1 is 'strongly disagree' and 5 is 'strongly agree').

CONCLUSION: The TtARP program supported the majority of patients to be discharged home, avoiding a sub-acute admission. Occupational therapy TtARP intervention improved functional outcomes, with most occupational therapy intervention targeted at the self care domain. Acute rehabilitation is a feasible way to reduce subacute admissions in a comprehensive hospital network.

34. GUARDIANSHIP IN HOSPITALS: A VICTORIAN FIRST MODEL OF INTERAGENCY CARE REDUCES LENGTH OF STAY FOR HOSPITAL-BASED INPATIENTS WHO REQUIRE OFFICE OF THE PUBLIC ADVOCATE (OPA) APPOINTED GUARDIANS

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BACKGROUND AND AIM: The Office of the Public Advocate (OPA) may be appointed guardian for individuals lacking decision-making capacity. OPA risk assessments prioritise community applicants over hospital inpatients, delaying discharge decisions and increasing length-of-stay (LOS) and risk of hospital-acquired complications. Alfred Health has the greatest number of inpatients needing OPA guardianship across Victoria. From July 2015 to June 2016, mean wait time for OPA guardian allocation at Alfred Health was 49.9 days (SD 27.0), costing an estimated $37,336 per patient. The Guardianship in Hospitals collaboration between OPA and three hospital social work services redesigns care and increases guardianship access for these vulnerable patients. The aim of the study was to measure the impact of the Guardianship in Hospitals model on time from VCAT order to OPA guardian allocation and overall LOS of inpatients who require OPA guardianship.

METHODS: This practice-based research used a quasi-experimental historical control group design with 12-month pre-implementation and post-implementation cohorts. Comparison of cohorts was conducted using data from hospital and OPA records, independent sample *t*-tests and N-1 chi-squared tests.

RESULTS: Mean guardian allocation wait time significantly decreased from 46.5 to 22.9 days (coef. -23.55, 95% CI -16.42 to -30.68, p<0.0001). Mean LOS decreased from 163.2 to 148.5 days. Estimated value of decreased allocation waits was $15,516 per patient, or $5 of resources released per $1 spent. For Alfred Health, allocation wait decreased from 49.9 to 29.9 days, valued at $8,299 per patient, and LOS from 167.3 to 163.1 days.

CONCLUSION: The Guardianship in Hospitals model has halved average OPA guardian allocation waits. This research is an example of collaboration between hospital social work departments and non-health services. It demonstrates social work innovation in designing interagency models of care, and patient advocacy. It is improving outcomes for vulnerable patients and translating research into practice. Further research will measure hospital-acquired complications, clinical reasoning and interdisciplinary decision-making.

35. THE AUSTRALIAN BREAST DEVICE REGISTRY AS A MODEL FOR MONITORING HIGH RISK DEVICES

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The Australian Breast Device Registry (ABDR) is a Commonwealth funded quality and safety registry to monitor the use of breast devices. Breast devices, including silicone breast implants and tissue expanders, are classified as high risk medical devices by the TGA. Systematically collected data on high risk medical devices is crucial for ensuring the safety of device recipients.

AIM: To report on the progress of the national roll out of the ABDR.

METHOD: The guiding document for the ABDR is the 'Operating Principles and Technical Standards for Australian Clinical Quality Registries'. Plastic, cosmetic and breast surgeons collaborate on the ABDR, contributing data from all of their patients, with endorsement by all societies. The registry employs an opt-out model, in which data from all patients is contributed and patients can choose to remove their data from the registry. A two-page minimum dataset is completed at the time of surgery and sent to the ABDR. Quality indicators will be examined.

RESULTS: At March 2019, the ABDR had engaged 514 surgeons representing 329 sites (85% of all eligible sites). Contributing surgeons were predominantly plastic surgeons (65%), with the greatest representation from NSW, Victoria and Queensland (76%). A total of 38,472 patients have data recorded in the ABDR encompassing 42,933 procedures (86% bilateral, 14% unilateral). Recorded at the individual breast level, 74% of the procedures were cosmetic, 19% reconstruction and 2% due to congenital deformity (0.1% not stated).

CONCLUSION: The ABDR is a model for post-market surveillance for high risk medical devices.

36. PATIENT PERCEPTIONS OF THE USE OF ARTIFICIAL INTELLIGENCE IN DIAGNOSTIC RADIOLOGY

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AIM**:** To examine patient perceptions of the use of Artificial Intelligence in Diagnostic Radiology

METHODS AND MATERIALS: 300 voluntary anonymous surveys were offered to all patients attending the Alfred hospital for an outpatient radiological investigation. Baseline information included age, gender, level of education, confidence with technology and hours spent on technology per week. Survey questions included awareness and perceptions of AI in Radiology, confidence with a Radiologist-generated report and computer-generated reports, accuracy required to trust computer-generated reports and perceptions around privacy of data and legal liabilities for missed and incorrect diagnoses.

RESULTS: 300 surveys were completed; 17 were incomplete and rejected, 283 were included for analysis. The average age group of the 150 male and 133 female participants was 41-50 years. Participants spent 5-10 hours on a technological device a week and were slightly comfortable with technology on self-analysis. 98% of patients were aware and very comfortable that a Radiologist was going to issue their report. 63% were unaware that AI or a computer program was used towards or could issue a diagnosis. Patients were more comfortable for a computer to issue a report with Radiologist input than without. Patients felt less comfortable with the safety of their privacy and data with an entirely computer-generated report. To trust an entirely computer-generated report, the median accuracy expected was 99.9%; 53% desired the computer to be more accurate and 41% desired equivalent accuracy. For major missed or incorrect diagnoses, 76% felt that some liability would lie with the hospital, 61% computer company, 37% Radiologist and 10% referring doctor.

CONCLUSION**:** Patients were trusting of Radiologist reports, were generally unaware of computer programs that could issue reports, were slightly uncomfortable with entirely computer generated reports and expected computer generated report accuracy to be at least on par or better than Radiologists to be acceptable.

37. A SINGLE CENTRE EXPERIENCE OF FLUOROSCOPIC GUIDED PERIPHERALLY INSERTED CENTRAL CATHETER (PICC) INSERTION BY NURSING STAFF: RATIONALE AND EARLY OUTCOMES

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At the Alfred, medical staff perform the majority of peripherally inserted central catheters (PICC) insertions. Centres that run nurse-led PICC services have higher malposition and reattempt rates than fluoroscopy guided insertion. The Alfred has a large cystic fibrosis and lung transplant cohort which accounts for a high proportion of clinically difficult PICC insertions.

AIM: We propose bedside insertion, blind or with navigation technology may be more susceptible to technical difficulties. A nurse led fluoroscopy guided PICC insertion service may be a viable alternative to the current model of care.

METHODS*:* Practical and theoretical PICC insertion training was completed using a standardised in-house education package. 20 PICC insertions were completed by nursing staff and signed off by an IR consultant. Data was collected on the first 50 unsupervised nurse inserted PICC lines.

RESULTS*:* 0% malposition, 100% insertion success, 0% arterial puncture, 4% developed a line associated DVT, 0% had a haematoma. 7 of the lines were found to have a complication over a total of 1367 days, 4 of these had lines that developed a sluggishness to bleed or flush at or after day 20 and 1 line became blocked at day 36. There were 5.12 complications per 1000 catheter days. The average number of days in situ without a line issue was 25.8. The average number of days in situ before a line developed a problem equated to 41.4.

CONCLUSION*:* Complication rates were within the ranges as described in the literature and malposition was significantly lower when inserted under fluoroscopy guidance. Our results show 100% insertion success based on accuracy of tip position within the lower third portion of the superior vena cava. We propose that a nurse-led fluoroscopy guided PICC service will be cost effective, not impact on fluoroscopy bookings and will see similar outcomes to medical staff insertions.

38. HIGH LEVEL CARE PATIENTS WITH HIP FRACTURES – DOES DISCHARGE DESTINATION FROM ACUTE CARE AFFECT OUTCOMES?

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BACKGROUND: Hospital presentations for management of hip fracture are increasing and a growing cohort are admitted from Residential Aged Care Facilities (RACFs). Whilst international hip fracture guidelines highlight the importance of rehabilitation post-operatively, the most appropriate setting is unknown.

AIM: To determine the factors associated with discharge destination for patients from RACFs who underwent hip fracture fixation, and to compare 12 month outcomes for those returning to their RACF with those admitted to a Sub-Acute Facility (SAF).

METHODS: A retrospective case series review of all patients from a RACF admitted to The Alfred hospital, Melbourne, for fixation of hip fracture in 2014-2015 was undertaken. Data including demographic and hospital event details, length of stay (LOS), discharge destination and 12 month functional outcomes measured by the Glasgow Outcomes Score – Extended (GOS-E) were collected.

RESULTS: Ninety patients from a RACF were included, with 68 patients (75.6%) returning directly to their facility and 22 (24.2%) admitted to a SAF. Those discharged to a SAF had an average LOS at this facility of 20.79 days (SD 8.02). This group also had a longer acute LOS [7 days (IQR 5, 10), compared to 6 days (IQR 4, 7.5) p value 0.02]. There was no difference between groups at 12 months in terms of mortality or function on the Glasgow Outcome Scale Extended (GOS-E), with 50% of all patients deceased at this time point and the other 50% reporting a poor functional outcome.

CONCLUSION: Patients from RACFs who underwent hip fracture fixation had poor 12 month functional outcomes and a high rate of mortality irrespective of discharge destination. Future research should explore opportunities to provide structured multidisciplinary rehabilitation in the RACF environment. Prospective economic modelling and a comprehensive suite of outcome measures to evaluate patient and stakeholder satisfaction with such a model of care are essential.

39. PRELIMINARY FINDINGS FROM PILOTING A NATIONAL CLINICAL QUALITY REGISTRY FOR OVARIAN CANCER INFORMED BY PRE-EXISTING CLINICAL DATABASES

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The National Gynae-Oncology Registry (NGOR) is a new multi-module clinical quality registry (CQR) which has recently piloted an ovarian cancer module, sourcing data from existing datasets maintained by private consulting rooms of gynaecological oncologists, and/or gynaecological oncology unit databases from ten public and private hospitals across Victoria, Tasmania and New South Wales.

AIM: To demonstrate the feasibility of using existing clinical databases to inform a set of nine quality indicators developed by a steering committee of clinical and registry specialists; and to demonstrate the usefulness of a CQR to monitor the management of ovarian cancer in Australia.

METHODS: Women who were eligible for the pilot were invited to participate under an opt-out method of recruitment. Clinical data about the participants was then sent from participating sites and clinicians to the registry. Quality indicator performance, and data completeness was assessed and reported back to participating hospitals and clinicians after approximately 18 months of data collection.

RESULTS: Over 270 participants were recruited during the pilot, during which it was found that each source database contained data of varied formats and definitions. Some databases did not contain sufficient detail to inform all indicators and/or did not contain some of the necessary data for risk-adjustment. However, it was found that minimal adjustments and greater clarity around data definitions would provide the registry the potential to achieve its' aim of improving quality of care and patient outcomes.

CONCLUSION: Despite missing data and other methodological issues during the pilot, it was successfully demonstrated that the use of existing clinical databases has the potential to greatly reduce time and costs associated with primary data collection. Furthermore, there is strong clinical support for a CQR with many relevant stakeholders expressing that it will be a valuable resource for the improvement of quality of care.

40. INTRAOPERATIVE TECHNIQUE USE IN BREAST DEVICE SURGERY ACROSS AUSTRALIA

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An estimated 20,000 Australian women undergo breast device surgery annually and various intraoperative techniques (IOTs) are used to optimise outcomes. The Australian Breast Device Registry (ABDR) collects information on IOTs and provides an opportunity to understand IOT use.

AIM: The primary aim is to explore the intraoperative technique (IOT) use in breast device surgery in Australia. The secondary aim to determine whether patient, surgeon or hospital factors explained these differences.

METHOD: Participants were patients who had undergone breast device surgery for breast augmentation (BA) or reconstruction (BR). Seven IOTs included for analyses were prophylactic antibiotics, antibiotic dipping solution, glove change for insertion, sleeve/funnel, antiseptic rinse, drains, occlusive nipple shields. Regression analyses were performed to determine the reasons for variations in IOT use.

RESULTS: Data on 24,096 procedures were analysed. Prophylactic antibiotics used in almost all (BA=95.8%; BR=96.9%) procedures. Antiseptic rinse (BA=86.3%; BR=75.7%), glove change for insertion (BA=67.4%; BR=73.5%), and antibiotic dipping solution (BA=59.2%; BR=45.2%) used in most procedures. Occlusive nipple shields used in most (70.3%) BA and drains in most (57.7%) BR procedures. Sleeve/funnel use was least (BA=29.9%; BR=13.2%). Regression results for BA were significant (p<0.001) for all seven IOTs in the univariate and multivariate models. In the two mixed effects models which tested for surgeon and hospital factors two IOTs (glove change for insertion and sleeve/funnel) were significant (p<0.001) but none of the other results were significant. BR regression results were significant (p<0.001) in the univariate and some multivariate models but the two mixed effects models did not have significant results.

CONCLUSION: There is high usage of prophylactic antibiotics across Australia. In augmentation surgery, the variation in most IOT use is explained by surgeon or hospital factors. In reconstruction surgery, the variation in IOT use is lower than augmentation and are explained by patient, surgeon and hospital factors.

41. PRESSURE INJURY DATA IN AN AUSTRALIAN ACUTE CARE SETTING: A COMPARISON OF THREE DATA SETS

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Hospital-acquired pressure injuries (HAPIs) represent a serious clinical and economic problem. The cost of treating HAPIs in Australian public hospitals was recently reported at AUS$983 million per annum. There are three main sources of data for documenting pressure injury (PI) occurrence in Australian hospitals: incident reporting (RiskMan), medical record coded data and real time surveys of pressure injury. PI data reported at hospital level and to external agencies using these three different sources is variable. This coding and reporting issue may lead to inaccurate data interpretation and hinders improvement in accuracy of PI identification, coding and prevention.

AIM: The study compared 3 different data sources at The Alfred to investigate PI data collection quality & to develop data harmonisation.

METHODS: We compared available data sets from the Alfred Health 1) incident reporting, 2) medical record coded data, and 3) PUPPS/PIPPS data for inpatients from point prevalence studies conducted in 2015, 2016, and 2017. We used the International Classification of Diseases 10th edition Australian modified (ICD-10AM) coding classification system.

RESULTS: Of the 507 PIs recorded in PUPPS, there were 136 (26.8%) (95%CI 23.0-30.9) PI recorded in RiskMan. PIs present on admission were reported more accurately in RiskMan. Of the 175 of PI recorded in PUPPS, 55 (31.4%) (95%CI 24.6-38.9) were recorded in RiskMan. The True Positive Fraction (TPF) of ICD 10 codes and RiskMan for PI greater than stage II was assessed using PUPPS as the gold standard. The calculated agreement of RiskMan and coding with PUPPS: RiskMan TPF 109 (36.2%) (95%CI 30.8-41.9). Some PI location sites recorded in PUPPS were reported more accurately in RiskMan e.g. ischium-buttocks PI (30.0%) and lower back (21.7%), comparing with head (11.1%), heel (16.5%) and toe (5.7%), which were underreported. The main limitations were related to PI coding, i.e. PI coded in PUPPS may not be the same as documented in RiskMan as stage I PIs are not included in RiskMan.

CONCLUSION: RiskMan may not be the most reliable system for PI reporting. There is a need to better understand the correlation between the three data sets to allow a more efficient and effective sharing of data sources and to improve capacity to collect high quality PI incidence data over time; thereby facilitating capacity to benchmark performance with other hospitals and ultimately reduce incidence of preventable pressure injury in hospitalised patients.

INFECTIOUS DIESEASE AND INFECTION CONTROL

42. IMPROVING EARLY RECOGNITION AND TIMELY CARE OF SEPSIS – AN ELECTRONIC SEPSIS CARE BUNDLE

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INTRODUCTION**:** Sepsis is life-threatening organ dysfunction caused by a dysregulated response to infection. Delayed recognition and treatment are associated with high mortality. Sepsis care bundles implemented internationally have demonstrated improvements in process and clinical outcomes. AIM: To measure the effect of an electronic Sepsis Care Bundle on time to antibiotic administration and completion of care bundle components. Improvements were anticipated to reduce sepsis related mortality and ICU admission rate.

METHODS**:** As part of the Better Care Victoria Sepsis Scaling Collaboration, The Alfred developed and piloted an electronic Sepsis Care Bundle linked with the hospital's deteriorating patient processes. The bundle consisted of four components (antibiotics, fluids, blood cultures and lactate) to be completed within 60 minutes of emergency department presentation or inpatient sepsis recognition. Multi-disciplinary education and audit and feedback were employed. Pre-intervention period data was collected retrospectively using coding. Post-intervention data was collected retrospectively using coding and prospective active surveillance.

RESULTS**:** Data were collected for 100 patients in the pre-intervention period (November 2017 – January 2018), and 143 patients in the post-intervention period (November 2018 – January 2019). Median time to antibiotic administration improved from a median of 99 to 48 minutes and the proportion of patients receiving antibiotics within 60 minutes increased (30% vs. 68%, p<0.001). There was improvement in completion of the sepsis bundle (6% to 35%, p<0.001). There were non-significant decreases in sepsis-related mortality (10% vs. 8.4%, p=.66), sepsis-related ICU admission (17% vs. 11%, p=.25) and hospital length of stay (median 6.6 vs 5.3 days, p=0.25).

CONCLUSION**:** Implementation of an electronic Sepsis Care Bundle accompanied with education, audit and feedback resulted in improvements in timely sepsis treatment, and the care bundle is now being implemented service wide. Larger studies are required to evaluate associations between the electronic sepsis care bundle and patient outcomes including mortality and length of stay.

43. A NURSE-LED, COMMUNITY BASED MODEL OF HEPATITIS C CARE IN MELBOURNE, AUSTRALIA

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AIM: Hepatitis C virus (HCV) testing and treatment at community based services', including alcohol and other drug, mental health and homeless services, will be a critical component of HCV elimination goals. We conducted a retrospective analysis of a nurse-led service at nine sites to evaluate progression through the HCV care cascade during 2017 and 2018.

METHODS: Clients from nine sites in both inner and outer metropolitan areas were either referred to or engaged by nurses directly during regular visits. Nurses' provided HCV education, testing and follow-up services. Clients who tested HCV RNA positive were contacted by the nurse to discuss treatment and prescription was provided by an affiliated doctor or nurse practitioner.

RESULTS: Overall, 569 clients were referred to or engaged by the HCV nurses during 2017 and 2018. HCV testing was completed by 459 people of whom 354 (77%) were HCV RNA positive. Of those who were HCV RNA positive, 240 (68%) reported recent injecting drug use and 191 (54%) reported a diagnosed mental health illness. A total of 251 (71%) were known to have commenced treatment; the majority, 169 (67%), were prescribed treatment by a general practitioner or nurse practitioner rather than a specialist gastroenterologist or infectious disease physician. By the end of 2018, 169 people who had commenced treatment were eligible for sustained virological response (SVR) testing among whom 96 (57%) had a test; all were HCV RNA negative.

CONCLUSION: HCV testing and treatment through a nurse-led community based model of care is feasible and effective. Despite this, more work is needed to identify how drops in the HCV care cascade regarding treatment uptake may be overcome, including through the combined use of point of care rapid testing and same day treatment prescription. Similarly, efforts to increase follow-up testing for SVR are warranted.

44. A STUDY OF INFECTED DRIVELINES FROM VENTRICULAR ASSIST DEVICE PATIENTS: THE PRESENCE OF MICROBIAL BIOFILMS AND MICRO-GAPS IN THE DRIVELINE TUNNEL

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BACKGROUND AND AIM: Driveline infections remain a major complication of ventricular assist device (VAD) implantation. To characterise *in vivo* microbial biofilms causing driveline infections and the degree of tissue integration into the velour of explanted driveline.

METHODS: Drivelines were obtained from ten VAD patients undergoing heart transplantation at The Alfred, Melbourne and St Vincent's Hospital, Sydney between June 2017 and October 2018. Four uninfected and six infected drivelines were aseptically sectioned into ten 1.5 cm pieces, from the smooth tube section at the exit-site to the velour section adjacent to the VAD. Organisms on each section were isolated and identified. Microbial biofilms on the infected driveline sections were assessed using scanning electron microscopy (SEM) and viable counts. Computed tomography (micro-CT) and SEM were used to assess tissue integration into each section. All sections were analysed histologically to confirm human matrix protein deposition.

RESULTS: No organisms were isolated from non-infected drivelines using microbiological culture. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Staphylococcus epidermidis* were found on the velour sections of infected drivelines and correlated with the microbiological culture from swabs of the infected exit-site. Although histological analysis found considerable collagen fibre and fibroblast deposition on the smooth tube and velour, SEM and micro-CT suggested insufficient tissue integration throughout the driveline velour. Micro-gaps were observed between the velour fibres, with evidence of microbial biofilms within these gaps. Such biofilms were *morphologically distinct* from *in vitro* biofilms grown on biomaterials and might be responsible for the antimicrobial treatment failure.

CONCLUSION: This study demonstrated inadequate tissue integration of clinical drivelines in the subcutaneous tissue tunnel, with associated microbial biofilms formed within the micro-gaps between velour fibres. These data provide important insights into a potentially novel therapeutic strategy against driveline infections that is focused on enhancing tissue integration into the velour, thereby preventing microbial adherence, biofilm formation and migration.

45. THE PREVALENCE AND DYNAMICS OF *MYCOPLASMA* AND *UREAPLASMA* SPP. IN PREGNANCY AND POSTPARTUM IN EAST NEW BRITAIN, PAPUA NEW GUINEA

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With growing concern for the rapidly increasing numbers of antimicrobial-resistant sexually transmitted infections (STIs), such as *M. genitalium*, there is renewed interest in their global surveillance and intervention. The prevalence and negative impacts of a *Chlamydia*, *Gonorrhoea* or *Treponema pallidum* infection in pregnancy are well described. However, despite the association of *Mycoplasma* and *Ureaplasma* spp. infections with poor maternal and birth outcomes, little is known about their prevalence, dynamics and risk factors, particularly in resource-poor settings.

We determined the prevalence of *Mycoplasma* and *Ureaplasma* spp. in a cohort of pregnant women attending antenatal care in East New Britain (ENB), Papua New Guinea. A vaginal swab was collected at enrolment (n=625) and six months after delivery (n=327). DNA extractions and real-time PlexPCR® (SpeeDx) were performed to detect *U. parvum, U. urealyticum, M. hominis* and *M. genitalium* at both time points. The prevalence of these infections at enrolment was high: 59.9% *M. hominis* and 75.2% *U. parvum*. The prevalence of these infections was significantly lower six months after delivery, with a minimum decrease of 26%. At enrolment, 94.1% of women had at least one STI, with most women having two (33.5%), three (24.8%) or more (11.2%) simultaneous infections. Pairwise and cluster analysis identified that many of these infections grouped together. A multivariate analysis indicated that the odds of having a detected case of each of these infections decreased for multigravidae women, those currently employed and women whom reported having ever used family planning. It also indicated that the presence of clinical symptoms was a poor predictor of STI detection. Given their association with poor maternal and birth outcomes, the high prevalence of *Mycoplasma* and *Ureaplasma* spp., in this cohort, particularly in women who are primigravidae, indicates the need for better detection and targeted intervention in resource-constrained areas like ENB.

46. NK CELL-MEDIATED KILLING OF HIV-INFECTED MACROPHAGES

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INTRODUCTION: HIV-infected macrophages are largely resistant to HIV-induced cell death, certain antiretroviral drugs, and can harbour HIV in tissues for long periods of time, yet cure strategies overlook this reservoir. Macrophages may be vulnerable to natural killer (NK) cell-mediated killing by either natural cytotoxicity (NC), requiring human leukocyte antigen (HLA) downregulation or antibody-dependent cytotoxicity (ADCC), requiring antibody opsonisation of HIV epitopes on the cell surface. The expression of these factors on HIV-infected macrophages is largely unknown.

AIM: To identify factors on the surface of HIV-infected macrophages that can be utilised in HIV targeting/elimination strategies.

METHODS: Human NK cells purified from healthy blood donors were cultured in media + IL-2 alone or IL-2/15/18. NC was assessed against the K562 target cell line. Human monocyte-derived macrophages (MDM) and T cells were infected *in vitro* with HIV_{BaL} for 7-10 days. Flow cytometry and fluorescence microscopy were used to assess productive infection (intracellular p24), HLA expression, and surface Env expression using anti-Env antibodies targeting distinct epitopes.

RESULTS: IL-2/15/18-induced NK-derived cells upregulated CD56 and CD16 and exhibited high NC activity over 14 days. In some donors, infected MDM downregulated HLA-A/B/C, rendering these cells potentially susceptible to NC-mediated killing. A subset of HIV-infected MDM expressed Env on their surface, but some anti-Env antibodies (i.e. PGT151 and 10E8) exhibited differential binding to infected MDM as compared to T cells, suggesting differences in expression of specific Env epitopes.

CONCLUSIONS: $CD56^{high}$CD16+ NK-derived cells may be useful for killing HIV-infected cells such as macrophages in immunotherapy-based HIV cure strategies. A subset of infected MDM express surface Env, suggesting ADCC-mediated elimination strategies are possible, however we show that HIV-infected MDM and T cells display distinct Env epitope expression profiles. This highlights the importance of testing the ability of HIV cure strategies to target both macrophage and T cell populations.

47. NEUROTOXICITY WITH HIGH DOSE DISULFIRAM AND VORINOSTAT USED FOR LATENCY REVERSAL

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BACKGROUND: The histone deacetylase inhibitor, vorinostat (VOR), and disulfiram (DSF), a drug used to treat alcohol dependence, reverse HIV latency in vivo by different pathways and have been safely administered to people with HIV. Three days of 2000mg DSF has been safely given as a latency reversal agent. This study aimed to determine if these two agents (i) reverse HIV latency more potently than a single agent and (ii) are safe and tolerable.

METHODS: HIV-infected adults on suppressive antiretroviral therapy (ART) were enrolled in a prospective single arm study of DSF 2000mg daily for 28 days and VOR 400mg daily on days 8-10 and 22-24. The primary endpoint was plasma HIV RNA on day 11 relative to baseline. We quantified cell associated (CA) unspliced (US) and multiply spliced (MS) RNA and HIV DNA in CD4+ T-cells from blood; HIV RNA in plasma using a single copy assay; and p24 expression by SiMoA and histone acetylation by flow cytometry from PBMCs. Plasma concentrations of ART, VOR and DSF were quantified.

RESULTS: The first two participants (P1 and P2) experienced grade 3 neurotoxicity (altered mental status possibly and probably related to DSF respectively), which led to trial suspension. P1 was a 67 year-old male on ABC/3TC/DTG with a CD4 count of 762 cells/μL and VL <50 copies/mL for 16.7 years. On study day 24 (having missed DSF and VOR on day 10 and stopped DSF and all ART from day 17-24) he presented with confusion, lethargy, and ataxia. Neuroimaging revealed sagittal sinus thrombosis and chronic vertebral artery occlusion. He was admitted to hospital, anticoagulated and symptoms resolved by day 29. P2 was a 61 year-old male on TAF/FTC + RAL with a CD4 of 1085 cells/μL and VL <50 copies/mL for 4.8 years. On day 11 he presented with paranoid ideation, emotional lability, lethargy and ataxia. He was admitted to hospital; brain CT scan was normal and his symptoms resolved by day 23. Both participants had increased CA-US RNA following study drugs, which persisted for weeks after drug cessation. P2 also had increased plasma viremia from day 8-37 (peak 81 copies/mL on day 21) with therapeutic ART drug levels. Low but detectable levels of VOR and histone acetylation were seen in both participants.

CONCLUSION: The study drug combination was not safe with significant but reversible neurotoxicity, which we suspect was related to prolonged high dose DSF. There was evidence of latency reversal in both participants. Prolonged high dose DSF, with or without VOR, should not be further pursued.

48. COMMUNITY AND PROVIDER ATTITUDES TOWARDS TREATMENT INTERRUPTIONS IN HIV CURE TRIALS

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BACKGROUND: Analytical treatment interruptions (ATI) assess effects of interventions aimed at curing HIV or achieving antiretroviral therapy (ART)-free HIV remission. Understanding of ATI acceptability and how ATI should be conducted amongst people living with HIV (PLHIV) and their HIV healthcare providers (HHP) is limited.

METHODS: Online surveys for PLHIV and HHP assessed understanding and acceptability of different monitoring strategies during ATI (frequency of CD4, viral load (VL), clinical assessment), potential risks of ATI and the prospect for HIV cure. Responses were collected from July 2017-January 2018. Survey results were compared using $\chi 2$ test between PLHIV and HHP for ATI monitoring strategies and perceptions of cure research.

RESULTS: 442 PLHIV completed the survey: 21% female, 61% ≤ 50 years old, 24% identified as heterosexual, 95% on ART, 83% reported undetectable VL. 55% thought HIV cure would be achievable within 10 years. Preferred frequency of CD4, VL and clinical monitoring during ATI was monthly (31%, 35%, and 39% respectively). 59% stated they would be more willing to undergo ATI if home based VL testing was available, 51% if nurses could perform home visits, and 54% if pre-exposure prophylaxis was offered for HIV negative partners. 144 HHP completed the survey: 72% practiced in Australia, 51% work in teaching hospitals, 24% in community based family practices and 15% in sexual health clinics. 19% HHP believed a HIV cure would be achievable within 10 years. Responses from questions comparable in both surveys demonstrate: higher optimism for cure amongst PLHIV, higher awareness of ATI in HHP, decreased acceptability of sustained viremia in PLHIV and similar acceptability of changes in CD4.

CONCLUSION: PLHIV were more optimistic of a HIV cure than HHP, but were less aware of ATI or willing to have periods of sustained viraemia. Clear education messages in relation to ATIs should be developed for both PLHIV and HHP.

49. STRUCTURE GUIDED PREDICTION OF PYRAZINAMIDE RESISTANCE IN TUBERCULOSIS

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Pyrazinamide, a first-line drug with remarkable sterilizing activity, plays an important role in the treatment of tuberculosis, especially in multi-drug resistant strains. Pyrazinamide use, however, is complicated by its side-effects and challenges with reliable drug susceptibility testing. Resistance to pyrazinamide is largely driven by mutations in pyrazinamidase (pncA), responsible for drug activation, but large genetic diversity and heterogeneity has hindered the development of a comprehensive molecular diagnostic test. Our objective was to use information from the proteins 3D structure to accurately identify resistance mutations in pncA. To achieve this, we curated 610 pncA non-synonymous single nucleotide mutations with associated high confidence experimental and clinical information on pyrazinamide susceptibility. The molecular consequences of these mutations were assessed using the mCSM platform, which provided insights into changes in protein stability, conformation, and interactions for each mutation. Using these structural and biophysical effects, we were able to correctly classify mutations as either susceptible or resistant with an accuracy of 78%. Our model was validated against a previously documented set of non-redundant clinically resistance mutations achieving 77% accuracy and 81% accuracy across all pncA missense mutations recently reported in the CRyPTIC dataset. Applying this structural analysis to a novel set of previously unreported Victorian clinical mutations with experimental drug susceptibility testing, our model showed clinical resistance in pyrazinamide could be predicted with 71% accuracy. We also performed a real-time analysis on a Victorian tuberculosis patient and showed pyrazinamide treatment would not be effective and led to its discontinuation, the first use of structural information to guide clinical resistance detection. We have made this model freely available through a user friendly web interface called SUSPECT-PZA, StrUctural Susceptibility PrEdiCTion for pyrazinamide, at: http://biosig.unimelb.edu.au/suspect_pza/. This will be a valuable resource to analyse any *pncA* missense mutation, providing structural insight to help guide patient treatment decisions and screening programs.

50. CONSUMER KNOWLEDGE AND ATTITUDES TOWARDS PUBLIC REPORTING OF HEALTHCARE ASSOCIATED INFECTION DATA

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BACKGROUND: There is little information regarding consumer knowledge of healthcare associated infection (HAI) in the Australian setting. Furthermore, it is also unclear how meaningful publicly reported HAI data is to consumers, how they may use it, and the most appropriate format for data to be presented. The purpose of this study was to explore consumer knowledge and attitudes towards HAI and public reporting.

METHOD: A qualitative study design characterised by a series of semi structured interviews was undertaken with purposively selected, elective surgical inpatient adults at a large metropolitan acute hospital in Melbourne. Interviews were digitally recorded and transcribed verbatim. Analysis of the data was conducted using thematic analysis.

RESULTS: Twenty interviews were conducted. Three major themes were identified, each with 3-4 sub themes; 1) Awareness of HAI – Patient understanding of HAI; MyHospitals data; Patient contribution to infection prevention; Previous experience of HAI. 2) Patient Priorities – Primary focus on current illness; Relationships and reputation; Confidence in staff to manage risk. 3) What patients want to know – Current source of patient information; Preferred source of information; Information content; Influence on choice of hospital.

DISCUSSION: We found broad variation in knowledge, sources of information, and preferences for the type and delivery of information. A significant cohort of participants preferred not to be informed, whilst others were neutral or only mildly interested. If public reporting of HAI data is to be aimed at consumers, further engagement with consumers is crucial to ensure information is provided is fit for purpose.

51. A COMPREHENSIVE *IN VITRO* EVALUATION OF MEDIHONEY AS AN ANTI-BIOFILM AGENT IN PREVENTING VENTRICULAR ASSIST DEVICE DRIVELINE INFECTIONS.

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BACKGROUND: Medihoney is routinely applied to the exit-site of Ventricular Assist Device (VAD) drivelines in patients in many Australian hospitals to prevent driveline infections. Its effectiveness as a prophylactic measure remains unclear. We performed a comprehensive *in vitro* study using microbiological assays that closely mimic the *in vivo* environment of the driveline exit-site to assess the effectiveness of medihoney in preventing biofilm-related driveline infections.

METHODS: Antimicrobial efficacy testing of medihoney was performed against 24 clinically-relevant bacterial and fungal strains grown as planktonic and biofilm cells. The minimum inhibitory concentration (MIC), minimum biofilm inhibitory concentration, minimum eradication concentration, and the activity of individual components of medihoney were assessed. A colony biofilm assay and a drip-flow biofilm reactor assay that mimic chronic wounds and the driveline exit-site were used to evaluate medihoney activity in inhibiting early adherent organism monolayers and mature biofilms.

RESULTS: Medihoney demonstrated activity against planktonic organism cells in 5/6 *S. aureus*, 6/6 *S. epidermidis*, 1/6 *P. aeruginosa* and 4/6 *Candida* strains using a qualitative disk diffusion susceptibility assay and a quantitative broth microdilution assay [MICs, 10% weight/volume (W/V) medihoney concentrations]. Only higher concentrations of medihoney (30-50%, W/V) inhibited the growth of biofilm cells. Eradication of biofilms could not be achieved by medihoney, even at the highest concentration studied. Medihoney's antibiofilm properties were multi-faceted, including sugar content, pH, osmolality and the proposed active ingredient, methylglyoxal (MGO). MGO actually played a less important role than other medihoney characteristics. The colony biofilm assay and the drip flow biofilm reactor showed that medihoney was unable to prevent the maturation of biofilms after early organism adherence, and only had a weak activity against established biofilms.

CONCLUSION: Our work suggests a suboptimal effectiveness of medihoney in preventing driveline exit-site infections due to biofilm development, warranting further clinical trials before its widespread use can be justified.

52. THE IMPACT OF AN ANTIMICROBIAL STEWARDSHIP TEAM ON THE APPROPRIATENESS OF ANTIMICROBIAL THERAPY IN SUSPECTED SEPSIS: A RANDOMISED CONTROLLED TRIAL

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AIM: To determine the impact of Antimicrobial Stewardship (AMS) team review in patients with Medical Emergency Team (MET) calls for suspected sepsis at The Alfred Hospital.

METHODS: Randomised controlled trial of non-ICU inpatients who had a MET call for suspected sepsis. Patients were randomised to standard care (management of antimicrobial therapy by the treating unit) or intervention (standard care plus AMS review 48 hours following the MET call). The primary outcome was appropriateness of antimicrobial therapy 72 hours post MET call, which was determined by a panel of blinded Infectious Diseases physicians.

RESULTS: Between February and August 2018, 90 patients were enrolled; 45 were randomly allocated to the intervention group, and 45 to the control group. A significantly greater proportion of patients in the intervention group were receiving appropriate antimicrobials 72 hours following the MET call (67% vs. 44%, difference 23%, 95% CI: 2.2%, 42%, p=0.03). There were differences observed in the total duration of antimicrobial therapy (8.7 vs. 10.7 days), time to appropriate therapy (1.8 vs. 3.1 days), sepsis-related ICU admission rates (13% vs. 22%) and sepsis-related in-hospital mortality (7% vs. 9%), however these were not statistically significant. In the intervention group, 27 recommendations were made by the AMS team; 74% of recommendations were accepted, including 30% of cases where antimicrobials were discontinued or de-escalated.

CONCLUSION: Internationally, this is the first randomised-controlled trial examining AMS team review in patients with suspected sepsis. AMS team review resulted in a significant improvement in the appropriateness of antimicrobial therapy 72 hours following MET calls due to suspected sepsis. Patients with suspected sepsis are an identifiable group that may benefit from routine AMS team review.

INTENSIVE CARE

53. EARLY REHABILITATION DOES NOT AFFECT RESPIRATORY OR HAEMODYNAMIC PARAMETERS IN PATIENTS ON EXTRACORPOREAL MEMBRANE OXYGENATION

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The number of publications reporting on rehabilitation of patients whilst on extracorporeal membrane oxygenation (ECMO) has increased over the past decade. Early rehabilitation in the intensive care unit (ICU) is recognised as safe and feasible in other ICU populations, but little is known about the respiratory and haemodynamic effects of rehabilitation in patients on ECMO.

AIM: The primary aim of this study was to describe the respiratory and haemodynamic effects of early rehabilitation compared to standard care physiotherapy over a 7-day period in patients requiring ECMO.

METHODS**:** Single-centre randomised controlled trial. Consecutive patients undergoing ECMO were recruited within 72 hours of ECMO commencement. These patients formed part of a larger multicentre randomised safety and feasibility trial on early rehabilitation versus standard care physiotherapy in patients on ECMO. Respiratory and haemodynamic parameters, along with ECMO settings, were recorded 30 minutes pre and post each rehabilitation session, and during the session (minimum and maximum values). In addition, the minimum and maximum values for these parameters were recorded outside of the rehabilitation or standard care sessions for each 24-hour period over the 7 days. The number of minutes of rehabilitation was recorded per session.

RESULTS**:** Fifteen patients (age 51.5 ± 14.3 years, 80% male) received ECMO; 10 venoarterial, 5 venovenous. The rehabilitation group (n=7) spent more time exercising per session than the standard care group (n=8); mean 28.7 versus 4.2 minutes respectively, p<0.0001. Four patients stood or walked at the bedside; three in the rehabilitation group and one in the standard care group. There was no difference between the groups for any of the respiratory, haemodynamic or ECMO parameters. The minimum and maximum values for each parameter occurred outside of the rehabilitation or standard care sessions.

CONCLUSION**:** Early rehabilitation of patients on ECMO has minimal effect on acute physiological parameters.

54. EXTREME HYPEROXIA IN PATIENTS WITH CARDIOGENIC SHOCK POST MYOCARDIAL INFARCTION TREATED BY VENOARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION

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INTRODUCTION: Patients with cardiogenic shock following acute myocardial infarction (AMI) have mortality rates in excess of 40-50%. Extracorporeal membrane oxygenation is an emerging technology that improves blood flow and oxygen delivery to patients through the use of a pump and oxygenator. The oxygenator is highly efficient and delivers hyperoxic blood to the patient. Recent studies have suggested potential harm from hyperoxia in critically ill patients, but little is known about the oxygen levels that occur in patients during venoarterial (VA) ECMO support.

OBJECTIVES: Describe the oxygen levels in patients on VA-ECMO post AMI, to compare this to a cohort of patients on intraaortic balloon pumps (IABP), and to investigate the association of hyperoxia and outcomes.

Methods: We performed a retrospective observational study in a quaternary ICU of all consecutive patients who presented with AMI and received VA ECMO between January 2012 and March 2018. We described their oxygen levels over the first 3 days, and then compared them to patients with cardiogenic shock who received intraaortic balloon pump who acted as controls. A census sample of 60 patients (30 in each group) was conducted and analysed.

RESULTS: Hyperoxia was present in the first 24hrs in the ECMO group. Comparison of the ECMO group with IABP group: at 0-6 hours (361 vs 113mmHg), 6-12 hours (306 vs 102mmHg), 0-24 hours (286 vs 103mmHg), and 24-48 hours (173 vs 90) ($p<0.01$ for all). ECMO group mortality was highest in the ≥300mmHg population in the 0-6 and 6-12 hour periods. In hospital mortality for ECMO was 63.3% versus IABP 38.3%.

CONCLUSION: VA-ECMO patients post AMI have extreme hyperoxaemia for the first three days and mortality is high. Further research is required to assess the impact on coronary perfusion and myocardial reperfusion injury, and whether interventions to reduce oxygen will result in improved outcomes.

55. FAMILIES' PERSPECTIVES OF PARTICIPATION IN PATIENT CARE IN ADULT ICU: A DESCRIPTIVE STUDY

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INTRODUCTION: When a relative is admitted to the intensive care unit (ICU), stress, anxiety and failure to cope may place families, and the patient, at risk for adverse psychological outcomes. Participation in patient care, a central tenet of Patient- and Family-Centre Care (PFCC), may reduce the families' psychological morbidity after ICU discharge. However, to date, little is known about how families perceive and participate in ICU, nor research to guide clinicians about supporting family participation in this context.

AIMS: To describe family perspectives of participation in patient care in adult ICUs.

METHODS: Using a mixed methods design, survey, observation and interview data were collected from a convenience sample of 30 family members in the ICU's at two metropolitan hospitals in Melbourne, Australia. Surveys collected data about families' preferences for participation in direct patient care and decision making in ICU. Naturalistic observations and semi-structured interviews explored families' actions and perceptions of participation. Analyses integrated descriptive statistics and thematic analysis.

RESULTS: Of 194 family participation activities observed, 74% related to activities, such as communication with staff or psychosocial-emotional support for the patient. Participation in physical care was a less frequent activity (24%). The major theme *Families as part of the healthcare team* reflected family perspectives of their own significant contribution to supporting their relative's recovery while they were in ICU. Several subthemes characterised their role in the healthcare team and included *Advocating for them, Knowing them better than anyone else* and *Maintaining social connections*.

CONCLUSION(S): Families are integral members of the ICU health team providing a necessary conduit for communication and emotional support. These results can be used to inform clinical practice, educational initiatives and further research to test the effectiveness of interventions that lead to high quality PFCC.

56. INSUFFICIENT PLASMA CONCENTRATIONS OF EMPIRIC ANTI-PSEUDOMONAL BETA-LACTAM ANTIBIOTICS IN CRITICALLY ILL PATIENTS WITH SUSPECTED SEPSIS

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Critically ill septic patients have disproportionately high mortality and early administration of empirical broad-spectrum antibiotics (typically beta-lactam agents with activity against *Pseudomonas aeruginosa)*, is an important component of management.

AIM: To determine if empirical anti-pseudomonal beta-lactam dosing achieves adequate drug exposure, as measured by the plasma drug concentration to MIC ratio, in high-risk critically ill patients with suspected severe bacterial infection.

METHODS: Adults aged > 18-years admitted to the intensive care unit with suspected sepsis treated empirically with either meropenem (MEM) or piperacillin/tazobactam (TZP). Plasma samples were drawn at point mid-way (concentration A) and at the end (concentration B) of a single dosing interval, after the patient had received at least 4 prior doses. The susceptibility breakpoint of *Pseudomonas spp.* (TZP-16mg/L, MEM–8mg/L), as defined by The European Committee on Antimicrobial Susceptibility (EUCAST) was used in analysis. Plasma levels were measured using high performance liquid chromatography.

RESULTS: Samples from 37 patients (20 on TZP and 17 on MEM) were analysed. The dose for TZP was 4/0.5g every 6 hours (65%) and MEM was 1g every 8 hours (94%). 17 (46%) were mechanically ventilated and 22 (59%) required vasopressor support. Sub-therapeutic levels (concentration B<MIC) were seen in 27 (73%) patients, 17 TZP (85%) and 10 MEM (59%). Patients with subtherapeutic levels had numerous risk factors – hypoalbuminemia (65%), heart or lung transplant (29%), multi-trauma (24%), altered body size, extra-corporeal membrane oxygenation, renal replacement therapy (12%, each) and neutropenia (6%).

CONCLUSION: In nearly three-quarters of the study cohort, anti-pseudomonal beta-lactam antibiotic concentrations were sub-therapeutic, when receiving 'standard' dosing in the ICU. These data remind the prescriber that critically ill septic patients often manifest altered physiology that has significant effects on drug handling. Prospective studies are needed to assess the utility of routine therapeutic drug monitoring to individualise doses and potentially improve outcomes.

57. PERIPHERALLY INSERTED CENTRAL CATHETERS (PICCS): FOR CORRECT POSITIONING, REAL-TIME MAGNETIC TIP TRACKING APPEARS SUPERIOR TO BLIND INSERTION

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Blind insertion of PICCs with post-insertion X-ray tip position confirmation is associated with a significant incidence of PICC tip mal-position. Tip mal-position requires manipulation or re-insertion of the PICC and additional X-ray confirmation. An accepted alternative insertion approach utilises real-time magnetic PICC tip tracking.

AIM: To retrospectively compare magnetic tip tracking with blind insertion for percentage of correctly positioned PICCs on the first insertion and complication rate.

METHODS: Data was collected on ICU patients who had a PICC inserted in 2018. A comparison was constructed for:

- A single operator using magnetic tip tracking for 50 sequential PICC insertions and then subsequently using the blind technique for a further 50 sequential PICC insertions.
- A single operator using magnetic tip tracking versus multiple operators using the blind technique over the same time period (March - June 2018).

RESULTS: Single operator: using magnetic tip tracking the PICC tip was correctly positioned in 90% (45/50) of insertions. Further manipulation of the PICC was required in 3/50 patients and re-insertion was required in 2/50 patients. Using the blind technique, the PICC tip was positioned correctly in 82% (41/50) of insertions. Further manipulation of the PICC was required in 1/50 patients and re-insertion was required in 8/50 patients. There were no complications.

Multiple operators: using the blind technique, the PICC was correctly positioned in 17% (5/30) of insertions. Further manipulation of the PICC was required in 10/30 patients and re-insertion was required in 15 patients. There was 1 complication (arterial insertion).

CONCLUSION: In this retrospective observational study, a single experienced operator appears significantly superior to multiple operators irrespective of insertion technique. For the single operator, the success rate is higher using magnetic tip tracking. Magnetic tip tracking has the potential to improve efficiencies: PICC insertion workload, time to PICC availability for use and minimisation of X-rays.

58. INCIDENCE AND IMPACT OF PATIENT AGGRESSION AND VIOLENCE IN AN INTENSIVE CARE UNIT

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Violence and aggression directed towards health staff is a complex issue with potentially significant consequences. To date, research in this area has primarily focussed on these events occurring in emergency departments or general wards; there is a deficit of research regarding workplace violence in the Intensive Care Unit (ICU) setting.

AIM: To identify the prevalence of aggression and/or violence against ICU nurses and to establish patient, environmental and worker related factors associated with behaviours of concern directed towards nursing staff.

METHODS: A 28 day prospective study of episodes of aggression and violence directed towards nursing staff within our intensive care unit was conducted. A twice daily audit of each cubicle in the ICU was conducted by the research team. Bedside nursing staff were presented with a checklist of possible behaviours of concern (BOC) and asked if an episode had occurred during their shift. The BOC checklist was adapted from the Modified Overt Aggression Scale[5].

RESULTS: 126 episodes of aggression and/or violence during this period with an incidence of 91 episodes per 1000 ICU patient days. Seventy-two percent of these episodes involved physical aggression, 58.7 involved verbal aggression, and 4.8% sexualised behaviour. In only 10% of these episodes was a Code Grey activated.

CONCLUSION: The incidence of episodes of physical and verbal aggression and violence directed towards intensive care nursing staff was significant. Yet these experiences of workplace violence are under reported in data captured regarding code grey's or riskman incidents. Further practices and evaluation to reduce the incidence of workplace violence in the ICU setting is warranted.

59. THE ATLANTIC STUDY: ANTI-XA LEVEL ASSESSMENT IN TRAUMA INTENSIVE CARE

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AIM**:** To quantify pharmacodynamic activity of daily subcutaneous (SC) enoxaparin as venous thromboembolism (VTE) prophylaxis in trauma patients admitted to the intensive care unit (ICU).

METHODS**:** This was a prospective observational pharmacodynamic study, conducted in the ICU of a major trauma referral centre. The study cohort included adult trauma patients in ICU with high risk of VTE, as defined by at least one of: age > 40 years, prior VTE, spinal cord injury (SCI), traumatic brain injury (TBI), major venous injury, pelvic fractures, spinal fractures requiring treatment, severe lower limb injuries, and major surgery > 2 hours in duration. Standard prophylactic enoxaparin dosing was 40mg SC daily, unless amended by the treating clinician. Plasma anti-Xa levels were measured 60 minutes before dosing (trough activity), and 3-5 hours after dosing (peak activity). Target peak and trough activity were defined as >0.2 IU/mL and >0.1IU/mL respectively. Thromboembolic and haemorrhagic complications were collected.

RESULTS**:** Twenty-five patients were enrolled. Median [IQR] age, weight, and creatinine were 59 years [36,70], 85kg [76.5,93.5] and 70umol/L [60.5,109] respectively. Median APACHE III and Abbreviated Injury Score were 54 [42.5,66.5] and 27 [17,34] respectively. Twenty-two patients received enoxaparin 40mg SC daily, two 60mg, and one 20mg. Median peak and trough anti-Xa levels were 0.21IU/mL [0.125,0.25] and 0.01IU/mL [0,0.05] respectively. Twelve (48%) patients had low peak levels $\leq$0.2IU/mL. Twenty-one (91%) patients had low trough levels $\leq$0.1IU/mL and in six (26%) cases, these were undetectable. Eight (32%) patients had documented VTE of whom seven had a low trough level $\leq$0.1IU/mL. There were no major haemorrhagic complications.

CONCLUSION**:** A significant proportion of high risk ICU trauma patients receiving daily SC enoxaparin VTE chemoprophylaxis have inadequate measured peak and trough plasma anti-Xa activity, which may infer greater VTE risk. Further systematic investigation concerning dose optimisation in this population appears warranted.

MENTAL HEALTH

60. EFFICACY, EFFICIENCY AND SAFETY OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION APPLIED MORE THAN ONCE A DAY IN DEPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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BACKGROUND**:** Repetitive transcranial magnetic stimulation (rTMS) is an established treatment for treatment-resistant major depression but a standard, 4-6 week course of treatment can be time-consuming. We present the first systematic review and meta-analysis of studies that investigated rTMS applied more than once a day and determined its effect size relative to once-daily or sham rTMS. Efficacy, efficiency and safety outcomes of so called accelerated rTMS are reviewed. The value of this study is in establishing evidence for accelerated rTMS regimens and inform clinical decision-making.

METHODS**:** Systematic searches were conducted on MEDLINE, CINHAL Plus, Embase, PsycINFO and the Cochrane Database of Systematic Reviews. Accelerated rTMS's efficacy, efficiency and safety are reviewed and quantitative analysis conducted to determine effect size relative to once-daily and sham rTMS.

RESULTS**:** 12 studies met inclusion criteria for qualitative review. Accelerated rTMS was equally efficacious compared with once-daily rTMS and superior to sham stimulation in treating depressive symptoms. Accelerated rTMS may induce faster therapeutic response over once-daily rTMS. 5 studies were included for meta-analysis. Minimal study bias or heterogeneity were found. A small effect size of Hedge's g -0.253 (95% CI: -0.61 to 0.1), p=0.17, favoured accelerated rTMS over standard or sham rTMS in treating depressive symptoms.

CONCLUSION**:** This is the first systematic review and meta-analysis addressing the efficacy, efficiency and safety of rTMS (excluding theta burst stimulation protocols) applied more than once-daily to treat depression. Our results suggest therapeutic equivalence and tolerability between accelerated and once-daily rTMS. More studies investigating accelerated rTMS regimens are needed to validate its clinical utility.

61. MINDFULNESS-BASED INTERVENTION TO REDUCE BURNOUT, PSYCHOLOGICAL DISTRESS, AND IMPROVE WELLBEING IN PSYCHIATRY TRAINEES: A PILOT STUDY

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BACKGROUND: Healthcare professionals including psychiatry trainees experience high amounts of occupational stress. Mindfulness-based intervention (MBI) is an emerging approach to address occupational stress. Practicality of mindfulness is appealing in a busy healthcare setting given its flexibility of usage. This pilot study aims to assess the impacts and feasibility of an MBI program as an occupational intervention in a metropolitan hospital.

METHODS: 16 psychiatry trainees participated in Therapeutic Relaxation and Enhanced Awareness Training (TREAT), an MBI program. TREAT consisted of 1-hour weekly sessions of theory and practice over 8 weeks. Levels of burnout, distress and mindfulness were measured pre and post-intervention. These were analysed using paired t-tests. Qualitative data collected through an open-ended feedback survey underwent thematic analysis with the aid of a thematic map.

RESULTS: Total mean of participants' personal burnout pre-intervention was 55.37 (SD 14.52) which is indicative of general fatigue. Post-intervention, this decreased to 44.36 (SD 16.00, hedges g = -0.64, p = 0.03). Their mean mindfulness score increased from 3.26 (SD 0.65) to 3.94 (SD 0.77, hedges g = 0.84, p = 0.01). Participants highlighted gains including better stress management, wellbeing and work performance. Positive feedback of the TREAT program emphasised the compassionate facilitator and the program being tailored to healthcare staff. Limiting factors to attending the MBI program included time restraints and clinical responsibilities.

CONCLUSION: Psychiatry trainees can benefit from an occupational MBI program in both their health and work performance. The study also identified a number of factors important for implementation. Despite the program being abbreviated compared to traditional MBI programs, participants still found it difficult to attend all sessions. Therefore, research is needed for innovative ways to allow staff to regularly access mindfulness practice. Moreover, MBI programs may be a useful intervention for other health disciplines in the hospital as well.

62. ACCEPTANCE AND COMMITMENT THERAPY (ACT) FOR PSYCHOSIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Schizophrenia spectrum and other psychotic disorders are severe mental health problems that affect approximately 21 to 23 million people globally. Acceptance and commitment therapy (ACT) is a third wave psychological treatment that has attracted considerable clinical and research interest. A systematic review and meta-analysis of ACT in psychosis has not been previously reported.

AIM: To conduct a systematic review and meta-analysis of randomised controlled trials comparing ACT and any comparator in patients with a psychosis.

METHODS: We systematically searched databases for published studies. These searches were supplemented by searches on trial registration sites for unpublished trials. Title and abstract, full-text screening and data extraction of identified articles were done by two reviewers independently. Discrepancies was resolved by another two authors. A standardised form was used to extract data for evidence synthesis. Study quality of included study was determined using the Cochrane risk of bias tool.

RESULTS: Eight studies met eligibility criteria. Data were extracted from five published and one unpublished trial. The summary effect size (Cohen's d) for symptom outcomes was -0.21 (95% CI: -0.60 to 0.18). A third were rated as having a low risk of bias. Harms were not appropriately reported in any of the trials.

CONCLUSION: Despite considerable clinical interest in the application of ACT in psychosis, the evidence that it is a safe and effective intervention is limited.

63. INTEGRATING HEPATITIS C CARE WITHIN COMMUNITY MENTAL HEALTH AND ADDICTION SERVICES

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BACKGROUND: Among many people with a lived experience of severe mental illness (SMI), there is a complex overlap with alcohol and other drug (AOD) use, including injecting drug use. As a result, people with SMI are at increased risk of blood borne infections, including hepatitis C virus (HCV). Despite this, engagement in HCV care among people with SMI has been historically low due to a range of personal, service and system level barriers.

METHODS: A nurse-led hepatitis C clinic was established across Alfred Mental & Addiction Health (AMAH) community programs. The fortnightly clinic was run by a hepatitis C Clinical Nurse Consultant alongside a Nurse Practitioner specialising in addiction and mental health, in collaboration with Alfred infectious diseases and gastroenterology departments. Treatment workup was undertaken by the nurses with treatment for those who were HCV positive prescribed by either the nurse practitioner or collaborating physicians.

RESULTS: Of 116 people referred to the clinic, 97 (84%) were HCV PRC positive and 8 were identified as cirrhotic. All participants reported a history of IDU, including 70% with current or recent IDU. Nearly all (81%) were unemployed and 55% lived in supported or unstable housing, including 12% who were currently homeless. The majority (79%) suffered with a severe psychotic illness or mood disorder.

Despite multiple failed appointments, 81% (94) completed initial screening, 62% (58) of whom have commenced treatment. Of the 74% (43) treated at the clinic, 51% (22) were treated by the Nurse Practitioner. Among 43 people who were due for sustained virological response (SVR) testing as of end February 2019, 31 people have had a test and all have been cured.

CONCLUSIONS: Through a nurse-led model of care, among this group of people with complex co-occurring psychiatric, psychosocial and addiction issues, most people who were HCV positive started treatment and of those who underwent SVR testing, all were cured. While specialist referral is important for people with cirrhosis, the majority did not require it, indicating replication of this model may be viable in other mental health settings.

64. CRISIS RESOLUTION TEAMS FOR PEOPLE EXPERIENCING MENTAL HEALTH CRISES: THE CORE MIXED-METHODS RESEARCH PROGRAMME INCLUDING TWO RCTS

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BACKGROUND**:** Crisis resolution teams (CRTs) seek to avert hospital admissions by providing intensive home treatment for people experiencing a mental health crisis. The CRT model has not been highly specified. CRT care is often experienced as ending abruptly and relapse rates following CRT discharge are high.

AIMS: The aims of CORE (Crisis resolution team Optimisation and RElapse prevention) workstream 1 were to specify a model of best practice for CRTs, develop a measure to assess adherence to this model and evaluate service improvement resources to help CRTs implement the model with high fidelity. The aim of CORE workstream 2 was to evaluate a peer-provided self-management programme aimed at reducing relapse following CRT support.

METHODS**:** Workstream 1 was based on a systematic review, national CRT manager survey and stakeholder qualitative interviews to develop a CRT fidelity scale through a concept mapping process with stakeholders (n = 68). This was piloted in CRTs nationwide (n = 75). A CRT service improvement programme (SIP) was then developed and evaluated in a cluster randomised trial: 15 CRTs received the SIP over 1 year; 10 teams acted as controls. The primary outcome was service user satisfaction. Workstream 2 was a peer-provided self-management programme that was developed through an iterative process of systematic literature reviewing, stakeholder consultation and preliminary testing. This intervention was evaluated in a randomised controlled trial: 221 participants recruited from CRTs received the intervention and 220 did not. The primary outcome was re-admission to acute care at 1 year of follow-up.

RESULTS**:** Workstream 1 – a 39-item CRT fidelity scale demonstrated acceptability, face validity and promising inter-rater reliability. CRT implementation was highly variable. The SIP trial did not produce a positive result for patient satisfaction. The programme achieved modest increases in model fidelity. Intervention teams achieved lower inpatient admission rates and less inpatient bed use. Qualitative evaluation suggested that the programme was generally well received. Workstream 2 – the trial yielded a statistically significant result for the primary outcome, in which rates of re-admission to acute care over 1 year of follow-up were lower in the intervention group than in the control group (OR=.66).

CONCLUSIONS**:** The CRT SIP showed promise as a means to increase CRT model fidelity and reduce inpatient service use. The peer-provided self-management intervention is an effective means to reduce relapse rates for people leaving CRT care.

65. MISDIAGNOSIS OF DELIRIUM IN REFERRALS TO A MAJOR TEACHING HOSPITAL CONSULTATION-LIAISON SERVICE

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Delirium, a frequent diagnosis made by Consultation-Liaison (C-L) Psychiatry, is often missed or misdiagnosed by referrers, correlated with longer mean length of hospital stay. In a study from Minnesota, 36 of 99 cases of psychiatry diagnosed delirium were correctly identified by non-psychiatric staff, whereas 63 were misclassified.

Several patient and clinician factors are suggested as increasing likelihood of missed or misdiagnosis, including previous psychiatric diagnoses, age, treatment setting and knowledge and attitudes and delirium subtype.

AIM: This project aims to determine a) the proportion of total cases seen by C-L Psychiatry diagnosed as delirium (by psychiatry) within a large teaching hospital, b) the proportion misdiagnosed by referrer, c) explore factors relating to missed or misdiagnosis and d) determine impact of missed or misdiagnosis on length of hospital stay.

METHODS: A retrospective cohort study was conducted. Using electronic records, referrer's diagnosis and referral questions were obtained. Data was collected pertaining to putative factors underlying missed or misdiagnosis.

Group membership (missed or misdiagnosis versus accurate delirium diagnosis prior to referral) was assigned to cases. T-test for scale and chi-square for class variables was performed to explore differences between the two groups for putative factors underlying missed or misdiagnosis. Factors found to be significantly different were then entered into an omnibus multivariate model. A second model predicting hospital stay (in days) versus group membership (missed/misdiagnosis versus accurate diagnosis), was fitted with analysis of variance.

RESULTS: 584 cases were referred to C-L Psychiatry from November 2018 to March 2019. There were 81 cases of CL-Psychiatry diagnosed delirium (14%). 43 cases were under consideration as delirium. 38 of 81 cases (47%) were missed or misdiagnosed by the referrer. A range of factors were identified that may underlie these cases, and recommendations were generated for referrers.

CONCLUSIONS: 47% of C-L Psychiatry diagnosed delirium is initially misdiagnosed by referrers to Alfred C-L Psychiatry, with service and patient care implications. Further education in delirium identification should be a priority.

NEUROSCIENCE

66. CHRONIC WHITE MATTER PATHOLOGY AFTER PAEDIATRIC TRAUMATC BRAIN INJURY IN THE MOUSE

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Traumatic brain injury (TBI) is particularly prevalent in the paediatric population (age 1-4 years). This is also an age when the brain is particularly vulnerable to insult, in part due to the ongoing development of new white matter tracts and resulting brain networks. The aim of this project was to characterise the extent of white matter disruption after injury using diffusion weighted imaging (DWI) a magnetic resonance imaging (MRI) technique. Controlled cortical impact (CCI) or sham-surgery was performed on male C57Bl/6 mice at postnatal day 21, and brains were collected at 6 months post-injury for *ex vivo* MRI. Major white matter tracts were identified for region-of-interest (ROI) quantification of DWI metrics including fractional anisotropy (FA), radial diffusivity (RD), axial diffusivity (AD) and mean diffusivity (MD) as well as track-weighted images (TWI) including the average pathlength map (APM), track-density imaging (TDI) and mean curvature. Region-of-interest analyses revealed a bilateral decrease in FA of the corpus callosum and external capsule. No changes in RD, AD or MD were observed. Tract-based spatial statistics (TBSS) confirmed these findings of a particular vulnerability of the corpus callosum and external capsule at this chronic post-injury time point. Future studies will evaluate changes in white matter over time following paediatric TBI with the aim of identifying new biomarkers that can be used as predictors of chronic atrophy and associated behavioural deficits.

67. DEVELOPMENT OF A SENSORY MODULATION PATHWAY WITHIN ACQUIRED BRAIN INJURY REHABILITATION

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Sensory modulation interventions are an emerging area of practice in acquired brain injury (ABI) rehabilitation. Clinician knowledge around methods for exploring individuals' sensory preferences, along with strategies for optimising arousal levels is paramount in maximising participation in rehabilitation and quality of life following ABI.

AIM: To describe the process of developing and implementing an evidence-based sensory modulation clinical pathway for patients with ABI.

METHODS: An interdisciplinary sensory modulation work group was developed, and a literature review completed to establish evidence-based sensory screening tools and intervention approaches to guide development of a sensory modulation clinical pathway for patients with ABI. Consultation with clinical experts and researchers in sensory modulation was undertaken to inform both pathway development and associated education strategy. A survey was developed in alignment with the theoretical domains framework that explored clinicians' perceived knowledge, skills, and beliefs in relation to sensory modulation practices. This survey was implemented pre- and post-implementation of the clinical pathway, with outcomes used to inform development of targeted education for staff.

RESULTS: Pre-implementation survey data indicated low confidence, perceived knowledge and skills by the interdisciplinary team in relation to sensory modulation practices. An education package comprising five education sessions was developed that targeted different subgroups of staff based on skills and knowledge required of their roles within the pathway. Three interdisciplinary sensory modulation champion roles were developed, with assigned responsibilities including support for education delivery and guiding practical application of the sensory modulation pathway. Following delivery of targeted education, the post-implementation survey data indicated increased staff confidence, knowledge and skill, with the clinical pathway reported to be routinely applied within practice.

CONCLUSION: Development of an evidence-based clinical pathway, in combination with a targeted education strategy that is developed through clinician engagement, can facilitate knowledge translation and embed sensory modulation practices in an ABI rehabilitation setting.

68. DOES A CALD BACKGROUND INFLUENCE ARRIVAL TO EMERGENCY DEPARTMENTS FOR STROKE CARE?

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Delay to Emergency Departments continues to limit patients benefiting from effective stroke care. The relationship between patients of culturally and linguistically diverse (CALD) backgrounds and access to acute stroke care is inconclusive, and importantly lacking an Australian perspective.

AIM: To analyse the association between delay in stroke presentation (pre-hospital time-delay, and arrival by ambulance) and CALD background (country of birth, language spoken at home, and use of interpreter service).

METHOD: A three-year retrospective data-analysis of patients diagnosed with stroke presenting to three-Australian Emergency Departments was undertaken for patients who presented <12-hours from stroke onset.

RESULTS: During the study period, of 2,557-patients 52% (n=1,337) were male, and the mean age was 70-years (23-years IQR). The pre-hospital mean time delay was 2:57-minutes, and arrival by ambulance occurred for 80% (n=2,043). The sample was stratified by CALD background demographics, to form four groups- (i) born in Australia and English speaking in the home (52%, n=1,353); (ii) born-outside of Australia and English speaking in the home (34%, n=870); (iii) born-outside of Australia and non-English speaking in the home (2%, n=58); and (iv) born-outside of Australia and interpreter required (10%, n=276). Ordinal logistic regression modelling for pre-hospital time delay and non-arrival by ambulance rates indicated that there were no significant relationships between the stratified groups (p=0.751).

CONCLUSION: Interestingly, these findings suggest that people with and without CALD background demographic access acute stroke care comparatively. These results are encouraging as accessing without delay to Emergency Departments is critical for stroke management to be initiated.

69. A NOVEL QUANTITATIVE BEDSIDE TEST OF BALANCE FUNCTION: THE VIDEO VISUALLY ENHANCED VESTIBULO-OCULAR REFLEX (VVOR)

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BACKGROUND: Initially utilized to investigate the visual-vestibular interaction, the visually enhanced vestibulo-ocular reflex (VVOR) has only recently found clinical utility in the form of a qualitative bedside test. We describe the next increment in the evolution of the clinical application of the visual-vestibular interaction, by describing the *quantitative* bedside VVOR, which employs rapid video-oculographic (rVOG) diagnosis of vestibulo-cerebellar disease. Portable rVOG is a new field of diagnostic eye movement quantification, whose utility has been facilitated by the recent development of a lightweight, minimum-slip high-speed video eye tracking system. Underlying the efficacy of the VVOR as a robust and sensitive clinical sign is the knowledge that its perturbation represents a compromise in all three key compensatory oculomotor reflexes; smooth pursuit (SP), optokinetic nystagmus (OKN) and vestibulo-ocular reflex (VOR). The clinical utility of the VVOR sign is it's unique ability to simultaneously test for the co-existence of vestibular and cerebellar pathology. Conditions where this compound deficit may been found include spinocerebellar ataxia 3 and 6, Friedreich's ataxia, Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS), multiple system atrophy of the cerebellar subtype (MSAc) and idiopathic cerebellar ataxia with bilateral vestibulopathy (iCABV).

AIM: To identify a robust and easily performed quantitative bedside clinical test of vestibular and cerebellar function.

METHODS: A prospective observational study.

Results: We present data on 156 patients with combined vestibular and cerebellar pathology; 81 with Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS), 23 with Friedreich's ataxia, 16 with SCA6, 7 with SCA3, 15 with MSAc, 9 with iCABV and 5 patients with rare presentations.

CONCLUSION: The video VVOR readily allows identification and quantification of combined vestibular and cerebellar pathology at the time of consultation. This process previously involved referral for specialized neuro-otology testing and so, improves clinical pathway efficiency and directs the diagnostic algorithm.

70. GENE EXPRESSION SUGGEST ALTERED GLUTAMATERGIC, DOPAMINERGIC AND ESTROGEN CLASSICAL PATHWAYS IN WORKING MEMORY DEFICIT IN SCHIZOPHRENIA

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As cognitive impairments are poorly treated by antipsychotics, it is imperative to understand the molecular mechanisms influencing these deficits. While candidate gene studies have extensively explored cognitive performance in schizophrenia, there is a lack of studies investigating gene expression, which gives detailed insight to potential pathways involved. Research has shown that cognitive deficits should be investigated by separate domains rather than global cognition. As one of the most replicated deficits in schizophrenia is in working memory, the study aimed to determine the changes in gene expression associated with working memory deficit in schizophrenia.

Thirty-six patients with a DSM-IV diagnosis of schizophrenia completed the Digit Span Backwards and Letter Number Span tasks as a measure of WM. Patients were clustered into WM deficit (N=17) and intact WM (N=19) groups. mRNA was extracted from peripheral blood samples and levels were measured using the AffymetrixTM Human Exon 1.0 ST Array. Ingenuity Pathway Analysis was used to identify the pathways that most impacted by changes in gene expression and that differentiated the two groups.

There was a significant difference between the two groups in both WM tasks ($p<0.001$), but no significant difference in age, years of education, premorbid IQ, symptom severity (PANSS) or duration of illness. There was a significant variation in mRNA levels between the two groups in 164 genes. IPA identified the following as top pathways that differentiated the WM deficit and intact WM groups: NRG1 interactome (p=1.70x10-2), Estrogen 2 group (p=2.94x10-2), COMT (p=4.35x10-2) and Glutamate (p=7.35x10-2) pathways.

Overall, our data suggests that working memory deficits can be attributed to an interplay between glutamatergic, dopaminergic and estrogen classical pathways. This is consistent with previous literature indicating dopamine-glutamate interactions influencing cognition in schizophrenia and is also consistent with previous research providing evidence for protective effects of estradiol on dopamine and glutamate systems.

71. TEMPORAL DISTRIBUTION PATTERN OF TISSUE-TYPE PLASMINOGEN ACTIVATOR (TPA) ACTIVTY IN THE CENTRAL NERVOUS SYSTEM (CNS) DELIVERED VIA THE INTRANASAL ROUTE: IMPLICATIONS FOR TARGETED DELIVERY OF TPA TO THE CNS.

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BACKGROUND: Tissue-type plasminogen activator (tPA) is now well known to play significant roles in the brain, particularly in the pathogenesis of Alzheimer's Disease (AD) via its ability to clear the amyloid beta peptide, modulate levels of the mature form of brain derived neurotrophic factor (BDNF) and to stimulate neuroprotective microglial cells. Mice prone to develop AD display a more severe phenotype when tPA levels are reduced by 50%. These findings raise the possibility that elevated levels of tPA in the brain may attenuate AD onset or severity. Intranasal (IN) administration of tPA may offer a therapeutic approach, however the time course and distribution pattern of tPA in the brain delivered via the IN route is not known.

AIM: To determine the temporal expression pattern in the brain of IN-delivered tPA.

METHODS: IN-tPA was administered to anaesthetised wildtype or $tPA^{-/-}$ mice (100□g in 30□l). Brains were harvested at various time points and 10□m fresh frozen sections were subjected to in situ zymography.

RESULTS: IN-delivered tPA was detected within 30 minutes in brain sections of $tPA^{-/-}$ mice. Activity was particularly prominent in the olfactory bulb, but also in distinct areas throughout the brain, including hypothalamus and cerebellum. tPA activity remained high after 3h but was decreased by ~50% by 6h and was almost absent by 24h. To determine the safety profile of repetitive delivery of IN-tPA, wildtype mice were delivered tPA 3 times per week for 8 weeks with no adverse neurological effects and no apparent accumulation of tPA.

CONCLUSION: These results indicate that tPA can enter the brain and remain active for more than 6h, which is much longer than the 5 minute plasma half-life. Our future studies will address the therapeutic potential of IN-delivered tPA and other plasminogen activators with extended half-lives, in the APP/PS1 mouse model of AD.

72. ONABOTULINUMTOXINA TREATMENT FOR MS-TREMOR MODIFIES FMRI TREMOR RESPONSE IN CENTRAL SENSORY-MOTOR INTEGRATION AREAS

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Treatment of tremor in multiple sclerosis (MS) is an unmet need. OnabotulinumtoxinA (BoNT-A) has shown promising results; however, little is known regarding its central effects.

AIM: To identify effects of BoNT-A on neural plasticity in MS and upper-limb tremor using functional MRI.

METHODS: Forty-three MS participants were randomized to receive intramuscular injections of placebo (n=22) or BoNT-A (n=21). Tremor was quantified using the Bain score (0-10) for severity, handwriting and Archimedes drawing at baseline, 6 weeks and 12 weeks. Functional MRI activation within two previously identified clusters, ipsilateral inferior parietal cortex (IPL) and supplementary motor cortex (SMC) of compensatory activity, was measured at baseline and 6 weeks.

RESULTS: Treatment with BoNT-A resulted in improved tremor severity -0.79 (p=0.007) and handwriting -0.53 (p=0.014) scores over 12 weeks. The BoNT-A group showed a reduction in activation within the IPL (p=0.034), but not in the SMC. The change in IPL activation correlated with the reduction in tremor severity from baseline to 12 weeks (β =0.608; p=0.015) in the BoNT-A group. No fMRI changes were seen in the placebo treated group.

CONCLUSION: Reduction in MS-tremor severity after intramuscular injection with BoNT-A is associated with changes in brain activity in sensorimotor integration regions.

73. OCULAR MOTOR ABNORMALITIES AND SHORTENED TELOMERES IN COLLISION SPORT ATHLETES

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Mild brain injuries as a consequence of collision sport participation have been linked to a range of neurological consequences, with evidence suggesting that collision sport athletes are more vulnerable to developing neurological syndromes later in life. Consequently, there is a need to understand how potential neurological changes manifest and whether abnormalities are specific to concussion history or whether sub-concussive impacts also contribute. With female participation in collision sports rising, there is further need to determine whether changes manifest differently between sexes.

AIM: To investigate the neurological implications of collision sport participation using novel biomarkers.

METHODS: Male (n = 72) and female (n = 28) amateur Australian rules footballers, with and without a history of concussion, were compared to male (n=29) and female (n =21) non-collision sport athletes. The effects of collision sport participation was investigated in two ways: (1) ocular motor assessment, a demonstrated sensitive marker of neurological function in a range of collision sports; (2) telomere length, reduced telomere length is a marker of mild brain injuries in rodents.

RESULTS: Footballers exhibited reduced spatial accuracy to a remembered location on an ocular motor memory guided task ($F_{(1, 93)}$ = 7.259, $p < 0.01$), and reduced telomere length ($F_{1, 128}$ = 4.496, $p < 0.05$) in comparison to controls; both findings were independent of concussion history and sex. Notably, shortened telomere length was associated with shortened memory guided latencies among Australian rules footballers (r^2 = 0.432, $p < 0.001$).

CONCLUSIONS: Although preliminary, these finding demonstrate that, even at the amateur level, Australian rules footballers have demonstrable neurological changes. Importantly, these changes are measurable through ocular motor assessment and analysis of telomere length, suggesting these methodologies might be sensitive biomarkers to monitor long-term neurological health of collision sport athletes.

74. LOSS OF GLT-1 AND GLUTAMINE SYNTHETASE ARE ASSOCIATED WITH EARLY STAGE OF ALZHEIMER'S DISEASE IN MICE

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Alzheimer's disease (AD) can increase the risk of epileptogenesis up to 10-fold in patients, compared to healthy age-matched controls. However, the underlying mechanisms leading to this increased risk have not been discovered.

AIMS & HYPOTHESIS: Here we proposed that changes in the brain occurring early in the AD disease process contribute to a susceptibility to epileptogenesis. Early disruption in the brain's glutamate homeostasis has been reported in both epilepsy and AD and therefore this study aimed to explore the potential role of glutamate in the pathogenesis of acquired epilepsy in AD. It also aimed to identify potential early biomarkers for acquired epilepsy in AD.

METHODS: Brain tissue was excised from 6 month-old Tg2576 AD mice along with their wild-type (WT) littermate. Western blotting and mass spectrometry were performed on the extracted brain samples.

RESULTS: Tg2576 mice had significantly lower amounts of GLT-1 and Glutamine synthetase in the cortex, compared to the WT ($p<0.01$). Results from Mass spectrometry have shown that metabolites such as glutamate and glutamine have the potential to be the early biomarkers for acquired epilepsy in AD.

CONCLUSION: The results show disruptions to the glutamate-glutamine cycle in Tg2576 mice, suggestive of impairment in astrocytic function. These findings support the hypothesis that the brain's glutamate homeostasis is affected early in AD and that this might lead to a higher susceptibility of the brain to epileptogenesis via the extracellular glutamate spill-over in the synaptic cleft. The findings from the metabolomics analysis also suggest that there are changes in different brain's metabolites early in AD.

75. GETTING SLAMMED: THE EFFECTS OF ACUTE AND CHRONIC ALCOHOL CONSUMPTION ON TBI OUTCOMES IN LATE ADOLESCENT FEMALE RATS

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Alcohol is the most commonly abused drug by adolescents. Differences in maturation rates of various brain structures make risky behaviours more alluring for adolescents. Alcohol use, particularly binge drinking, is prevalent amongst adolescents and young adults. Research suggests that females are more susceptible to the detrimental effects of alcohol. While alcohol consumption itself may incur a risk of neurological damage, it's also a significant risk factor for traumatic brain injury (TBI). TBI among adolescents is described as a modern healthcare epidemic within North America. The drastic changes occurring within their neurological networks put them at a greater risk for developing long-term post-traumatic deficits. Recent studies have indicated contradictory findings regarding the effects of alcohol consumption on TBI outcomes in adults, with some studies indicating detrimental effects while others suggest neuroprotective abilities.

AIM: To identify the effects of alcohol consumption on TBI outcomes during the sensitive stage of adolescent development.

METHODS: Late adolescent female Sprague Dawley rats were randomly assigned to one of six experimental conditions: Pre-injury alcohol+mTBI (8F); Pre-injury alcohol+Sham (8F); Pre- and Post-injury alcohol+mTBI (8F); Pre- and Post-injury alcohol+Sham (8F); No alcohol+mTBI (8F); No alcohol+Sham (8F). The alcohol consumption groups received a 10% w/v ethanol solution in an amount based on the animals' weight. Following the injury, the rats were subjected to a behavioural test battery, which included beamwalking, elevated plus maze, openfield, novel context mismatch, and forced swim, to assess post-concussive symptomology.

RESULTS: Overall, alcohol consumption at the time of TBI significantly ($p<.05$) improved motor coordination and balance and decreased depressive-like behaviours in comparison to the sham animals that consumed alcohol, while alcohol consumption in general significantly ($p<.05$) decreased anxiety-like behaviours.

CONCLUSION: The inhibitory effects of alcohol may counteract the neurological excitotoxicity caused by TBI. Thus, alcohol may exhibit neuroprotective abilities in the context of adolescent TBI.

76. IDENTIFYING RISK AND RESILIENCE FACTORS TO COGNITIVE DECLINE AND DEMENTIA - ASPREE

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BACKGROUND**:** Large prospective studies of deeply-phenotyped individuals, with regular assessments of cognitive function and rigorous dementia diagnosis, will enable better characterisation of factors associated with both risk of and resilience to cognitive decline and dementia.

METHODS**:** ASPirin in Reducing Events in the Elderly (ASPREE) is a randomised placebo-controlled trial of daily low-dose (100 mg) aspirin. Eligibility criteria included age ≥70 years (≥65 years for US minorities groups) without cardiovascular disease, physical disability or dementia, and with a Modified Mini-Mental State examination (3MS) score >77. Participants underwent regular systematic assessment of general cognition, language/verbal fluency, delayed recall, attention and processing speed. Dementia diagnosis was adjudicated by an international expert panel according to DSM-IV criteria.

RESULTS**:** 16,703 Australian and 2,411 US participants were recruited. Mean cognitive scores at baseline varied according to race/ethnicity, country, age, education and gender. Over a mean 4.7 years of treatment, aspirin compared to placebo did not prolong disability-free survival (a composite of death, dementia or persistent physical disability); component analysis showed no independent effect of aspirin on dementia. Although the treatment phase of the trial has ended, all individuals will continue to be followed with regular cognitive testing and adjudicated dementia diagnosis as part of the ASPREE-XT (extension) cohort study.

CONCLUSION**:** Given the depth and breadth of high quality data which has been gathered, and will continue to be obtained on such a large population of older individuals, this study will provide a valuable resource to study both protective/resilience and risk factors for cognitive decline and dementia.

77. COMMENCING CONTINUOUS EEG AT THE ALFRED

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Continuous EEG (cEEG) monitoring is essential for the optimal diagnosis and management of non-convulsive seizures. We audited the use of cEEG at the Alfred Hospital as part of a new epilepsy program and cEEG service. There are no reported case series of cEEG in Australia.

METHOD: Data was collected retrospectively from consecutive patients who underwent cEEG monitoring as part of their acute inpatient care between Jan 2018 to Dec 2018 at the Alfred Hospital. All inpatient EEG studies over 1hr were included. Elective cases from the epilepsy monitoring unit were excluded. Demographic and clinical information regarding their admission was collected. Descriptive statistics, and comparative analysis was performed.

RESULTS: There were 40 patients identified that underwent cEEG. 24 were male and 16 female, with an average age of 53yrs. 48% were performed in the ICU, and 52% on the acute medical ward. The average duration of recording per patient was 98.3hrs or 4.1days. Seizures were seen in 43%, the majority being non-convulsive. Interictal discharges were seen in 55%. 7(18%) patients were dead at the time of the audit.

CONCLUSION: Non-convulsive seizures and non-convulsive status epilepticus is common and widely underrecognized without cEEG. We present 40 cases as part of our newly expanding cEEG program at the Alfred over a one year period, 43% with seizures which were predominantly non-convulsive. A prospective database will be designed for further quality improvement and future research.

78. TRKB AGONISM PRESERVES KEY WHITE MATTER STRUCTURES FOLLOWING PAEDIATRIC TRAUMATIC BRAIN INJURY IN MICE

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Tragically, young children (0-4 years) are more likely to both sustain a traumatic brain injury (TBI) and experience life-long resultant health and behavioural complications compared with all other age groups. The human brain is especially vulnerable to injury during key developmental processes early in life such as myelination and oligodendrocyte maturation. One reported signalling mediator of these two processes is the tropomyosin receptor kinase B (TrkB), and we hypothesised that stimulation of this receptor following paediatric TBI would support functional recovery of key white matter tracts and confer improved behavioural outcomes.

AIM: To investigate the effect of TrkB agonist on white matter tract pathology and associated behavioural deficits following paediatric TBI.

METHODS: 24 male C57Bl/6J mice underwent sham-controlled experimental TBI surgery at postnatal day 21, followed by vehicle-controlled treatment with synthetic TrkB agonist LM22A4 (5 mg/kg/d, 14 d, intranasal). A battery of neurobehavioural tests were performed 4 weeks post-injury, then brains collected 5 weeks post-injury for sectioning. Myelinated tracts were visualised by spectral confocal reflectance microscopy (SCoRe) and immunofluorescence staining for myelin basic protein (MBP), and volumetric analyses of key regions-of-interest were performed on cresyl violet-stained sections.

RESULTS: TrkB agonism preserved ipsilateral white matter volume following TBI, and ameliorated pathological anxiety-like behaviours observed in TBI/veh mice. LM22A4-treatment additionally conferred broad neuroprotective effects, implied by preservation of perilesional cortical volume in TBI/LM22A4 mice. Hyperactivity was observed in TBI mice that was not altered by treatment with LM22A4. Analysis of white matter integrity by MBP and SCoRe is underway.

CONCLUSION: Treatment with TrkB agonist LM22A4 significantly reduces loss of white matter and perilesional tissue after paediatric TBI, and ameliorates some injury-induced behavioural deficits. Ongoing investigations will characterise the effect of TrkB-agonism on white matter tract integrity, clarify the role of TrkB in neuroprotection and/or regeneration, and elucidate its mechanisms of action.

79. TRAINING IN HEADACHE IN AUSTRALIA, NEW ZEALAND AND ASIA

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AIM**:** We aimed to assess 1) The quantity of teaching in headache subjects during undergraduate and postgraduate years; 2) The effects of teaching provided at the Headache Master School on knowledge and opinion.

METHOD**:** This is a cross-sectional survey study where questionnaires were sent to 137 delegates from Australia, New Zealand and Asia, prior to the two-day Headache Master School in Sydney in August 2018. The main outcome measured are recalled number of hours of teaching in undergraduate year and postgraduate years in: 1) Migraine; 2) Trigeminal autonomic cephalalgias (TACs); 3) Asthma; 4) Myasthenia gravis (MG) and performance in knowledge assessment before and after Headache Master School.

RESULTS**:** The questionnaire response rate was 73% (100 of 137), of which 29 delegates were within 10 years of completing their undergraduate degree. In undergraduate training, there was much greater quantity of teaching in asthma than migraine ($Z=5.007$, $p<0.000$) despite both being high-prevalent (asthma 11%, migraine 15-20%) conditions. Similarly, for diseases of medium-to-low prevalence, there was less training in TACs (1/1000), compared to MG (1.2/10,000) ($Z=6.196$, $p<0.000$). These major differences in training were also seen in postgraduate years even though overall headache teaching was greater in postgraduate than undergraduate training ($p<0.000$). In the knowledge assessment, candidates improved their test score by a mean of 7.67 ($p<0.01$) after training. Opinion questions also changed in key areas of migraine. Confidence improved from “mild confidence” prior to “moderate confidence” as a headache specialist after the HMS. The preferred mode of learning was in the workplace with mentors (54.25%; 51/94 responses).

CONCLUSIONS**:** Despite the high prevalence and morbidity of headache disorders, they receive less attention in training than conditions with similar prevalence. We propose that headache training opportunities should be improved in our region, particularly in the undergraduate course and through preceptorships or fellowships in postgraduate years. The Headache Master School has shown to be a highly effective method to enhance headache knowledge and confidence, at least in the short-term.

80. THE ROLE OF P2X7 RECEPTOR ANTAGONISM ON GLIOMA PROGRESSION

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Gliomas account for 80% of all brain cancers. These tumours predominantly manifest as high-grade glioblastomas that are vastly infiltrative and extremely difficult to treat. Patients only survive for a median of 14-15 months post diagnosis. Despite advancements, current treatment is limited and the prognosis remains bleak. Previous research has demonstrated the upregulation of a purinergic receptor, P2X7R, in human gliomas. P2X7R is known to be expressed on both glioma cells and microglia within the glioma microenvironment. It is hypothesised that P2X7R contributes to tumour growth by activating immunosuppressive microglia and thus inhibiting P2X7R may prevent tumour proliferation. We sought to elucidate this by inhibiting P2X7R on both the U251 human glioblastoma cell line and human glioma samples obtained during surgical resection at the Royal Melbourne Hospital, Victoria, Australia. We treated U251 and human glioma cultures for 72 hours with P2X7R antagonists: brilliant blue G (BBG), oxidised ATP (oxATP) and AZ10606120. Cell counting via fluorescence confocal microscopy was conducted thereafter. We observed no significant reductions in tumour proliferation following P2X7R antagonism with BBG (20μM) and oxATP (250μM) in both U251 cells and human glioma samples. Interestingly, tumour cell numbers were significantly lower than the controls in both U251 cells ($p<0.0001$) and human glioma samples ($p=0.001$) treated with varying concentrations of AZ10606120. Our results demonstrate a potential trophic role of P2X7R where its inhibition by AZ10606120 hinders glioma growth directly or through the inactivation of immunosuppressive microglia. This sheds new light on P2X7R as a therapeutic target for human gliomas.

81. PRELIMINARY EVIDENCE FOR GENETIC PREDICTORS OF FINGOLIMOD RESPONSE IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS OF EUROPEAN DECENT

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Multiple Sclerosis (MS) is the leading cause of neurological disability worldwide, affecting over 25,000 Australians. Without a cure, patients rely on disease-modifying treatments (DMTs) to manage symptoms. Most patients experience disease breakthrough on treatment and the length of time before this occurs differs for each patient. Fingolimod is the most prescribed DMT in Australia for relapse-remitting multiple sclerosis (RRMS), yet no genetic predictors of response have been identified.

AIM: To identify genetic predictors of fingolimod response in RRMS patients of European descent.

METHODS: This study used a genome-wide approach to identify Single Nucleotide Polymorphisms (SNPs) associated with treatment response in 204 fingolimod-treated RRMS patients of European decent. Association testing was completed using a survival analysis measuring 'time to failure' by genotype at each SNP; where failure was defined as a relapse or three-month confirmed disability progression.

RESULTS: Of 204 individuals analysed, we identified a failure rate of 53% (n=108) over a four-year period. The two most significant SNPs with hazard ratios of 3.23 (95% CI=2.05-5.07, $p=3.81\times10^{-7}$) and 5.78 (95% CI=2.93-11.40, $p=4.17\times10^{-7}$), respectively, approached genome-wide significance. Both SNPs increased the risk of disease breakthrough on fingolimod. Combined analysis demonstrated that carriage of the minor allele at the two top identified loci significantly increased risk of failure on fingolimod with a hazard ratio of 3.17 (95% CI=2.22-4.53, $p=2.24\times10^{-10}$).

CONCLUSION: The effect size and significance of the observed associations strongly suggest association and warrant additional investigation. The results of the combined analysis of the two most significantly associated SNPs strongly suggest that response to fingolimod could be influenced by multiple unrelated SNPs, and therefore a genetic testing panel with multiple SNPs would be a more accurate predictor of fingolimod response.

82. ASSOCIATION OF *APOE* HAPLOTYPE WITH COGNITIVE FUNCTION IN A HEALTHY ELDERLY COHORT

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ASPirin in Reducing Events in the Elderly (ASPREE) was a randomized clinical trial of daily low-dose aspirin for primary prevention in 16,703 Australians aged over 70 years and 2,411 Americans aged over 65 years. ASPREE examined the impact of aspirin on a range of clinical outcomes over a five-year period. At baseline, median age of ASPREE participants was 74 years with no CVD history, no Alzheimer's disease (AD) and Modified Mini-Mental State Examination (3MS) score ≥ 78. DNA sequencing on 11,541 samples from ASPREE Healthy Ageing Biobank was performed for >750 genes used in clinical testing. We present genotyping results for *Apolipoprotein E* (*APOE)* gene, a strong genetic risk factor for AD. We stratified on *APOE* genotype; ε3/ε3 = 7127 (61.7%), ε3/ε4 = 2448 (21.2%), ε2/ε3 = 1479 (12.8%), ε2/ε2 = 64 (0.6%), ε1/ε3:ε2/ε4 = 254 (2.2%) and ε4/ε4 = 169 (1.5%). We identified 64 ε2 homozygotes and 169 ε4 homozygotes, both rare in the population. A slightly higher learning and memory measures (HVLT-R) in ε2/ε2 and ε2/ε3 (HVLT-R mean = 8.0, SD = 2.8) compared to ε3/ε3 (HVLT-R mean 7.0, SD = 2.8) which remained after controlling for smoking, gender, age, BMI, education, LDL and alcohol use (P = 0.02, adjusted difference in means = 0.17, 95% confidence interval (CI) = 0.02 to 0.32). We investigated 46 *APOE* ε4/ε4 individuals aged > 75 years and observed a similar difference in episodic memory (HVLT-R mean = 6.0, SD = 3.0) compared to 2871 ε3/ε3 at age > 75 years (HVLT-R mean = 7.0, SD = 2.9) which was explained by controlling for above-mentioned covariates (P = 0.11, adjusted difference in means = -0.67, 95% CI = -1.50 to +0.15). This uniquely ascertained and well-phenotype population provides a significant opportunity to examine the role of *APOE* in ageing and health.

83. AGED RATS HAVE AN ALTERED IMMUNE RESPONSE AND WORSE OUTCOMES AFTER TRAUMATIC BRAIN INJURY

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Initial studies suggest that increased age is associated with worse outcomes after traumatic brain injury (TBI), though the pathophysiological mechanisms responsible for this remain unclear. Immunosenescence (i.e., dysregulation of the immune system due to aging) may play a significant role in influencing TBI outcomes.

AIM: To examine neurological outcomes and immune response in young-adult (i.e., 10 weeks old) compared to middle-aged (i.e., 1 year old) rats following a TBI (i.e., fluid percussion) or sham-injury.

METHODS: Rats were euthanized at either 24 h or one-week post-injury to analyze immune cell populations in the brain and periphery via flow cytometry, as well as telomere length (i.e., a biomarker of neurological health). Behavioral testing, as well as volumetric and diffusion-weighted MRI, were also performed in the one-week recovery rats to assess for functional deficits and brain damage.

RESULTS: Middle-aged rats had worse sensorimotor deficits and shorter telomeres after TBI compared to young rats. Both aging and TBI resulted in worse cognitive function and reduced cortical volume. These changes occurred in the presence of fewer total leukocytes, fewer infiltrating myeloid cells, and fewer microglia in the brains of middle-aged TBI rats compared to young rats.

CONCLUSION: These findings indicate that middle-aged rats have worse functional deficits, decreased cortical volume, and shorter telomeres after TBI than young rats, and this may be related to an altered neuroimmune response. Although further studies are required, these findings have important implications for understanding the pathophysiology and optimal treatment strategies in TBI patients across the life span.

84. A RANDOMISED TRIAL OF EARLY ACTIVE REPETITIVE MOTOR TRAINING TO PREVENT DEVELOPMENT OF UPPER LIMB CONTRACTURE AFTER STROKE.

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There is limited research to date on using massed practice to prevent or reverse upper limb contractures following stroke.

AIM: To determine if 1-hour/day of active, repetitive motor training using the SMART Arm™ robotic device in addition to usual upper limb therapy prevents / reduces upper limb (UL) contracture.

METHODS: Randomised controlled trial, with assessor blinding and concealed allocation. We included inpatients <6 mo post stroke were randomly allocated to receive either a maximum of 1 hour/day of active repetitive motor training using the SMART Arm robotic device plus usual UL therapy, five days a week (experimental; Exp); or usual UL therapy only (control; Con). Outcome measures were taken at baseline, post intervention (5 weeks) and follow-up (7 weeks). Primary outcomes were passive range of wrist extension, elbow extension and shoulder flexion. Clinical trial registration information: ACTRN:12614001162606.

RESULTS: Fifty participants completed the trial. The addition of 1-hour/day of robotics to usual UL therapy had no statistically or clinically significant effect. At 5 weeks, between-group differences (Exp – Con) for wrist extension was 0.8° (95% CI -5.8 to 7.6); elbow extension was 0.5° (95°%CI 0.3 to 0.8); and passive shoulder flexion was 4.6° (95%CI -7.7 to 16.9). Loss of passive range (i.e. degree of contracture developed) across both groups during the trial was not clinically important in any measured joints.

CONCLUSION: The addition of one hour daily of repetitive motor training using the SMART Arm robotics device did not prevent or reduce upper limb contracture over a 5-week period in patients undergoing rehabilitation following stroke.

85. EVALUATING TEMPORAL LOBE EPILEPSY SEIZURE PROGRESSION, BEHAVIOURAL AND STRUCTURAL COMORBIDITIES AND POTENTIAL DISEASE MODIFYING THERAPIES USING A MODIFIED POST-STATUS EPILEPTICUS MODEL.

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RATIONALE: Current pharmacotherapy for mesial temporal lobe epilepsy (MTLE) does not impact the development or progression of the disease. In this study we set out to validate a modified kainic acid (KA)-induced post-status epilepticus (SE) model as a tool to evaluate seizure progression and to test if novel drug treatments would be disease modifying: reverse/reduce the progression of epilepsy, including the frequency and severity of the seizures, behavioural comorbidities and neuroimaging changes in chronically-epileptic rats.

METHODS: Wistar rats(n=24) underwent KA induced-SE for 4h. Shams(n=15) did not receive KA. 9 weeks post-SE, rats were implanted with EEG recording electrodes and video-EEG was recorded for one week at 10-, 12-, 14-, 18-, 22- and 26-weeks post-SE. Rats received a 4-week levetiracetam(200mg/kg/day) treatment at 11-week(n=9) and 24-weeks(n=7) post-SE to evaluate disease modification and resistance to drug treatment, respectively. Behavioural tests were performed to evaluate anxiety, depression, sociability, neuromotor and cognition. Post-mortem MRI was performed 28wk post-SE.

RESULTS: Rats showed a progressive increase in the number, severity and duration of seizures. Average seizure per day was different between 10-week 18- and 22-week post-SE ($p<0.05$ for both comparisons) after SE. Post-SE rats show depressive like behaviour, impaired cognition and sociability deficits. Levetiracetam treatment did not reduce the number of seizures during treatment at 12-, 14- or 26-weeks post-SE. Volumetric MRI analysis revealed that Post-SE animal had a reduced cortical, hippocampal and amygdala volume($p<0.01$), corpus callosum($p<0.05$) and increased ventricular volume ($p<0.05$).

DISCUSSION: This modified post-SE model shows evidence that epilepsy worsens over time, indicated by the increased number of seizures and pharmacorresistance to drug treatment, similar to the human condition. Moreover, we shown that behavioural and structural comorbidities commonly presented in MTLE patients. In conclusion, our proposed paradigm can aid the understanding of the nature and progression of seizures and accelerate the discovery of novel disease modifying therapies for drug-resistant MTLE.

86. EXPRESSION LEVELS OF NEUROINFLAMMATORY CYTOKINES IN BLOOD RELATE TO PATHOLOGICAL OUTCOMES IN THE BRAIN IN A MODEL OF TEMPORAL LOBE EPILEPSY IN MALE WISTAR RATS

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AIM: Epilepsy is a chronic neurological disorder characterised by recurrent unprovoked seizures. To date there is no biomarker for patients that are at high risk for acquiring epilepsy after an epileptogenic brain insult nor for the brain pathology relevant to epileptogenesis that could direct novel anti-epileptic treatments. Neuroinflammation plays an important role in epilepsy pathogenesis and its markers are reported to increase in the peripheral blood due to a leaky blood-brain barrier. This study aimed to measure inflammatory cytokines in blood for their potential to reflect brain pathology and seizure susceptibility.

METHODS: Blood samples and brain tissues were collected at cross-sectional timepoints (7, 14 and 84 days) covering the epileptogenesis phases following kainic acid-induced status epilepticus (KASE) in a rat model of temporal lobe epilepsy. mRNA expression of neuroinflammatory cytokines such as interleukin-1β, HMGB-1, interleukin-10, interferon-γ, TGF-β and TNF-α was evaluated in whole blood using RT-PCR and compared with expression in control animals. Moreover, the measured mRNA expression in KASE animals were correlated with autoradiographic and immunohistochemical markers of brain inflammation such as translocator protein (TSPO), microglial activation, astrocyte reactivity and neurodegeneration in relevant brain regions.

RESULTS: Expression of inflammatory cytokines did not differ significantly between KASE and control rats. Nonetheless at 84d timepoint, the distribution of mRNA expression of interleukin-1β in blood of KASE animals correlated with the TSPO signals and fluorojade counts (a marker of neurodegeneration) in the brain. Similarly, interferon-γ mRNA levels correlated with the fluorojade counts at 84d timepoint. Furthermore, at this time point, interleukin-1β mRNA expression in the blood correlated positively with TSPO signals in the brain. This was consistently observed over different brain regions relevant to epilepsy pathology.

CONCLUSION: The present study provides evidence that the molecular alteration of inflammatory cytokines in blood during chronic epilepsy can represent the cellular changes in the brain.

87. KETOSIS IMPROVES PROGNOSIS: THE EFFECTS OF THE KETOGENIC DIET ON MILD TRAUMATIC BRAIN INJURY IN ADOLESCENT RATS

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A mild traumatic brain injury (mTBI) is caused by an insult to the head and may result in transient neurological dysfunction, with a proportion of individuals experiencing prolonged clinical and cognitive symptoms, referred to as post-concussion symptomology (PCS). Interestingly, the biphasic nature of these injuries is less publicly recognized. The resulting cascade of molecular imbalance that follows the initial impact includes altered glucose metabolism, mitochondrial dysfunction, and increases in reactive oxygen species (ROS). Glucose is the primary energy source for the brain, however following brain injury glucose becomes an inefficient energy substrate, and the brain is primed to use alternative substrates for cerebral function. The ketogenic diet (KD), a high fat, low carbohydrate diet, forces the body to burn fat rather than carbohydrates thus utilizing ketones over glucose for energy. Ketones can supply up to 70% of the energy required for brain function, improve mitochondrial metabolism, and reduce production of ROS.

AIM: To examine the effects of the KD on PCS in adolescent rats.

METHODS: Male and female Sprague Dawley rats were randomly assigned to receive either a standard diet (n=23), or the KD – either pre-injury (n=16) or post-injury (n=27), then further randomized into a sham (n=30) or mTBI (n=36) condition. All animals were then tested on 6 behavioral tasks validated to examine PCS. Gene expression analysis in the brain and gut were performed following sacrifice.

RESULTS: Exposure to the KD prior to injury had some neuroprotective properties, improving short-term working memory $p < .05$. The KD post-injury may have been therapeutic, reducing both anxiety- and depressive-like behaviours p's $< .05$. The KD also altered gene expression in the prefrontal cortex, hippocampus and intestine p's $< .05$.

CONCLUSION: This study demonstrates the promise of the KD as both a neuroprotective and therapeutic agent for mTBI and warrants further investigation.

88. INCREASED BRAIN ACTIVITY DURING A COGNITIVE EYE MOVEMENT TASK IN EARLY MULTIPLE SCLEROSIS

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BACKGROUND: Cognitive impairment is a common symptom in multiple sclerosis (MS), including patients with clinically isolated syndrome (CIS). However, the underlying neural processes driving cognitive impairment in CIS is largely unknown. Saccadic eye movement is a validated approach used to probe the neural processes of cognitive function in a sensitive and objective manner. Integrating functional magnetic resonance imaging (fMRI) with a saccadic eye movement paradigm provides the opportunity to assess the neural activation associated with cognitive dysfunction in patients with CIS.

OBJECTIVE: We sought to examine the neural processes of cognitive impairment in CIS patients using a saccadic eye movement task.

METHODS:18 CIS patients and 17 healthy controls completed an fMRI eye movement task across four runs. The task involved switching between interleaved pro-saccades (direct eyes towards the target) and anti-saccades (divert eyes away from the target). For each trial, saccadic response time, error rate, and spatial accuracy were recorded. Contrast images for antisaccade vs. prosaccade between patients and controls were examined and thresholded at $z > 2.3$ with a cluster significance of $p = 0.05$.

RESULTS: Saccadic measures did not differ significantly between groups. However, patients demonstrated increased neural activation in the right parietal operculum, and postcentral and supramarginal gyrus compared to controls for antisaccade > prosaccade.

CONCLUSION: Despite comparable saccade performance, CIS patients reported stronger neural activation relative to healthy controls during the eye movement task. This change in neural activation suggests that there are neuroplasticity changes occurring in the earliest stage of MS to enable CIS patients to achieve the same cognitive outcomes. Furthermore, this study demonstrated that the saccadic eye movement task is an approach to examine the neural correlates of cognition in early MS.

89. SEIZURE SUSCEPTIBILITY AND INFLAMMATION AS RISK FACTORS FOR POST-TRAUMATIC EPILEPSY

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Post-traumatic epilepsy (PTE) is a common long-term consequence of traumatic brain injury (TBI). The ability to predict an individual's risk of PTE, by delineating biomarkers associated with disease development, would be invaluable to identify patients who would most benefit from early intervention strategies. Emerging evidence suggests that neuroinflammation might contribute to the development of seizures and epilepsies.

AIM: To investigate whether neuroinflammation after TBI is associated with the risk of developing seizures using selectively-bred rats that are seizure-prone (FAST) or seizure-resistant (SLOW), compared to their parental control strains (Long Evans and Wistar).

METHODS: 10-week old male rats either received a moderate fluid percussion injury (n=8-16/group), or sham-surgery (n=2-8/group). Rats then underwent acute injury measures, serial blood collection and neuromotor assessments, followed by tissue collection at 7 days for immunofluorescent staining of inflammatory cells.

RESULTS: As expected, FAST rats showed an exacerbated physiological response acutely post-injury, with a 100% seizure rate and mortality within 24 hours. SLOW rats, on the other hand, showed a reduced response, with no acute seizures and a rapid neuromotor recovery, returning to baseline by 7 days post-injury. Interestingly, differences were also apparent between the control strains, with TBI Long Evans rats performing significantly worse physiologically in the angle board test compared to the TBI Wistar rats (Day 2, 7: $p<0.0001$, $p<0.01$) as well as showing significantly higher microglia/macrophage and astrocyte activation on the ipsilateral brain compared to the contralateral side, in the lateral cortex (CD68: $p<0.05$, GFAP: $p<0.0001$), external capsule (CD68: $p<0.001$, GFAP: $p<0.01$), thalamus (CD68: $p<0.001$ GFAP: $p<0.05$), and hippocampus (CD68: $p<0.05$, GFAP: $p<0.05$).

CONCLUSION: The results together indicate strain differences in the response to TBI as well as seizure susceptibility. Findings support further investigation into whether strain differences are associated with chronic PTE development, with the aim to identify biomarkers indicative of epileptogenesis.

90. IMPLEMENTING ACUTE BLOOD PRESSURE LOWERING IN INTRACEREBRAL HAEMORRHAGE: EXPERINCE FROM A SINGLE COMPREHENSIVE STROKE CENTRE

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Spontaneous intracerebral haemorrhage (sICH) remains a significant cause of morbidity and mortality throughout the world. National Clinical guidelines advocate (weak recommendation) acute blood pressure (BP) lowering within 6 hours of onset of sICH to systolic 140 mmHg – with the aim of reducing haematoma expansion.

AIM: We audited the barriers to implementing this in a comprehensive stroke centre having established a sICH protocol containing an acute BP lowering regime in the ED.

METHODS: We retrospectively reviewed consecutive patients with sICH in our stroke department sICH registry between 1/1/2018 to 28/2/2019 after implementation of our sICH protocol. Patients were categorised based on onset-to-door time ≤6 hours and >6 hours.

RESULTS: Of 102 patients with sICH during study period, 43 patients (42.2%) presented ≤ 6 hours from onset (mean age 70.4 years, 53.5% male) including 37 patients presenting ≤4.5 hours, and 59 patients (57.8%) > 6 hours (mean age 74.1 years, 49.2% male). Compared with patients with onset > 6hours, patients who presented ≤6 hours had better pre-morbid function (median mRS score 0 vs 2, p = 0.02), higher initial systolic BP (mean 168 vs 155 mmHg, p =0.03), lower GCS (median score 12 vs 14, p= 0.01) and higher NIHSS on presentation (median score 16 vs 5, p =0.01). Among patients with onset-to-door time ≤ 6 hours and initial SBP > 140 mmHg, 78.8% (26/33) received acute BP therapy, and 19.2% (5/26) had SBP lowered to target within one hour of presentation in the ED, despite protocol.

CONCLUSION: ICH patients presenting early were found to have more severe stroke. Despite protocol, acute BP lowering in ED was effective in only 1 in 5 eligible cases. A dedicated Hyper Acute Stroke Unit (HASU) with high level non-invasive physiological monitoring and antihypertensive dose escalation is planned to improve this in our centre.

OBESITY

91. MECHANISMS OF BOLUS TRANSIT FOLLOWING SLEEVE GASTRECTOMY

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Sleeve gastrectomy has rapidly gained popularity due to its ability to induced and sustain substantial weight loss; with over 22,000 performed annually in Australia. Rapid uptake of the procedure has outstripped understanding of the physiological effects of the procedure, although there is substantially altered anatomy.

AIM: To determine the nature of gastric emptying and oesophageal function mediating bolus transit and clearance post-surgery.

METHODS: There were 26 participants post-surgery demonstrating optimal progress (by structured clinical interview) and 21 obese controls. Protocolised nuclear scintigraphy, dynamic contrast swallows, with SF-36 quality of life assessment and structured symptom scores.

RESULTS: Sleeve gastrectomy participants had a mean age of 48.9±11.7 years, 19 females. Excess weight loss was 56.2±45.2% and duration from surgery 15±23 months. Post-surgery; mild to moderate delay in oesophageal transit during swallows (liquid; n=15, semi-solid; n=14). Gastric emptying half time was 25.4±12.5 minutes (gastric sleeve) compared to 70.7±44.7 minutes (controls) ($p<0.0001$). Post gastric sleeve, 35±17% of radio-labelled meal transited into the small bowel, compared to 19±13% in controls ($p<0.004$). More than 50% of gastric sleeve participants demonstrated immediate post-deglutitive (triggered) reflux events during their swallows. Dynamic contrast swallows illustrated consistent patterns of oesophageal peristalsis based gastric filling leading to trans-pyloric flow correlating with triggered reflux events. Quality-of-life in optimal participants was good; five of eight health concepts measured had scores greater than 80. Regurgitation occurring less than once per month was reported in 73% of participants. The dysphagia score was 30.3 ±13.9 out of 40 (with 0 representing no dysphagia to any food and 45 being total dysphagia, i.e. unable to swallow water).

CONCLUSIONS These, data suggest a new paradigm of sleeve clearance proposing oesophageal function as a central mechanism of action of emptying and mediator of reflux. Reflux events observed during normal clearance processes, making it a response intrinsic to this procedure.

92. ALTERED PHYSIOLOGY OF THE DISTAL OESOPHAGUS FOLLOWING SLEEVE GASTRECTOMY

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BACKGROUND: Gastroesophageal reflux disease (GORD) following sleeve gastrectomy (SG) negatively impacts quality of life and potentially requires lifelong medical treatment or reoperation. The effect of SG on the physiology of GORD and symptom severity, however, remains uncertain.

AIM: To identify physiological mechanisms associated with GORD symptom severity following SG.

METHODS: This study is a retrospective review of SG patients of a prospectively maintained database of bariatric surgery patients from the last five years. Patents were classified as asymptomatic (n=32), moderate reflux (n=34), or severe reflux (n=9) based on a structured clinical interview. Patients underwent a standardised protocol of oesophageal manometry and 24-hour pH monitoring.

RESULTS: Between the groups, age was 48.2 vs 40.4 vs 45.4 (p=0.0279), excess weight lost was 58.1% vs 52.6% vs 57.9% (p=0.672), and duration since surgery was 16.0 months vs 13.6 months vs 14.3 months (p=0.8828).

Severely symptomatic patients had increased total acid exposure compared to the moderate and asymptomatic groups (15.5%, 7.91%, and 6.56%, over 24 hours; p=0.005). Impaired oesophageal peristalsis was associated with decreased lower oesophageal sphincter (LOS) basal tone (9.73 vs 20.7mmHg, p=0.001) and increased acid exposure over 24 hours (10.9% vs 6.88%, p=0.039). Hiatus hernia was associated with decreased LOS basal tone (12.6mmHg vs 20.1mmHg, p=0.017), increased acid exposure over 24 hours (11.3% vs 6.30%, p=0.009), and increased silent reflux events (92.2 vs 51.4, p=0.013).

CONCLUSION: We have defined expected physiological values for asymptomatic, moderately symptomatic, and severely symptomatic states following SG. More severe reflux symptoms following SG are characterised by increased oesophageal acid exposure that is partially explained by impairments in peristalsis and presence of a hiatal hernia. Given the altered anatomy and physiology involved with SG, it would appear that novel physiological mechanisms relating to these alterations are driving GORD post-SG.

93. DELETION OF TRIM28 IN ADIPOSE TISSUE PROMOTES ADIPOSITY BUT PRESERVES METABOLIC HEALTH

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White adipose tissue (WAT) plays a significant role in metabolic regulation and energy homeostasis, which can be disrupted in the setting of obesity. Obesity can lead to health complications including insulin resistance, type 2 diabetes and fatty liver disease, which are caused in part by the deposition of lipid in peripheral tissues following saturation of WAT depots. Recent studies have shown that activating adipogenesis, or enhancing healthy WAT expansion, can reduce obesity induced complications and results in a metabolically healthy phenotype. Thus, by redirecting fat from non-adipose tissues back into adipose tissue, complications associated with obesity may be alleviated. Indeed, a protein recently shown to promote metabolically healthy obesity is tripartite motif containing 28 (Trim28), which was suspected to act in an epigenetic manner during development and not directly in adipose tissue per se. However, to our knowledge there have not been any studies to definitively demonstrate the role of Trim28 specifically in WAT.

Here, we demonstrate that adipose specific Trim28 KO mice have increased adiposity on a normal chow and high-fat diet. Consistent with previous findings, this increased adiposity was not associated with decrements in glucose tolerance, and was demonstrated to increase the expression of genes consistent with lipid storage and browning in both visceral and subcutaneous WAT depots. We also demonstrate that triglycerides are elevated in visceral fat depots and reduced in the plasma and liver of KO mice compared to controls. Furthermore, we show that the magnitude of this effect was exacerbated in female mice, suggesting that Trim28 could play a role in gender specific differences in relation to complications associated with obesity. These data suggest that Trim28 expression may be a potential mechanism important for promoting healthy adipose tissue expansion and improving lipid storage in the setting of obesity.

OTHER

94. INVESTIGATION OF COMPENSATION AND SPILLOVER SPREADING ERROR MATRICES UNDER DIFFERENT SETUP CONDITIONS.

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AIM: With recent advancement in Flow Cytometry, we have investigated compensation and spillover spreading matrices on 4 different instruments (Canto, LSR, LSR Fortessa, LSR Fortessa X-20) on the AMREP Campus using the BD CD4 Evaluation kit. We also investigated the differences between the matrices when baseline voltages were set up using the application template set up on FACSDiva software compared to the BD CD4 evaluation kit recommendations of setting the positive peak at 10^4 MFI (Mean Fluorescence Intensity).

METHOD: Fresh Human PBMC's were isolated from a healthy donor and stained using the CD4 Evaluation kit, once stained the cells were acquired using two different methods. Method A used voltage settings which standardised all the positive population MFI's to 10^4, Method B used the software derived application settings to set the baseline voltages. The results generated were used to develop heat map tables illustrating where issues may arise.

RESULTS: Using Method B resulted in a lower percentage of compensation values which were above the upper limit of 100% (0%, 0%, 0.9%, and 2.7%) compared to Method A – (10%, 3.6%, 11.8%, and 9.6%). Similar results were seen in regards to Spillover Spreading where the upper limit was set at a spillover spread of 5, Method B showed less - (3.3%, 0%, 6.4%, and 8.2%) compared to Method A – (30%, 5.4%, 29%, and 26%).

CONCLUSION: The data indicates that by using Method B and adjusting the baseline voltages accordingly, we can achieve lower compensation and spillover values when compared to Method A. This information can serve as a guide for flow-users when building/adding new fluorophores to existing panels, as well as a trouble shooting guide for established panel. This data also illustrates the importance of appropriate voltage settings for experiments and how inappropriate settings can influence compensation and spillover spread in downstream data analysis.

95. A 7-YEAR RETROSPECTIVE REVIEW OF THE TECHNICAL SUCCESS OF THE 'LOW PROFILE' HANGMAN TECHNIQUE FOR COMPLICATED INFERIOR VENA CAVA (IVC) FILTER RETRIEVALS

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Potentially retrievable inferior vena cava (IVC) filters have been in use in clinical practice since the early 2000s. Prolonged filter dwell times have been associated with increased difficulty of retrievability and potential complications relating to IVC stenosis or occlusion. It is good practice therefore, that all patients with potentially retrievable IVC filters should have an attempt made at filter retrieval as soon as no longer clinically indicated. Interventional Radiologists need therefore to be prepared to perform both standard and advanced, complex filter retrievals if offering an IVC filter service.

AIM: To assess the safety, efficacy and reproducibility of a new modified lower-profile hangman technique.

METHODS: A retrospective review of all filter retrieval procedures performed at a major trauma centre, from 2012 to 2019 was performed. Records were reviewed for patient demographics, device type, device dwell time, device tilt, embedded hook, success of device retrieval, evidence of caval injury and occurrence of complications.

RESULTS: From 2012 to 2019 there were 473 filter retrieval attempts. An advanced technique was documented in 66 (14%). The low profile hangman technique alone was documented in 23 procedures (5% of all procedures, 35% of advanced technique procedures). Average screening time was 28 minutes. At the time of retrieval attempt, 9 patients (41 %) were anticoagulated. The hangman technique was employed as isolated manoeuvre in 23 patients and was successful on initial attempt in 22 cases (96%). The average dwell time of filters retrieved by the hangman technique was 228 days (range 40 – 903, median 196). No procedure-related complications occurred.

CONCLUSION: The retrieval of IVC filters is an important part of offering an IVC filter service. Advanced techniques to retrieve caval filters are multiple, and the risk of complications is increased in these cases. We demonstrate the safety, efficacy and reproducibility of a new modified and lower-profile hangman technique. This new technique is able to employ only an 11 French venous access sheath using off the shelf equipment and this remains a cost-effective approach to complex filter retrieval.

96. INTERRUPTED TIME SERIES OBSERVATIONAL STUDY OF ALFRED HEALTH CLINICAL PHARMACISTS' DAILY ACTIVITIES

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Clinical pharmacists are involved in a variety of activities throughout a typical working day. The implementation of an electronic medical record system is expected to have major impacts on workflow on pharmacists' day to day activities.

AIM: To quantify the proportion of time a clinical pharmacist spends on a range of clinical and non-clinical activities pre and post electronic Timely Quality Care (eTQC) implementation.

METHODS: Pharmacists working on the surgical and general medical units (GMU) were observed performing their usual roles to evaluate time spent executing different activities. During an eight-hour shift, tasks were recorded using the Work Observation Method by Activity Timing (WOMBAT) tool, developed for direct observation of health professionals. Tasks were allocated to domains: WHAT, HOW, WHO and WHERE, which were further divided into categories and sub-categories.

RESULTS: A total of more than 200 hours of observation were conducted over 21 sessions between Jun-Aug 2018. A total of 7961 individual tasks were recorded with a median task time of 45 seconds. Both GMU and surgical pharmacists performed most tasks on their own (~60%); tasks performed with another person most frequently involved a patient within the surgical team (12.8%) and a doctor within the GMU team (17%). The most frequently performed task in the surgical unit was daily medication review (12.5%) and clinical discussion/provision of therapeutic advice (n=692 18.4%) in GMU. A large proportion of time was spent conducting inpatient clinical activities: Surgical 26% and GMU 40%. Pharmacists spent ~33% of time engaged in more than one task simultaneously. Post eTQC implementation data is yet to be analysed but will be included in this paper.

CONCLUSION: Pharmacists on the GMU and surgical teams spent most of their time performing tasks on their own, on the ward. A large proportion was within the inpatient clinical activities category, in both the surgical and GMU disciplines. This is the first study to describe and quantify daily clinical pharmacist activities at Alfred Health. The results of this study will allow comparison of pharmacist activities before and after eTQC implementation and to determine the changes to work flow.

97. VITAMIN D LEVELS FROM A TERTIARY HEALTH CENTER IN VICTORIA AUSTRALIA: GENDER, AGE, SEASONAL AND SPECIALTY DIFFERENCES

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Vitamin D deficiency is a global health issue that afflicts more than one billion people worldwide. Low vitamin D status has been associated with an increased risk of rickets, osteoporosis, diabetes mellitus, cardiovascular disease and multiple sclerosis.

AIM: To investigate whether gender, age, monthly and seasonal variations in serum concentration of 25(OH)D are evident among the Victorian tertiary hospital population.

METHODS: Results of serum 25(OH)D lab tests of 38,385 patients (inpatient and outpatient) from Royal Melbourne Hospital, Australia in 2013-2017 were analyzed using R programming and statistical software. Dispensing records of vitamin D supplementation (cholecalciferol 1,000 IU or 50,000 IU) were derived from pharmacy records. Clinical variables that were recorded include gender, age and medical specialty each patient was admitted to as well as the season, month and year vitamin D test was measured. Univariate and multivariate analyses were undertaken to assess which clinical variables were associated with variations in vitamin D status.

RESULTS: Mean vitamin D level of study population was 67.39 nmol/L (SEM 0.16) with average age of 57.0 years. Univariate analysis showed females ($P<0.0001$), older age ($P<0.0001$), patients from Neurology ($P<0.0001$) and summer ($P<0.0001$) were associated with higher vitamin D status. Patients whose vitamin D levels were measured in 2013 were significantly lower compared to patients in 2014-2017 ($P<0.0001$, one-way ANOVA). Multivariate analysis showed that when the effects of other variables were accounted for, vitamin D status of Neurology patients was significantly higher than other specialties.

CONCLUSION: There is a gender, age, medical specialty, seasonal, monthly and yearly variation in vitamin D levels in a tertiary health center in Victoria. This highlights the importance of targeting certain subgroups to improve their vitamin D status. The association between low vitamin D status and winter despite supplementation suggests other interventions are required to boast vitamin D levels.

POPULATION HEALTH AND EPIDEMIOLOGY

98. DETERMINING THE CONTENT OF A PATIENT-REPORTED OUTCOME MEASURE FOR THE BARIATRIC SURGERY CLINICAL REGISTRY

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The Bariatric Surgery Registry (BSR) collects data and assesses the safety and efficacy of bariatric surgery across Australia and New Zealand. The focus of the longterm data collection is to record adverse events, mortality related to bariatric surgical procedures, as well as monitoring weight loss and diabetes status of patients. However, the Bariatric Surgery Registry is looking to expand the information collected from patients to include Patient-Reported Outcome Measures (PROMs).

AIM: Using newly developed conceptual and analytic framework for health-related quality of life dimensions, to examine both qualitative and quantitative data as the first step in the development of the BSR-PROMs.

METHOD: Two focus groups, which included a total of 12 patients who underwent a bariatric procedure, were conducted to examine patient perspectives as to the most important outcomes of their surgery, particularly in regards to their overall wellbeing. In addition, quantitative data from 198 participants with a BMI $\geq$ 40 from an Australia-wide survey measuring subjective wellbeing were also examined, utilising the Personal Wellbeing Index.

RESULTS: Quantitative results indicate that satisfaction with 6 of the 7 life domains for participants with BMI $\geq$ 40 fell substantially below the normative range for Australians. Findings from the focus groups provided important insights in terms of the impact of bariatric surgery on their overall quality of life. This includes the role of personal and professional relationships, outcome expectations, and attitudes to changes in lifestyle, and eating behaviours.

CONCLUSION: An overview of patient perspectives on bariatric surgery are provided, and discusses some of the critical issues in determining content of Patient Related Outcome Measures for the Bariatric Surgery Registry.

99. STUNTING AS AN (IN)ACCURATE MEASURE OF HEALTH AND NUTRITION OUTCOMES: A CASE FROM LAO PEOPLES' DEMOCRATIC REPUBLIC (PDR)

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BACKGROUND: Stunting is a form of chronic malnutrition, affects 156 million children worldwide and is a major public health issue. Globally, chronic malnutrition, measured by stunting, is a priority investment area not only due to its association with increased rates of childhood disease and death, but also due to its' effects on children's cognitive, motor and neurodevelopment. This in turn has significant implications for a country's future economic prosperity and productivity. Stunting is commonly used as an indicator of nutritional status and often applied as a proxy for poverty. However, several studies have reported that inaccuracies in age reporting can lead to errors in stunting measurements and interpretation. Our work in Savannakhet Lao PDR (2008-11) using a community-based nutrition model, reported on multiple anthropometric and nutrition outcomes and also found that stunting was an inaccurate measure of the impact of the project on health and nutrition outcomes.

AIM: To examine how stunting measurements can be improved to provide accurate data for nutrition policies and programs.

METHODS: We implemented a 3-year health/nutrition project in 12 villages in the highlands of Savannakhet province to reduce acute malnutrition in children. Monthly anthropometric measures were taken from children aged 6-59 months by volunteer nutrition teams in each village and an outreach multisectoral district committee. We conducted a cross-sectional assessment before project activities began and at the end of the project. Sixty percent of all households were surveyed at baseline, and at endline 82-100% of eligible, registered participants were surveyed. Statistical analyses were performed using Stata 13.

RESULTS: The prevalence of wasting declined from 12.4% to 6.1% and other non-anthropometric measures for health and nutrition outcomes (i.e. breastfeeding and infant feeding practices) improved from baseline to endline. Height and length measures were similar at both timepoints. Stunting and underweight (two measures that use age as a variable) increased from baseline to endline. Systematic differences in child age measurements were apparent between baseline with heaping at whole years and endline with older children and less or no heaping.

CONCLUSION: Our study found that anthropometric measures that were calculate based on age provided results that were inconsistent and contradictory to our other indicators to measure health and nutrition outcomes. Inaccuracies in age reporting is common in nutritional studies and both under- and over-estimate of age can affect calculated stunting prevalence. Given national and global malnutrition policy and programming is increasingly informed by stunting data, it is imperative that attention is given to accurate stunting measurements to enable accuracy of data for decision making.

100. ALCOHOL-RELATED HARMS AND RISKY DRINKING AMOUNG YOUNG PEOPLE IN VICTORIA, AUSTRALIA

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Most studies of alcohol-related harms have focused on the most severe and least common harms (e.g. physical assault). Multiple binge-drinking campaigns have targeted these severe harms, which young people have evaluated as unrelatable and ineffective. AIM: This study aimed to investigate a broader spectrum of alcohol-related harms and risky drinking among young people.

METHODS**:** *Sex, Drugs and Rock 'n' Roll* is an annual online survey of Australian 15-29 year olds. In 2017, participants reported on a range of alcohol-related harms across physical, social, criminal, transport and sexual domains. The AUDIT-C categorised participant's alcohol consumption as low (<6) or high (7-12) risk. Logistic regression identified if there was an association between each alcohol-related harm and high-risk alcohol consumption in the past year, adjusting for age, gender and age at first alcohol consumption.

RESULTS: Overall, 1272 participants completed the survey. In the past year, 1163 (91%) participants consumed alcohol. Sixty-five percent had experienced at least one alcohol-related harm in the past year. The most common harms included forgetting parts of the night (46%), not getting up for plans (26%), arguing (25%), difficulties getting home (18%) and regretted/unwanted sexual activity (14%). Participants categorised as high-risk drinkers had higher odds of experiencing each alcohol-related harm in the past year compared to low-risk drinkers.

CONCLUSION: Participants experienced a broad range of alcohol-related harms including low severity harms (e.g. arguing, not getting up in time for plans) and higher severity harms (e.g. memory loss, regretted/unwanted sexual activity). Harms were more common among high-risk drinkers. In order to design more effective alcohol harm prevention measures, it is essential to better understand the full range of negative effects experienced by young, risky drinkers. This knowledge can inform tailored alcohol risk reduction measures and broader population-level strategies.

101. PHYSICAL HEALTH OF TRANSITIONED ADF AND REGULAR ADF MEMBERS IN 2015: FINDINGS FROM THE TRANSITION AND WELLBEING RESEARCH PROGRAMME

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INTRODUCTION: Military service can involve exposure to physical and psychological stressors. There has been little systematic research into the health and wellbeing of military personnel after they leave the services.

METHODS: 4326 Transitioned ADF (transitioned from regular Australian Defence Force service between Jan 2010-Dec 2014) (18% response) and 8480 Regular 2015 ADF (42%) completed a questionnaire including symptoms, doctor-diagnosed medical conditions, respiratory health, injuries, pain, sleep problems, lifestyle factors, self-perceived health and quality of life and health service use.

RESULTS: Transitioned ADF reported a higher mean number of symptoms (16.4 vs 11.8), similar mean number of medical conditions (1.9 vs 1.5), were more likely to report some medical conditions (a circulatory, musculoskeletal/connective tissue or nervous system condition, high blood pressure, chronic low back pain, and hearing loss), a slightly higher mean number of service-related injury types (1.11 vs 0.96), and poorer self-perceived health and quality of life compared to 2015 Regular ADF. Service-related injuries were more likely to have been sustained during training than on deployment in both groups. The majority of Transitioned ADF and 2015 Regular ADF reported experiencing some pain intensity and disability.

In Transitioned ADF, poorer physical health outcomes overall were reported in Department of Veterans' Affairs (DVA) clients compared with non-DVA clients, in Ex-Serving compared with Active Reservists or Inactive Reservists, and in those who had been medically discharged compared with those discharged for other reasons.

CONCLUSION: This was one of the first studies internationally to investigate a comprehensive range of physical health indicators in recently transitioned military personnel. Overall Transitioned ADF were more likely to report poorer physical health across domains, some subgroups appeared particularly at risk. Findings in DVA clients were consistent with DVA being the conduit for care in veterans who have a service-related injury or mental health condition.

102. EFFECT OF ASPIRIN ON DISABILITY-FREE SURVIVAL IN THE HEALTHY ELDERLY

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The use of aspirin to increase healthy independent life-span in older individuals has not been studied.

AIM: To determine whether 5 years of daily low-dose aspirin extended disability-free life in healthy seniors in the ASPirin in Reducing Events in the Elderly (ASPREE) study.

METHODS: Community-dwelling individuals in Australia and the U.S., aged 70 or older (or 65 and older in U.S. minorities) without cardiovascular disease, dementia or physical disability, were recruited during 2010-14 and randomly assigned to receive 100mg enteric-coated aspirin or placebo orally. The primary endpoint was a composite of death, dementia, or persistent physical disability.

RESULTS: A total of 19,114 individuals were enrolled of median age 74; 56% were female, 9% were minorities and 11% reported prior regular aspirin use. Of these, 9525 were randomly assigned to aspirin and 9589, to placebo. The trial was terminated at 4.7 median years' follow-up after a determination that there would be no benefit on the primary outcome from continuing aspirin. At the time of trial termination the rate of the primary endpoint was 21.5 (aspirin) versus 21.2 (placebo) per 1000 person-years (hazard ratio [HR] 1.01; 95% confidence interval [CI] 0.92 to 1.11). Final year compliance with assigned medication was 62% (aspirin) and 64% (placebo). Aspirin had no effect on secondary endpoints of death, dementia, or persistent physical disability. The rate of major haemorrhage was higher with aspirin (HR 1.39; 95% CI 1.18 to 1.62; P<0.001).

CONCLUSION: Aspirin in healthy elderly individuals did not prolong disability-free survival over 5 years but increased the rate of major haemorrhage.

103. THE PREVALENCE, LOCATION AND IMPACT OF MODERATE TO SEVERE PERSISTENT PAIN AMONGST AMBULANT, COMMUNITY-DWELLING OLDER AUSTRALIANS

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AIM: There is limited information about the nature of persistent pain amongst otherwise healthy, ambulant community-dwelling older Australians. In light of significant Australian public health concern regarding the clinical management of persistent pain, this study aims to describe the prevalence, location and impact of moderate to severe persistent pain.

METHODS: Questionnaire based, cross-sectional study (2011-15), administered to ASPREE clinical trial participants who were generally healthy, ambulant, community-dwelling older Australians (aged at least 70 years old). The main outcome measure was prevalence of moderate (score 4 to 6) to severe (score 7 to 10) persistent pain (on a scale of 0 to 10), location of body sites affected, impact on life, and frequency of medication used to treat it.

RESULTS: Almost half of all 14155 questionnaire respondents (6454/14155=45.6%) experienced pain on most days of the week, with the remaining 7701 participants reporting no persistent pain. Moderate to severe pain affected 19.9% (n=1291) of males and 29.5% (n=2269) of females. One quarter of respondents (25.1%, n=3560) experienced moderate to severe pain, commonly involving at least three body locations: the lower back, knees, and upper back. With regards to impact on life for the 3560 respondents who experienced moderate to severe pain, pain often or always upset sleep (28.8%, n=1024), made walking difficult (34.8% n=1239), and made some day to day activities hard (41.2% n=1467). In 50.9% (n=1812) of respondents who experienced moderate to severe pain, it was often or always treated with medication. Of those reporting moderate (n=2737) or severe pain (n=823), 27.2% (n=741) and 44.6% (n=367) respectively reported taking medication to treat their pain on most days.

CONCLUSION: Study findings contribute new information regarding the nature of persistent pain amongst otherwise healthy, ambulant community-dwelling older Australians. Persistent pain is a common accompaniment of aging, even amongst otherwise healthy individuals.

104. TRADITIONAL SES STEROIDS AND KETOANDROGEN LEVELS BY MENSTRUAL CYCLE STAGE, AGE AND BODY MASS INDEX IN WOMEN AGED 18-39 YEARS

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Prior studies suggest androgen levels decline with age in women across the reproductive years. The aims of this study were to verify this, and report on traditional androgens as well as the more recently described 11ketoandrostenedione (11KA) and 11 ketotestosterone (11KT), measured by liquid chromatography, tandem mass spectrometry (LC-MS/MS) by age, menstrual cycle stage and body mass index (BMI).

The Grollo-Ruzenne Young Women's Health Study recruited a population-representative sample of 6,986 Australian women aged 18-39 years. 602 study participants, free from factors that would influence their hormone levels, provided serum samples for measurement of estradiol (E_2), estrone (E_1), androstenedione (A), dehydroepiandrosterone (DHEA), testosterone (T), dihydrotestosterone (DHT), 11KA and 11KT.

Cyclical variations were seen for E_1, E_2, T and A with mid-cycle levels [median (range)] of 291 (13.2- 1909) pmol/L, 455 (5.5-3,583) pmol/L, 0.35 (0.09-1.01) nmol/L and 2.08 (0.63-7.89) nmol/L respectively. The median (range) levels of DHEA, 11KT and 11KA, which did not vary across the menstrual cycle, were 4.91 (0.08-23.51) nmol/L, 1.27 (0.03-7.61) nmol/L and 7.94 (0.07-31.67) nmol/L respectively.

Taking into account BMI, each of T, A, DHEA, 11KT and 11KA declined with age. The percent decrease in the median values between the youngest age group (18-25 years) and the oldest age group (35-39 years) was T 25%, A 31%, DHEA 36%, 11KT 14% and 11KA 29%. The median ratios were T:11KT 0.26, A:11KA 0.23, A:T 5.95 and 11KA:11KT 6.52 with no age variation.

This study confirms findings from smaller studies, that both T and DHEA decline during the reproductive years. That 11KA and 11KT also decline with age in premenopausal women, but do not vary across the menstrual cycle, are novel findings. Importantly, this study provides reference values by menstrual cycle stage and by age for each of the sex steroids measured.

105. EFFECT OF ASPIRIN ON ALL-CAUSE MORTALITY IN A HEALTHY OLDER POPULATION

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ASPirin in Reducing Events in the Elderly (ASPREE), a placebo controlled randomized trial of daily aspirin in older adults, showed no benefit for the primary outcome of disability-free survival. An increase in the secondary endpoint of all-cause mortality in the participants on aspirin was observed.

AIM: To investigate causes of death over 5 years among healthy elderly randomised to low-dose aspirin or placebo.

METHODS: 19,114 Australian and US community-dwelling participants aged 70+ years (U.S. minorities 65+ years) without overt cardiovascular disease, dementia or physical disability, were recruited in 2010-2014 and followed to mid-2017. Deaths were classified according to the underlying cause by blinded adjudicators. Mortality was compared between aspirin and placebo groups using hazard ratios (HR) and post-hoc exploratory analyses of specific causes of death were undertaken.

RESULTS: 1052 deaths occurred during a median 4.7 years of follow-up. The death rate in the aspirin group was 12.7 per 1000 person-years of follow-up compared with 11.1 in those on placebo (HR 1.14, 95% CI 1.01 to 1.29). Cancer was the major contributor to the excess mortality, with cancer-related deaths occurring in 3.1% of the aspirin group and 2.3% of the placebo group (HR 1.31, 95% CI 1.10 to 1.56).

CONCLUSION: An increase in all-cause mortality was observed in older apparently healthy adults randomized to daily aspirin that was primarily attributed to an increase in cancer mortality. In the context of previous studies, this result was unexpected and should be interpreted with caution.

106. SOCIOECONOMIC INEQUALITY IN THE HEAT-HOSPITALIZATION ASSOCIATION IN BRAZIL: A NATIONWIDE TIME-SERIES STUDY DURING 2000-2015

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OBJECTIVE: This study aims to evaluate how the heat-hospitalization association in Brazil during 2000−2015 could be modified by local socioeconomic level.

METHODS: We collected data on hospitalization and meteorological conditions from 1,814 Brazilian cities during the 2000−2015 hot seasons. City-specific urbanization rate, average family income and GDP per capita were used to represent each city's socioeconomic level. We used Quasi-Poisson regression with constrained lag model to obtain city-specific estimates, and then pooled them together according to different socioeconomic quartiles or levels using random-effect meta-analyses. Meta-regressions adjusting for mean temperature, temperature range and population structure were used to evaluate how the city-specific heat-hospitalization could be modified by each socioeconomic indicator.

RESULTS: A total of 49,145,997 hospital admissions during 2000-2015 were included in the analyses. At the national level, every 5°C increase in daily mean temperature was associated with 4.0% (relative risk [RR] = 1.040, 95% confidence interval [CI]:1.037-1.043) increase in hospitalization. This association showed a clear strengthening trend with socioeconomic quartiles decreasing from the highest to the lowest. The RR (95%CI) for cities of lower middle income, upper middle income and high income according to World Bank's classification were 1.053 (1.045-1.062), 1.040 (1.036-1.043) and 1.026 (1.020-1.032), respectively. After adjusting for city-level mean temperature, temperature range, and population structure by meta-regression, the city-specific RRs still showed significant negative association with the urbanization rate (*P*=0.030), average family income (*P*=0.015) and log(GDP per capita) (*P*=0.008).

CONCLUSIONS: There is a socioeconomic inequality in the heat-hospitalization association. People live in less developed cities in Brazil are suffering from higher vulnerability to heat exposure, despite their less responsibility to the global warming. The results suggest that more efforts should be invested in less developed areas in Brazil under a changing climate.

107. EFFECT OF ASPIRIN ON CARDIOVASCULAR EVENTS AND BLEEDING IN HEALTH ELDERLY

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Aspirin is a well-established therapy for secondary prevention of cardiovascular events. However, its role in primary prevention of cardiovascular disease is unclear, especially in people whose older age increases their absolute risk.

AIM: To investigate cardiovascular events and bleeding among healthy elderly randomized to low-dose aspirin or placebo in the ASPirin Reducing Events in the Elderly (ASPREE) study.

METHODS: We conducted a randomized, double-blind trial of 100 mg enteric-coated aspirin versus placebo in community-dwelling men and women in Australia and the U.S. Participants were aged 70 years or older (or 65 years of age or older for U.S. African Americans and Hispanics) at enrolment, and free of known cardiovascular disease, dementia or disability. Secondary endpoints included major haemorrhage and cardiovascular disease, defined as coronary heart disease death, non-fatal myocardial infarction, fatal and non-fatal stroke, and hospitalisation for heart failure.

RESULTS: Between 2010 and 2014, 19,114 individuals were enrolled and assigned to aspirin (9525 participants) or placebo (9589 participants). After a median of 4.7 years of follow-up, cardiovascular disease rates were 10.7 and 11.3 events per 1000 person-years in the aspirin and placebo groups respectively (hazard ratio [HR] 0.95, 95% confidence interval [CI] 0.83 to 1.08). Rates of major haemorrhage were 8.6 and 6.2 events per 1000 person-years in the aspirin and placebo groups respectively (HR 1.38, 95% CI 1.18 to 1.62, P<0.001)

CONCLUSION: Low-dose aspirin as a primary prevention strategy in older adults significantly increased the risk of major haemorrhage and did not substantially reduce cardiovascular disease rates.

108. CANCER PREVALENCE AND ASSOCIATION WITH RISK FACTORS IN A HEALTHY OLDER POPULATION

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Cancer is a leading cause of death globally, and the risk of developing this disease increases with age. ASPirin in Reducing Events in the Elderly (ASPREE) was a placebo controlled randomised trial of daily aspirin in older adults, which collected self-reported history of cancer, including subtype, from participants at study enrolment.

AIM: To investigate the prevalence of past cancer history among healthy elderly and to identify any associations with known risk factors.

METHODS: At study enrolment, self-reported personal cancer history, cancer subtype and cancer risk factor data were sought from 19,114 participants (Australia n=16,703; U.S. n=2,411). 19,030 participants provided a complete cancer data set by responding to all cancer history questions. Eligible participants were healthy, free of major disease and expected to survive 5 years. Odds ratios, adjusted for age, gender and country, were used to describe the associations between cancer history and known cancer risk factors, and for cancer subtype prevalence with past aspirin use.

RESULTS: Nearly 20% of ASPREE participants reported a prior cancer diagnosis at enrolment. 22% of males and 18% of females, with females diagnosed at a younger age (diagnosis <50 yrs for females=16% and males=6%). Prevalence of prostate and breast cancer history were higher in the U.S. participants; melanoma and colorectal cancer were higher in Australian participants. Prior aspirin use was associated with a history of cancer whilst obesity, smoking, alcohol consumption and diabetes were not.

CONCLUSION: Personal cancer history in healthy older ASPREE participants was as expected for the most common cancer types in the respective populations, but was not aligned with known cancer risk factors. Potential survivor bias, partly driven by the study's entry criteria, may play a role in this population.

RESPIRATORY MEDICINE / LUNG TRANSPLANT

109. SHARING EXPERIENCES AND OFFERING MUTUAL SUPPORT: AN EVALUATION OF THE PEER CONNECT SERVICE FOR PEOPLE WITH PULMONARY FIBROSIS

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INTRODUCTION: People living with pulmonary fibrosis (PF) report unmet needs for information and support. Lung Foundation Australia (LFA) developed the Peer Connect Service to facilitate telephone support between people with PF across Australia. This project aimed to evaluate the resources required to deliver the Peer Connect Service, and to document the experiences of participants.

METHODS: Number of matches undertaken over 12 months was recorded, along with the number of contacts between LFA staff and participants required to establish each match. People with PF who had participated in the Peer Connect Service took part in a semi-structured interview by telephone. Primary Peers (registered patient peers who agreed to initiate contact) and Secondary Peers (eligible patients who had sought a peer match) were interviewed. Thematic analysis was undertaken by two independent researchers.

RESULTS: 60 peer matches were made, with a minimum of seven contacts from LFA staff to establish every match, mostly via telephone. Interviews were conducted with 32 participants with PF, consisting of 17 primary peers, 13 secondary peers and two who were both. Ages ranged from 53 to 89 years. A prominent theme was the value of shared experience, allowing information and emotional support needs to be met. Most participants perceived that Peer Connect provided mutual support, however a small number of Primary Peers had unmet support needs or were concerned that their phone calls were intrusive. Shared personal characteristics (eg gender, family background, hobbies) were important to the success of a match. Participants saw face-to-face contact with peers as highly desirable, whilst acknowledging the practical difficulties with achieving this.

CONCLUSION: The Peer Connect Service provides a unique opportunity for people with PF to share experiences and offer mutual support. This telephone matching model may be useful to provide peer support for individuals with rare diseases who are geographically dispersed.

110. THE UTILITY OF THE SIT-TO-STAND TEST IN ACUTE HOSPITAL INPATIENTS FOLLOWING LUNG TRANSPLANTATION.

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Measurement of physical function is important to guide physical therapy for patients post-lung transplantation (LTx). The sit-to-stand (STS) test has proven utility in chronic disease, but psychometric properties post-LTx are unknown.

AIM: To assess the reliability, validity, responsiveness and feasibility of the 60-second STS test post-LTx.

METHODS: This measurement study was conducted on 62 inpatients post-LTx (31 acute postoperative; 31 medical readmissions). Inter-rater reliability was assessed with two STS tests undertaken by different assessors at baseline. Known groups validity was assessed by comparing STS repetitions in postoperative and medical participants. Content validity was assessed using comparisons to quadriceps and grip strength, measured with hand-held dynamometry (HHD). Criterion validity was assessed by comparison of STS repetitions and six-minute walk distance (6MWD) postoperatively. Responsiveness was assessed using effect sizes over inpatient admission, via repeated STS on inpatient discharge.

RESULTS: Median age was 62 years (range 21-80); time post-LTx was 5(3-8) days postoperative and 696(99-7940) days for medical readmissions. Inter-rater reliability was excellent ($ICC_{2,1}$ 0.96) with a mean learning effect of 2 repetitions. Repetitions were greater for medical compared to postoperative participants at baseline only (baseline mean 18 vs. 9, p<0.01; discharge 19 vs. 14, p=0.05). More STS repetitions was associated with greater quadriceps strength (postoperative r=0.57; medical r=0.47) and 6MWD (postoperative r=0.68). Effect sizes were 0.94 and 0.09, with a floor effect of 23% and 3% at baseline (postoperative/medical) improving to 10% at discharge. Patients incapable of attempting a STS test at baseline were excluded, reducing generalizability to critical care. Physical rehabilitation was not standardized, possibly reducing responsiveness.

CONCLUSION: The 60-second STS test demonstrated excellent inter-rater reliability, moderate validity and was responsive to change postoperatively. The 60-second STS represents a safe, feasible physical outcome for post-LTx inpatients. Two tests should be completed at each time point.

111. THE ALFRED WELLNESS SCORE IN ADULTS WITH CYSTIC FIBROSIS: STABILITY, VALIDITY AND RESPONSE TO PULMONARY EXACERBATIONS

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The recently-developed Alfred Wellness Score (Awescore) questionnaire (Qx) is a brief patient-reported measure of 5 domains with 10 items two for each of the five domains: pulmonary, physical activity, nutritional, psychological and general health.
OBJECTIVES**:** To assess Awescore stability and validity compared to the CFQ (Cystic Fibrosis Qx); to assess the effects of pulmonary exacerbation on Awescore compared to baseline values.
METHODS**:** In two separate studies participants completed (1) Awescore and CFQ (time 1, time 2) one month apart while clinically stable; and (2) the Awescore during clinical stability and at diagnosis of a pulmonary exacerbation using recognised criteria.
RESULTS**:** (1) No significant difference was seen between the Awescore measures for 20 participants (time 1: mean 65 [SD 14], time 2: 65 [13]; mean difference -0.2 [95%CI -3.5 to 3.1]); these scores were significantly and strongly correlated (Pearson's r=0.854, p=< 0.005). The CFQ scores (time 1: mean 813 [SD 125], time 2: 789 [131]) were moderately correlated with the Awescore (Pearson's r=0.632; p=0.003). (2) Sixty patients completed the Awescore during clinical stability and exacerbation (age mean 33 [SD 10] years, BMI 22 [2] kg/m^2, FEV_1 median 50 [IQR 40,65] %predicted). A significant reduction in Awescore from clinical stability (mean 76 [SD 10], range 48-95) to exacerbation (47 [13], 17-69) was demonstrated (mean difference -29 [95%CI -32 to -25]) and observed in all domains (p< 0.0005).
Conclusion: The Awescore is a stable and valid measure when compared with the CFQ. Pulmonary exacerbations impact negatively and significantly on all health domains of wellness in adults with CF.

112. ADVANCE CARE PLANNING IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ASSESSED FOR LONG TERM OXYGEN THERAPY

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Advance Care Planning assists end of life care and improves patient, clinician and family satisfaction. This study demonstrated a low ACP rate, despite high mortality, in patients with Chronic Obstructive Pulmonary Disease assessed for Long Term Oxygen Therapy.

AIM: To identify patients with Chronic Obstructive Pulmonary Disease (COPD) on Long Term Oxygen Therapy (LTOT) and to determine uptake rates of an Advance Care Plan (ACP) and factors which correlate to the presence of an ACP.

METHODS: Data was retrospectively collected from consecutive patients with COPD assessed for continuation or commencement of LTOT who attended Oxygen Clinic at The Alfred, a tertiary hospital in Melbourne, between 1st July 2015 and 30t June 2016. Factors recognised to be associated with an ACP were analysed using independent t-tests for continuous variables and Chi-squared tests for ordinal variables.

RESULTS: 79 patients were included; age (mean ± SD) 71±11years, FEV1%predicted 38±15%, PaO2 60±11mmHg, PaCO2 45±10mmHg, arterial pH 7.43±0.04, Body Mass Index 28±8kg/m2. 21.5% had an ACP. 40.5% were on continuous home oxygen, 36.7% used intermittent oxygen, 11.4% used nocturnal oxygen and 11.4% did not qualify for oxygen, were not advised to have oxygen for safety reasons or refused oxygen. 43.0% lived at home with community supports, 35.8% home with family, 12.8% family and supports, 3.8% home alone, 5% not known. 26.6% died within the study period. The only factor significantly associated with the presence of an ACP on univariate analysis was number of hospital admissions within the preceding 12 months ($p<0.002$).

CONCLUSION: ACP assists end of life care and improves patient, clinician and family satisfaction. This study demonstrated a low ACP rate, despite high mortality, in patients with COPD assessed for LTOT. Patients who were hospitalised within the last 12 months were more likely to have an ACP in place. No other factor was identified that correlated with increased uptake of ACP. We recommend that all patients with COPD attending oxygen clinic should have discussions about ACP. Appropriate resource allocation and training should be implemented towards achieving this outcome.

113. WAKE UP TO SLEEP! PATIENT PERCEPTION OF SLEEP QUALITY IN THE WARD SETTING – A PILOT STUDY

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Sleep is essential for good health and is important for recovery from injury or illness. Poor sleep is common in adults during acute care hospitalisations and has the potential to worsen outcomes. Perception of sleep quality is subjective, highly variable and not universal.

AIM: To evaluate patients' perception of sleep quality during an acute inpatient hospitalisation in a ward setting.

METHODS: Patient perception of sleep quality was audited on a 33 bed medical ward. The Richards Campbell Sleep Questionnaire (RCSQ) was administered and rated using the Total Sleep score (TSC) on 4 consecutive nights. Charlson Comorbidity Index (CCI) was measured. Exclusion criteria: language barrier, dementia, age <18 years, not on ward until after 2200hrs, asleep or not at bedside at the time of audit.

RESULTS: 72 encounters obtained from 132 beds (54%), 60 excluded, 31 patients participated. Age 23-88 yrs. 63.9% female. Using data from patients' first night, perception of sleep quality was rated as poor (16.1%), moderate (35.5%) and good (48.4%). Females TSC trended higher compared to males (65.4 v 59.2) but both remain in the moderate category. Similarly, TSC trended higher in a semi-private room compared to private (62.3 vs 50.8) but both remain in the moderate category. More females (63%) occupied semi-private rooms. CCI scores, mild (41.9%), moderate (25.8%) & severe (32.3%). No correlation between CCI and TSC. For those with repeat data, there was variation in perception of sleep quality.

CONCLUSION: Patient sleep quality perception was variable across the audited population. Perceived sleep quality trended towards a higher rating in females and those who occupied a semiprivate room. There was no relationship with Total Sleep Score and the Charlson Comorbidity Index. Further research is warranted to understand the factors affecting and promoting sleep in the acute inpatient ward setting.

114. ATRIAL ARRHYTHMIAS POST LUNG TRANSPLANTATION: MECHANISMS OF ACTION, EXPERIENCE AND SUGGESTED TREATMENT ALGORITHM

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BACKGROUND: Atrial arrhythmias are relatively common post-lung transplantation, and can confer considerable peri-operative morbidity including haemodynamic instability, pulmonary congestion, dyspnoea, or can mask other post-transplant complications such as infection or acute rejection. However, for most patients, arrhythmias are limited to the short-term perioperative period.

METHODS: We performed a retrospective case-control analysis of two hundred lung transplant recipients and identified the incidence, risk factors, and outcomes between the two groups. One hundred cases with atrial arrhythmias from June 2011 – August 2017 were identified and matched to the first 100 controls without arrhythmia retrospectively prior to August 2017. Furthermore, a literature review was performed for all protocols or guidelines or recommendations on atrial fibrillation or arrhythmias in the perioperative thoracic surgical setting. Evidence from eight guidelines was then reviewed by a local expert panel including Cardiologists, Cardiothoracic Surgeons, Intensive Care Specialists, and Lung Transplant Physicians, and a set of recommendations specific to lung transplant recipients were formulated.

RESULTS: Atrial arrhythmias following lung transplantation were more commonly present in older recipients and those with underlying COPD, but not in those previously noted structural heart disease, or in those undergoing single rather than double lung transplants. Atrial arrhythmias were associated with increased length of stay, but not short term mortality in our cohort. Based on our experience, we propose a suggested management algorithm for pharmacological and mechanical rate/rhythm control strategies, and for anticoagulation, and discuss the appropriate length of duration.

CONCLUSIONS: Atrial arrhythmias are relatively common post lung transplantation. Carefully managed, the associated risk of perioperative morbidity and mortality can be mitigated. Further prospective studies are required to validate these strategies.

115. LUNG IMAGING AT MEDICAL EMERGENCY TEAM CALLS FOR INPATIENTS: LIMIT CTPA

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BACKGROUND**:** Computed tomography pulmonary angiography (CTPA) is the gold standard test for pulmonary embolism (PE), but may be overused. This has not been well studied in the Australian inpatient setting. We aimed to evaluate CTPA use following inpatient medical emergency team (MET) calls for clinical deterioration at an Australian hospital. Specifically, we studied the diagnostic yield and presence of alternative diagnoses.

METHODS**:** We performed a retrospective study of all patients who underwent CTPA for suspected PE within 24 hours of a MET call at The Alfred Hospital, Melbourne between 1 January 2017 and 31 December 2017. Demographic details, clinical history and imaging results were analysed.

RESULTS**:** 155 patients underwent CTPA during the study period. PE was diagnosed in 19 patients (12.3%). 94.7% of detected PEs were segmental or larger. CTPA revealed clinically relevant alternative diagnoses in 91 patients (58.7%), most commonly consolidation (24.5%) or moderate to large pleural effusion (11.0%). These were not visible on initial chest x-ray in 40 cases, and had therapeutic consequences in 19 cases (12.3%). Chest x-ray was used as an initial test in 79.3% of patients. Normal chest x-ray predicted a higher rate of PE on CTPA (22.2% vs 9.2%, p=0.037). Other predictors of PE were recent orthopaedic or spinal surgery.

CONCLUSIONS**:** CTPAs performed at our centre in acutely deteriorating inpatients had a higher yield than predicted, revealing a diagnosis of significant PE or other clinically relevant pathology in 70% of patients. While the use of chest x ray as initial investigation may reduce the need for CTPA in some individuals, this retrospective study has demonstrated that the current use of CTPAs in this population in our centre impacted positively on their inpatient progression of care.

116. MATERNAL HIGH-FIBRE DIET REDUCES LUNG EMPHYSEMA AND INFLAMMATION IN OFFSPRING PREDISPOSED TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Currently, no cure exists for Chronic Obstructive Pulmonary Disease (COPD); a progressive lung disease that leads to airflow limitation in the lungs and comprises varying degrees of emphysema and chronic bronchitis. It is estimated that 251 million people are affected by COPD worldwide and treatments to prevent disease symptoms and complications are currently inadequate, therefore, novel treatment strategies are urgently required. Recent studies have shown that mice offspring of dams fed a high-fibre diet during pregnancy and lactation are protected from the development of asthma. However, the ability of a high-fibre maternal diet to modulate lung damage in offspring 'at risk' of developing COPD is unknown.

AIM: To determine if a maternal high-fibre diet will attenuate the development of lung emphysema, inflammation and mucus metaplasia in offspring, using a preclinical model of COPD, the $Hck^{up/up}$ mice.

METHODS: Pregnant $Hck^{up/up}$ mice were fed a high-fibre diet (SF11-029) or a standard control diet (AIN-93G) throughout pregnancy and weaning. Mice pups were reared onto the same diet administered through pregnancy and weaning until 4 or 12 weeks of age to examine the effect of high-fibre on lung emphysema, inflammation and mucus metaplasia.

RESULTS: Mice offspring of dams fed a standard, control diet developed severe mucus metaplasia at 4 weeks and increased immune cell infiltration and airspace diameter at 12 weeks. Comparatively, mice offspring of dams fed a high-fibre diet were protected against COPD, showing reduced inflammation and airspace enlargement at 12 weeks and reduced mucus metaplasia in the airspaces at 4 weeks, compared to the age-matched control diet fed mice offspring.

CONCLUSION: A maternal diet rich in high-fibre protects 'at risk' offspring from the development of COPD-like characteristics in adulthood. These findings provides novel insight into how dietary modulation during pregnancy can positively influence lung health in offspring susceptible to respiratory illnesses.

117. OPTIMISING THE ALFRED STEP TEST EXERCISE PROTOCOL (A-STEP) AS A MAXIMAL EXERCICE CAPACITY TEST FOR ADULTS WITH CYSTIC FIBROSIS

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After developing and feasibility testing the A-STEP an incremental, maximal exercise capacity test for adults with Cystic Fibrosis (CF) (replacing the previously used submaximal 3 Minute Step Test), a number of clinical concerns were identified.

AIM: To identify and address limitations to optimise usefulness of the A-STEP.

METHODS: A review of each patient's individual assessment information was undertaken to ascertain all parameters that restricted the test.

RESULTS: In the safety/ feasibility study A-STEP was maximal for 32/40 (80%). 42.5% reached [1] ≥ 90% age predicted HR max; 42.5% [2] ≥ 9 or 10/10 for maximal shortness of breath (SOB) and 55% [3] ≥ 9 or 10/10 for maximal leg fatigue (MLF). In order for the ASTEP to be a maximal test in the future patients must achieve at least one of the following: [1] ≥ 90% age predicted HR max; [2] ≥ 9 or 10/10 for SOB ; [3] ≥ 9 or 10/10 for MLF and an additional Level 16 has been added to the 15 Level test. For safety, a trained physiotherapist should perform the A-STEP with medical support as oxygen desaturation is allowed to 80% and a non-slip mat and therapist's foot to stabilise the step is now recommended. Instructions to patients to limit movement artefact have been included to ensure a steady oximetry trace. Patients should be well hydrated before testing with water available. Use of bronchodilators should be individualised as may result in pre-test tachycardia. Patients should be reminded to wear appropriate clothing, as this resulted in submaximal testing in a small number of patients.

CONCLUSION: A-STEP limitations were identified and addressed around objective physiological criteria, number of test levels, safety concerns, patient preparation and physical aspects of carrying out the test. The optimised A-STEP is a safe, maximal exercise capacity test for adults with CF.

118. WEIGHT AND BODY COMPOSITION CHANGES FOLLOWING ONE YEAR OF TREATMENT WITH LUMACAFTOR-IVACAFTOR IN SEVERE CYSTIC FIBROSIS LUNG DISEASE

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The impact of lumacaftor-ivacaftor (LUM-IVA) on body composition is not widely studied, particularly in severe cystic fibrosis (CF) lung disease.

AIM: To evaluate changes in body composition in adults with CF with FEV_1< 40% predicted over 12 months of LUM-IVA treatment.

METHODS: Data were analysed for 24 CF adults (13 male, baseline age: 32.6±8.6 years, FEV_1%predicted: 34.7±7.4%, BMI: 20.3±2.7kg/m^2), who received LUM-IVA for 12 months under a managed access program. Body composition (tetrapolar multifrequency BIA, SECA, Germany) was measured at baseline, 1, 6 and 12 months. Absolute changes (Δ) in BMI, weight, fat-free mass (FFM) and fat mass (FM); and %Δ in weight from baseline were determined. Analyses were performed using linear mixed effects regression modelling and Pearson's correlation.

RESULTS: No weight change was seen at one month. Weight increased significantly in the first 6 months (mean±SD %Δweight0-6mth: 3.9±1.7%, p=0.03) and was maintained by 12 months (%Δweight 0-12mth +4.9±7.3, p=0.003). BMI increased significantly at 6 months (+0.8±1.3kg/m^2, p=0.005), plateauing by 12 months (ΔBMI 6-12mth: 0.1±1.1kg/m^2, p=0.65). Fat mass increased significantly at 6 months (ΔFM-0-6mth: 1.8±2.5kg, p=0.003), but plateaued by 12 months (ΔFM6-12mth: 0.7±1.9kg, p=0.12). No changes were seen in mean FFM (ΔFFM-0-12mth: 0.02±2.2kg, p=0.96), indicating overall preservation of FFM. Lower baseline BMI was associated with higher weight gain (r= -0.54, p=0.006) and FFM (r= -0.57, p=0.005) at 12 months. The % of patients with BMI<18.5kg/m^2 decreased from 33% at baseline to 13% at 12 months (p=0.003, McNemar's test).

CONCLUSIONS: Gains in weight, BMI and fat mass seen over the first six months on LUM-IVA are attenuated by one year. In this cohort, underweight patients were more likely to improve BMI and body composition. Mechanisms underlying body composition changes require further investigation, including improved appetite, salt/hydration or exercise, or via amelioration of catabolism.

TRAUMA / EMERGENCY MEDICINE

119. THE POTENTIAL OF HEAD ACCELERATION MEASUREMENT TO AUGMENT CURRENT BEST PRACTICE IN CONCUSSION SCREENING IN THE AUSTRALIAN FOOTBALL LEAGUE (AFL) AND AUSTRALIAN FOOTBALL LEAGUE WOMEN'S (AFLW)

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Concussion is common in contact sports such as Australian football, with a reported incidence of 6 to 8 concussions per 1000 player hours at the elite level. Development of wearable sensor systems has facilitated in vivo measurement of the head's kinematics during sport. Limited options exist for non-helmeted mounted wearable accelerometer devices suitable for application in Australian football.

AIM: To explore the feasibility and potential utility of a non-helmeted mounted wearable accelerometer for detecting high head acceleration events (HAEs) to augment identification of elite Australian Football League (AFL) & Australian Football League Women's (AFLW) players for concussion screening.

METHODS: A prospective observational study with 92 AFL and 118 AFLW players recruited during the 2017 season. The X-Patch® wearable accelerometer identified players with high HAEs defined as > 95 g (males) and > 85.5 g (females) which were compared to players identified for sideline assessment. High HAEs were verified using video footage and a subset of videos were reviewed for players demonstrating concussive signs by a trained medical reviewer blinded to accelerometer outputs.

RESULTS: High HAEs were recorded for 26 players (50% male). Ten of these players were not visible on video at the time of the HAE, so head impacts could not be confirmed. Of the remaining 16 players, two were identified by club personnel and had signs of concussion on video. Among the 14 players not identified, seven had head impacts that could be confirmed on video, and seven were visible in the footage however no head impact was identified. Among 184 players who did not record high HAEs, five players were identified to have potential concussion.

CONCLUSION: HAEs as measured by the X-Patch® are not sufficiently reliable to be used in practice for screening AFL & AFLW players. This research demonstrates the challenges of using the X-Patch® to improve screening for concussion.

120. OUT-OF-HOSPITAL CARDIAC ARREST OUTCOMES ACCORDING TO THE LEVEL OF TRAINING AND THE RELATIONSHIP TO THE PATIENT OF THE PERSON PROVIDING BYSTANDER CARDIOPULMONARY RESUSCITATION.

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BACKGROUND**:** Bystander CPR (byCPR) has been associated with improved outcomes in Out-of-hospital Cardiac Arrest (OHCA). In this study, we describe the relationship to the patient of the person providing byCPR, their level of training and the influence these had on patient outcomes.

METHOD**:** Non-traumatic OHCA who received byCPR and Emergency Medical Services resuscitation from 1/1/2015 - 31/12/2017 were included from the Victorian Ambulance Cardiac Arrest Registry. Ambulance Victoria patient care reports were analysed to ascertain the relationship to the patient of the person providing byCPR and their level of medical qualification. We performed multivariable logistic regression to assess the association between survival to hospital discharge and 1) Related-byCPR (family, friends and colleagues), and 2) Med-byCPR (healthcare professional providing by-CPR).

RESULTS**:** We found that 2385 (53.4%) OHCA patients received byCPR from a relative, 468 (10.5%) from a friend or colleague and 1611 (36.1%) from a bystander unrelated to the patient. Of those providing byCPR 3703 (83%) were laypersons and 761 (17%) were healthcare professionals. Using multivariable regression analysis, adjusted for known Utstein factors, we found Med-byCPR was associated with increased odds of survival to hospital discharge (14.5% vs 13.8%, OR:1.4 [95% CI: 1.02 – 1.92]) compared to those who received Lay-byCPR. We found no association between the relationship to the patient and survival to hospital discharge.

CONCLUSION**:** Bystander CPR from a healthcare professional was associated with increased survival. This is an important finding and has implications when planning the dispatch of community responders to cardiac arrest patients.

121. REDUCTION IN OXYCODONE USE AFTER IMPLEMENTATION OF AN ANALGESIC LADDER IN THE EMERGENCY DEPARTMENT

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Opioids are increasingly being used to treat pain in the Emergency Department (ED) despite little evidence of benefit and long-term safety. The widespread misuse of prescription opioids is a current 'crisis' being faced in many countries, with Australia following the same path.

AIM: To assess the introduction of an analgesic ladder and targeted education on oxycodone use for patients presenting with back pain to the ED.

METHODS: This retrospective cohort study was conducted pre- and post-implementation of a new ED analgesic ladder and guideline in the EDs of a major metropolitan health service in May 2017. Data were collected from June to July 2016 and June to July 2017 including consecutive adult patients who presented to the ED with back pain and were admitted to emergency short stay units at The Alfred and Sandringham EDs in Melbourne, Australia. Outcome measures were the proportion of patients prescribed oxycodone and total doses administered.

RESULTS: There were 107 patients pre-intervention and 107 patients post-intervention included in this study. After implementation of the analgesic ladder, the proportion of patients who were prescribed oxycodone significantly decreased from 72.9% (78/107) to 51.4% (55/107; p=0.001). Among patients who received oxycodone during their stay in the ED, the total median dose administered was 14mg before (IQR: 5-20mg) and 5mg (IQR: 5-10mg) after implementation of the analgesic ladder (p<0.001). On discharge from hospital, a prescription for oxycodone was issued for 36 (33.6%) patients pre-intervention and 26 (24.3%) patients post-intervention (p=0.13).

CONCLUSION: Implementation of an analgesic ladder was associated with a statistically significant but modest reduction in oxycodone prescription for back pain. Rather than intensive interventions directed at changing clinician behaviour, serious consideration should be afforded to restricting supply of oral opioids in the absence of stringent indications.

122. PASSING STONES DOWN UNDER: A MULTICENTRE EVALUATION OF ACUTE URETERIC COLIC IN AUSTRALIA

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INTRODUCTION AND AIM: Ureteric lithiasis is among the most common acute urological presentations in Australia. With the number of stone procedures is increasing, the decision for intervention versus conservative management remains controversial. MIMIC is the largest international retrospective cohort study evaluating the management decisions and outcomes for patients presenting to hospital with confirmed stone disease. This study is an analysis of data contributed to the collaboration from health networks across Australia.

METHODS: This study is a multicentre international cohort coordinated by the Australian Young Urology Researchers Organisation (YURO) and British Urology Researchers in Surgical Training (BURST). Retrospective analysis of electronic medical records was performed at participatin Australian sites from 1/5/17-1/1/18. Inclusion criteria were patients presenting with acute renal colic and computed tomography (CT) evidence of a single obstructing ureteric calculi who were discharged with non-operative management. The primary outcome of stone passage was confirmed with repeat CT imaging after a minimum of 6 months. Patients with multiple stones or who had a subsequent presentation were excluded from the study. Data was entered into a centralised REDcap database and multivariate analysis was performed on: patient age, sex, previous history, location of presentation, stone size and position.

RESULTS: Data was collected from 400 patients entered from 6 health networks across Australia. Most patients (72%) were discharged with conservative management and of those over two thirds had a confirmed outcome of being stone-free or had another admission for intervention with the remainder being lost to follow up. Three quarters of Australian patients experienced spontaneous passage with the remainder requiring surgical intervention. Spontaneous resolution of ureteric lithiasis was dependant on calculus size, with 79% of stones under 6mm and one third of stones larger than 6mm passing spontaneously. Clearance was affected by anatomical location with proximal, mid and lower/distal ureteric stones passing with increasing rates respectively.

CONCLUSIONS: This study represents the most comprehensive data set for the contemporary management of ureteric colic both within Australia and internationally. The dataset collected from the Australian hospitals largely reflected the international cohort. Associations between stone size, stone position and need for intervention were identified. The results of this study can be used to inform management practice both within Australia and internationally.

123. LACTATE, BICARBONATE AND ANION GAP FOR EVALUATION OF PATIENTS PRESENTING WITH SEPSIS TO THE EMERGENCY DEPARTMENT: A PROSPECTIVE COHORT STUDY

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A serum lactate level > 2 mmol/L has been chosen as the preferred cut-off value for screening of patients with suspected sepsis, however it has been hypothesized that that alternate measures of acidaemia such as the anion gap or serum bicarbonate may also be useful in screening of patients with suspected sepsis.

AIM: To determine the outcomes of patients with initial lactate levels ≤2 mmol/l, but abnormal bicarbonate or anion gaps, in patients with suspected sepsis presenting to the Emergency Department.

METHODS: This prospective cohort study enrolled patients from an adult tertiary referral hospital who presented with suspected sepsis. The predictive value of lactate, bicarbonate and the anion gap for intensive care unit (ICU) admission and death at hospital discharge were evaluated using area under receiver operative curves (AUROC).

RESULTS: There were 441 patients with suspected sepsis enrolled from February 2016 to June 2017. There were 96 (22.0%) patients who were admitted to the ICU and at hospital discharge, 42(9.6%) patients had died. There was no statistically significant difference between the AUROCs of lactate or bicarbonate level or anion gap to predict ICU admission (p=0.17). There was no statistically significant difference between the AUROCs of lactate or bicarbonate level or anion gap to predict mortality at hospital discharge (p=0.44). Among the 73 patients with normal lactate levels, but abnormal bicarbonate or anion gap, there were 7 (9.6%) deaths.

CONCLUSION: A normal lactate level alone should not be used to exclude life-threatening sepsis. Patients with metabolic acidosis characterised by low bicarbonate or high anion gap levels, but with normal lactate levels, have high rates of ICU requirement and mortality and should also be considered for early, aggressive therapy.

124. HYPOCALCAEMIA IN SHOCKED TRAUMA PATIENTS: A RETROSPECTIVE COHORT STUDY

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BACKGROUND: Haemorrhagic shock continues to be the most common preventable process after major trauma. Haemorrhage-associated calcium loss leads to disruption of platelet function, intrinsic and extrinsic pathway-mediated haemostasis and cardiac contractility. Among shocked major trauma patients, we aimed to investigate the association between hypocalcaemia on presentation and adverse outcomes.

METHODS: Data were extracted from the Alfred Health Trauma Registry and Applications and Knowledge Management Department for all major trauma patients from 1st July 2014 to 30th June 2018 presenting directly from the scene with a shock index (SI) ≥1. Patients with pre-hospital blood transfusion were excluded. Ionized hypocalcaemia was defined as <1.11mmol/L and acute traumatic coagulopathy (ATC) was defined as an initial INR>1.5. Multivariable logistic regression analysis was used to assess the association between admission hypocalcaemia and ATC.

RESULTS: There were 226 patients included in final analysis with 113 (50%) patients recording ionized hypocalcaemia on presentation to the trauma centre prior to any blood product transfusion. Ionized hypocalcaemia was associated with coagulopathy in patients with SI≥1 (adjusted OR 2.9; 95% CI: 1.01-8.3, p=0.048). Admission ionized hypocalcaemia was also associated with blood transfusion requirement in the first 24 hours post-admission in 62.5% of hypocalcaemic patients as compared to 37.5% of normocalcaemic patients (p<0.001). Finally, admission ionized hypocalcaemia was associated with death at hospital discharge (25.6% among hypocalcaemic patients compared to 15.0% of normocalcaemic patients).

CONCLUSION: Hypocalcaemia was a common finding in shocked trauma patients and was independently associated with acute traumatic coagulopathy. Proactive administration of calcium to trauma patients in haemorrhagic shock may be beneficial and warrants further assessment in randomised controlled trials.

125. EFFECT OF EARLY SUSTAINED PROPHYLACTIC HYPOTHERMIA ON NEUROLOGIC OUTCOMES AMONG PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY: THE POLAR RANDOMISED CLINICAL TRIAL

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After severe traumatic brain injury, induction of prophylactic hypothermia has been suggested to be neuroprotective and improve long-term neurologic outcomes.

AIM: To determine the effectiveness of early prophylactic hypothermia compared with normothermic management of patients after severe traumatic brain injury.

METHODS: The POLAR study was a multicentre randomized trial in 6 countries that recruited 511 patients both out-of-hospital and in emergency departments after severe traumatic brain injury. There were 266 patients randomized to the prophylactic hypothermia group and 245 to normothermic management. Prophylactic hypothermia targeted the early induction of hypothermia (33°C-35°C) for at least 72 hours and up to 7 days if intracranial pressures were elevated, followed by gradual rewarming. Normothermia targeted 37°C, using surface-cooling wraps when required. Temperature was managed in both groups for 7 days. All other care was at the discretion of the treating physician.

RESULTS: Among 511 patients who were randomised, 500 provided ongoing consent (mean age, 34.5 years [SD, 13.4]; 402 men [80.2%]) and 466 completed the primary outcome evaluation. Hypothermia was initiated rapidly after injury (median, 1.8 hours [IQR, 1.0-2.7 hours]) and rewarming occurred slowly (median, 22.5 hours [IQR, 16-27 hours]). Favourable outcomes (Glasgow Outcome Scale-Extended score, 5-8) at 6 months occurred in 117 patients (48.8%) in the hypothermia group and 111 (49.1%) in the normothermia group (risk difference, 0.4% [95% CI, -9.4% to 8.7%]; relative risk with hypothermia, 0.99[95% CI, 0.82-1.19]; P=.94). In the hypothermia and normothermia groups, the rates of pneumonia were 55.0% vs 51.3% respectively, and rates of increased intracranial bleeding were 18.1% vs 15.4% respectively.

CONCLUSION: Among patients with severe traumatic brain injury, early prophylactic hypothermia compared with normothermia did not improve neurologic outcomes at 6 months. These findings do not support the use of early prophylactic hypothermia for patients with severe traumatic brain injury.

126. CLINICALLY SIGNIFICANT TRAUMATIC INTRACRANIAL HAEMORRHAGE FOLLOWING MINOR HEAD TRAUMA IN A GERIATRIC POPULATION: A RETROSPECTIVE COHORT STUDY

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Head trauma is a significant cause of morbidity and mortality in the elderly population, which may be complicated by intracranial haemorrhage (ICH). Anticoagulation is a risk factor for the development of ICH. Guidelines for the investigation of ICH following asymptomatic, minor head trauma are currently unclear.

AIM: The primary objective of this study was to determine the incidence of clinically significant traumatic intracranial haemorrhage (T-ICH) following minor head trauma in elders. Secondary objectives were to investigate the impact of anticoagulant and antiplatelet therapies on the incidence of T-ICH and to evaluate factors associated with the use of brain computed tomography (CT).

METHODS: This retrospective cohort study extracted data from electronic patient records. The cohort consisted of patients presenting after a fall and/or head injury and presented to one of 5 Quebec City emergency departments (ED) between 1st March 2010 and 31st July 2017. Inclusion criteria were age ≥ 65 years old and a minor head trauma defined as an impact to the head without fulfilling criteria for traumatic brain injury.

RESULTS: From the 1,000 electronic medical records evaluated, 311 cases satisfied inclusion criteria. The mean age was 80.1 (standard deviation 7.9) years. One hundred and eighty-nine (189) patients (60.8%) were on an anticoagulant (n=69), antiplatelet (n=130) or a dual therapy (n=16). Twenty patients (6.4%) developed a clinically significant T-ICH, of which one required neurosurgical intervention and one died after opting against surgery. Two hundred and five patients (65.9%) received a brain CT in the ED. Anticoagulation therapy was associated with greater use of brain CT by clinicians but not associated with an increased risk of clinically significant T-ICH in this cohort.

CONCLUSIONS: In this cohort of geriatric patients presenting to the ED following minor head trauma, the incidence of clinically significant T-ICH was 6.4%. Future research is required to better predict the need for CT brain. In the meantime, this type of imaging should always be considered in this patient group.

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