AlfredHealth

ABSTRACT BOOK

ALFRED HEALTH WEEK RESEARCH POSTER DISPLAY

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CONTENTS

CATEGORY PAGE

CARDIOVASCULAR DISEASES

DIABETES / DIABETIC COMPLICATIONS

GASTROENTROLOGY

HAEMATOLOGY / MALIGNANT HAEMATOLOGY

HEALTH SERVICES / PATIENT SAFETY

INFECTIOUS DISEASES / INFECTION CONTROL

INTENSIVE CARE

MENTAL HEALTH

NEUROSCIENCE

OBESITY

POPULATION HEALTH / EPIDEMIOLOGY

RADIOTHERAPY

RENAL MEDICINE

RESPIRATORY DISEASES / LUNG TRANSPLANTATION

TRAUMA / EMERGENCY MEDICINE

1. OPTIMISING THE BASOPHIL ACTIVATION TEST TO ASSESS EFFICACY OF PEANUT ALLERGY THERAPEUTICS

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BACKGROUND: Peanut allergy is the major cause of food induced anaphylaxis, and currently there is no cure. Gold standard diagnosis of peanut allergy is achieved using double-blind placebo-controlled food challenge, which can be associated with serious adverse effects such as anaphylaxis. More frequently utilised diagnostic tests measure allergen-specific IgE antibodies in the blood which indicates sensitisation, but not always clinical reactivity. The basophil activation test (BAT) is a reliable test of IgE reactivity that correlates closely to the clinical presentation of peanut allergy. The BAT, therefore, is an ideal tool for safely evaluating allergic responses in a clinically relevant manner.
METHODS: Whole blood from peanut allergic patients was incubated with whole peanut extract over a range of concentrations, and activation of basophils assessed by flow cytometry using the cell surface marker CD63. Sensitivity of patient basophils to peanut was assessed using CDsens calculations, and accuracy of different titration curves assessed using linear models.
RESULTS: Peanut allergic patients have different sensitivities to peanut as shown by titration curves and CDsens calculations. CDsens can be calculated accurately using different linear models. Basophil activation results are reproducible over time and laboratory sites.
CONCLUSIONS: The basophil activation test can be utilised as a reliable tool to evaluate peanut sensitivity in peanut allergic subjects. This measurement can be used to assess efficacy of peanut allergy therapeutics, as well as potentially replacing risky food challenges in the future.

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2. CD21 DEFICIENCY: AN UNUSUAL PRESENTATION

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BACKGROUND: Primary Immunodeficiencies are inherited conditions affecting 1 in 10000 individuals worldwide. Biallelic mutations in the CD21-gene impair antibody responses in adults. CD21 is expressed in complex with CD19, CD81 and CD225 on the surface of B-cells. Here, we identified a 9-year old boy with a history of presumed viral illness with fever, upper respiratory tract infection, mouth ulcers and a perianal fissure, accompanied by strongly reduced serum immunoglobulins, and absence of CD21 on mature B- cells.
AIM: To identify the genetic cause of CD21-deficiency and examine the nature of the severe clinical phenotype.
METHODS: We evaluated blood B and T cells with flow cytometry. Surface protein and mRNA transcripts of CD19, CD21 and CD81 were determined from B-cells of the patient and healthy controls. Genomic DNA of the patient was analysed for mutations in the CD21 gene. B-cell Somatic Hypermutations in IgA and IgG transcripts were quantified by sequence analysis.
RESULTS: The patient has normal numbers of B, T and NK cells, but a marked reduction in memory B-cells. CD21 expression was undetectable by one antibody (clone BL13), but detectable, although reduced expression was found with 3 other clones. In addition, CD19 was reduced, whereas CD81 was normal. The patient carried a homozygous missense mutation in exon 10 of CD21 (c.1676G>A; p.G559E), affecting a highly conserved residue in the SRC9 domain, the epitope of clone BL13. IgG and IgA transcripts of the patient showed strongly reduced somatic hypermutations, similar to that observed in CD19-deficient patients.
CONCLUSION: Patient B-cells harbour a unique mutation in CD21, potentially impairing the structure and resulting in reduced surface expression. The instability of CD21 affected CD19 expression, unlike mutations in previously described CD21 patients that showed increased CD19 expression. Taken together, the clinical and immunological characteristics demonstrated an unusual presentation of CD21-deficiency, more reminiscent of CD19-deficiency

3. CD11B REGULATES INFLAMMATION, AUTOIMMUNITY AND ASSOCIATED PATHOLOGY IN A MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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OBJECTIVES: Systemic Lupus Erythematosus (SLE) is a highly complex, heterogeneous autoimmune disease characterized by circulating self-reactive antibodies that deposit in tissues including the kidneys, alongside a chronic inflammatory response that leads to progressive tissue damage and impaired function. Genome-wide association studies have identified a number of receptors and signal transduction molecules specific for the immune system that predispose to the development of SLE. A loss-of-function single nucleotide polymorphism in the *Itgam* gene encoding leukocyte integrin CD11b (rs1143679) has been identified which associates with an increased incidence of SLE, implicating CD11b as a protective factor against disease development.

METHODS: To understand the role that CD11b plays in controlling autoimmune disease, we crossed CD11b deficient mice ($CD11b^{-/-}$) with Lyn deficient ($Lyn^{-/-}$) mice, a well-studied, robust model of human SLE. Double knockout $Lyn^{-/-}$ $CD11b^{-/-}$ mice were analysed over time for development of autoimmune disease and inflammation.

RESULTS: While aged mice lacking CD11b alone did not develop autoimmune disease, deficiency of CD11b on the Lyn-deficient autoimmune-prone background exacerbated disease, driving splenomegaly and lymphadenopathy, extramedullary haematopoiesis, autoantibody production and glomerulonephritis, which heavily impacted survival.

CONCLUSIONS: These findings confirm that CD11b is an autoimmune susceptibility gene that when mutated can exacerbate the severity of disease on a susceptible genetic background. This work highlights an important role for CD11b in regulating and controlling the progression of inflammation and autoimmune disease.

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4. CHANGES IN ANTIBODY RESPONSES INDUCED BY IMMUNOTHERAPY FOR GRASS POLLEN ALLERGY

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BACKGROUND: Melbourne has one of the highest incidences of grass pollen allergy worldwide, affecting approximately 32% of the population. Patients are typically affected by seasonal allergic rhinitis and are at risk of thunderstorm asthma. Currently, there is no cure, however, immunotherapy involving desensitisation to grass pollen allergens can ameliorate symptoms and protect against thunderstorm asthma. The impact of immunotherapy on the immune system is poorly understood.

AIM: To investigate the impact of immunotherapy on immunological memory in patients with ryegrass pollen allergy.

METHODS: 30 allergic patients (50% male) aged 19-59 years were started on preseasonal-only (4 months) sub-lingual immunotherapy for 3 consecutive years using a commercial tablet containing extracts from pollen of five grasses (Oralair®). Allergy symptoms were measured by Visual Analogue Score (VAS/100 mm) during peak season. Patient blood was collected each year prior to the start of Oralair treatment to quantify the antibody response to ryegrass pollen by enzyme-linked immunosorbent assay (ELISA) and examine immune cells by flow cytometry. Statistical significance was determined by t tests of paired variables ($p<0.05$).

RESULTS: Clinical efficacy was confirmed by significant decreases in VAS ($p<0.01$). Ryegrass pollen-specific IgE levels did not change, but specific IgG_2 and IgG_4 antibodies increased with immunotherapy. Furthermore, IgG_2-expressing and IgG_4-expressing memory B cell frequencies increased following treatment with Oralair.

CONCLUSION: Sublingual immunotherapy for grass pollen allergy altered B cell memory towards IgG_2 and IgG_4. As these isotypes are associated with secondary immune responses, it is likely that they are driven by repeated exposure to pollen allergens. IgG_2 and IgG_4 may compete with IgE for allergen binding. Ongoing studies are aimed at understanding how IgG_2 and IgG_4 might ameliorate allergic responses and through which mechanism these isotypes are preferentially induced, as this may lead to optimised strategies for treatment of allergic disease.

5. EFFECT OF HEAT PROCESSING ON IGE REACTIVITY AND CROSS-REACTIVITY OF ASIA-PACIFIC MOLLUSC SPECIES: IDENTIFICATION OF NOVEL SYDNEY ROCK OYSTER TROPOMYOSIN SAC G 1

Varese NP[1,2], Rolland JM[1,2], Abramovitch JB[1,2], Anania J[1,2], Nugraha R[3], Kamath S[3], Hazard A[2], Lopata AL[3], O'Hehir RE[1,2]

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Shellfish allergy is an increasing global health priority, frequently affecting adults. Molluscs are an important shellfish group causing food allergy but knowledge of their allergens and cross-reactivity is limited. Currently optimal diagnosis of mollusc allergy enabling accurate advice on food avoidance is difficult.

AIMS: To assess the IgE reactivity of proteins of four frequently ingested Asia-Pacific molluscs: Sydney Rock Oyster, Blue Mussel, Saucer Scallop and Southern Calamari, and the effect of heat processing on this reactivity. To determine the level of cross-reactivity between mollusc species and cross-reactivity with Blue Swimmer Crab tropomyosin, Por p 1.

METHODS AND RESULTS: Sera from 13 mollusc-sensitised, seafood-allergic subjects (mean age 33.8±9.2 years; 10F/3M) were assessed for IgE reactivity with mollusc extracts. Cooking of the molluscs increased IgE reactivity as measured by IgE ELISA and immunoblotting. Biologically relevant IgE reactivity was confirmed by basophil activation. Strong IgE reactivity of several proteins including a 37-40 kDa protein corresponding to the major shellfish allergen, tropomyosin, was observed for all species by immunoblotting. IgE-reactive Sydney Rock Oyster proteins were identified by mass spectrometry, and the novel major oyster allergen, tropomyosin Sac g 1, was cloned, sequenced and registered with the IUIS. Oyster extracts showed the highest cross- reactivity with other molluscs, while mussel cross-reactivity was weakest. Inhibition IgE immunoblotting demonstrated high cross- reactivity between tropomyosins of mollusc and crustacean species.

CONCLUSION: These findings inform novel approaches for reliable diagnosis and improved management of mollusc allergy.

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6. HUMAN DERIVED FEEDER CELLS AND HUMAN SERUM FOR THE XENO-FREE EXPANSION OF ADULT HUMAN KERATINOCYTES

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BACKGROUND - Cultured Epithelial Autograft (CEA) was the birth of skin tissue engineering, which described methodologies for isolation and expansion of autologous basal keratinocytes for burns treatment, and is currently practiced at some specialized units around the world. One of CEA limitations, however, is its reliance on animal-derived material. Despite all efforts, to date, no xeno-free alternative with proven efficacy has been reported.

OBJECTIVES - Here, we investigated whether human derived fibroblast feeders and human serum can sufficiently and effectively provide a suitable microenvironment for adult keratinocyte isolation and expansion.

METHODS - Human dermal fibroblasts and epidermal keratinocytes, isolated from skin, discarded during abdominoplasty and breast reduction procedures, were cultured in xeno-free conditions.

RESULTS - We report that such xeno-free adult keratinocytes form similar number of colony forming units as Green's method, however, they express lower levels of α6 integrin (CD49f; a progenitor and stem cell marker). We identified IL-8 as a potential growth factor secreted by adult fibroblasts that may enhance adult keratinocyte colony formation in human serum. Finally, we propose, a step-by-step xeno-free isolation and cultivation methodology for adult keratinocytes to be tested further in serial cultivation that can be adapted for clinical application.

CONCLUSIONS - Human derived fibroblasts and human serum can effectively support adult keratinocyte isolation and initial expansion *in vitro*. Future work is required to determine whether the xeno-free system proposed here is sufficient for serial subculture of adult keratinocytes required for grafting.

7. PSYCHOSOCIAL FACTORS OF BURNS PATIENTS ADMITTED TO THE ALFRED VICTORIAN ADULT BURNS SERVICE

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Psychosocial factors specific to acute burns patients have been found to impact on health care interventions and outcomes. The priority focus for psychosocial intervention has been on patients with a higher level of total body surface area (TBSA) burns (20% and above), on particular pre-existing issues (mental health/ drug and alcohol), and patients' reactions to the incident.

AIM: Our study explored the nature of psychosocial factors identified for burns patients given limited research to date into the breadth and impact of issues for this particular cohort. Our hypothesis was that the experience of a burn, irrespective of TBSA, has psychosocial impact across a variety of areas.

METHODS: A retrospective audit of 249 patient medical records and the VABS registry over a one year period using a comprehensive psychosocial assessment tool for data collection.

RESULTS: On average, eight psychosocial factors were identified per patient spread across all eleven domains examined, such as pre-admission issues, injury related issues, and family and social support needs. Nil dominant psychosocial factor or psychosocial domain was experienced across the population. Psychosocial factors were independent of the severity of the burn and pre-admission issues.

CONCLUSION: Given the diversity of psychosocial factors identified across the patient's acute admission (pre, during and post), the need for psychosocial assessment and support across the entire cohort was seen as an effective means of highlighting potential issues and barriers. This approach would also enable early intervention and planning for barriers to discharge.

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8. LOCALISED PROSTATE CANCER: EXAMINING BARRIERS AND FACILITATORS OF PATIENT ADHERENCE TO REPEAT TESTING PROTOCOLS.

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Increased Prostate Specific Antigen (PSA) testing has led to global overdiagnosis and overtreatment of localised prostate cancer. To address this, many clinicians are utilising Active Surveillance (AS), which involves closely monitoring disease by following a repeat testing protocol- PSA tests, digital rectal examinations and biopsies. AS delays active treatment (radical prostatectomy, radiotherapy) until test results indicate disease progression. Thus, AS reduces overtreatment and also delays urinary, sexual and bowel side effects associated with active treatment, improving quality of life. However, there is a worrying trend of low patient adherence to AS protocols, undermining the utility of AS to reduce overtreatment.

AIM: To identify barriers and facilitators of patient adherence to AS protocols, as reported by current literature.

METHODS: To find relevant articles for this literature review, four databases (MEDLINE, EMBASE, CINAHL, CENTRAL) were systematically searched, as is summarised: prostate cancer AND (active surveillance or watchful waiting) AND (adherence or compliance) AND (reasons or factors or barriers or facilitators or enablers.) Results were limited to English and articles were title and abstract screened. RESULTS: Few studies examined barriers and facilitators to AS protocol adherence. Notably, a lack of research reported on factors affecting specific protocol adherence. Instead, many papers investigated factors affecting the transition from AS to active treatment for non- medical reasons. Barriers and facilitators were grouped into non-modifiable factors (such as age, education, race) and psychosocial factors (such as anxiety, uncertainty, family opinions of AS). While psychosocial factors influence the transition from AS to active treatment, little evidence discussed provider delivery of AS protocols, indicating a significant research gap.

CONCLUSION: Despite concerning low patient adherence, this review found little evidence exists on barriers and facilitators to AS adherence. Survey or interview studies should be conducted in cohorts of AS patients to specifically identify reasons for low protocol adherence.

9. DEVELOPMENT OF A BI-NATIONAL THYROID CANCER CLINICAL QUALITY REGISTRY

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BACKGROUND: The occurrence of thyroid cancer is increasing throughout the developed world, including Australia, and since the 1990s has become the fastest increasing malignancy. In 2014, 2,693 Australians were diagnosed with thyroid cancer, with this number projected to rise to 3,300 in 2018.

OBJECTIVES: To establish a bi-national population-based clinical quality registry with the aim of monitoring and improving the quality of care provided to patients diagnosed with thyroid cancer in Australia and New Zealand.

PATIENTS & METHODS: The Australian and New Zealand Thyroid Cancer Registry (ANZTCR) captures clinical data for all patients, over the age of 18 years, diagnosed with thyroid cancer, confirmed by histopathology report, that have been diagnosed, assessed or treated at a contributing hospital. Data is collected by endocrine surgeons using a web-based interface, REDCap, primarily via direct data entry.

RESULTS: A multi-disciplinary Steering Committee was formed, and with operational support from Monash University the ANZTCR was established in early 2017. The pilot phase of the registry is currently operating in Victoria, New South Wales Queensland, Western Australia and South Australia, with over 30 sites expected to come on board across Australia and New Zealand in 2018. A modified-Delphi process was undertaken to determine the key quality indicators to be reported by the registry and a minimum dataset was developed comprising information regarding thyroid cancer diagnosis, pathology, surgery and 30-day follow up.

CONCLUSION: There are very few established thyroid cancer registries internationally, yet clinical quality registries have shown valuable outcomes and patient benefits in other cancers. The establishment of the ANZTCR provides the opportunity for Australia and New Zealand to further understand current practice in the treatment of thyroid cancer and reasons for variation in outcomes.

10. MONITORING QUALITY OF CARE IN PANCREATIC CANCER

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Best practice care can optimise survival and quality of life in patients with pancreatic cancer (PC), but there is evidence of variability in management and suboptimal care for some patients. Monitoring practice is necessary to underpin improvement initiatives.

AIM*:* We aimed to develop a core set of quality indicators that measure the quality of care across the disease trajectory.

METHODS: We performed a modified, three-round Delphi survey among experts with wide experience in the care of PC across three states in Australia. A total of 107 potential quality indicators were identified from the literature and presented to the panel for rating. A further six indicators were later added by the panel experts bringing the total potential quality indicators to 113. The spectrum of care was divided into five areas: diagnosis and staging, surgery, other treatment, patient management and outcomes.

RESULTS*:* Nineteen PC experts from New South Wales, Queensland and Victoria completed the first online consensus round. Thirteen experts met for a face-to-face Delphi meeting for consensus round two and further completed a short online consensus round three. From the 113 potential quality indicators, 34 were considered the most important and feasible indicators to measure quality of care in PC, of which 27 are recommended for inclusion in the final set.

CONCLUSIONS: This study provides a core set of quality indicators to measure quality of care in PC. This indicator set can be applied as a tool for internal quality improvement, comparative quality reporting, public reporting and research. Inclusion of these quality indicators into monitoring databases such as clinical quality registries will enable opportunities for benchmarking and feedback on best practice care to clinicians involved in the management of PC.

11. INTERVENTIONAL RADIOLOGY'S ROLE IN THE MANAGEMENT OF METASTATIC COLORECTAL CARCINOMA. AN ALGORITHM BASED ON CURRENT LITERATURE.

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BACKGROUND: Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the fourth leading cause of death in the world. Hepatic disease accounts for two-thirds of CRC deaths,[i] emphasizing the importance of managing patients with hepatic metastasis. Metastatic colorectal cancer in not a uniform disease. Patient and tumour characteristics vary widely, and current era of treatment is necessarily complex, with the emergence of personalised cancer care. There may be a range of therapies in the armamentarium to choose from which can be suited to the patient and their clinical situation. Choosing the right treatment requires a multidisciplinary approach and is patient dependent.

AIM: To present a treatment al algorithm for management of patients with hepatic metastasis from colorectal cancer.

METHODS: A thorough literature review was conducted, information was assimilated and an algorithm constructed based on potential clinical presentations and treatment options for hepatic metastasis from colorectal cancer.

RESULTS: We outline the methods available to IR for treatment, and describe the nuances for that treatment. We review the evidence for standard and novel IR treatment options including ablation, infusion therapies, embolization (including DEBIRI and radioembolisation), combined and adjunctive techniques (for example Portal vein embolisation).

CONCLUSION: While previously interventional radiology (IR) management in metastatic colorectal carcinoma was directed toward symptom relief and supportive treatment, in recent years there have been rapid advances in IR treatment options. IR treatments are increasingly becoming recognised as disease modifying image-guided therapies that can sometimes be applied with curative intent. We suggest a treatment algorithm for management of patients with hepatic metastasis from colorectal cancer. Knowledge of all treatment options is essential as there continues to be advances in management of CLM.

[i] Donadon M, Ribero D, Morris-Stiff G, Abdalla EK, Vauthey JN New paradigm in the management of liver-only metastases from colorectal cancer. Gastrointest Cancer Res. 2007 Jan; 1(1):20-7

12. WHEN TO RESECT? MANAGEMENT OF PATIENTS WITH ADVERSE HISTOPATHOLOGICAL FEATURES POST COLONOSCOPIC POLYPECTOMY

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Most bowel cancers commence as benign, non- threatening growths, termed polyps, which are usually harmless but can develop into cancerous tumours. Evidence based management of colorectal polyps with residual malignancy is poor and advising patients on the best course of action after removal is difficult. The pathological examination of the malignant polyp can provide important prognostic information, essential in clinical management.

AIM: The aim of this study was to assess the surgical management and overall survival of patients with residual foci of malignancy and/or adverse histopathological features post polypectomy where major resection is undertaken as definitive treatment.

METHODS: An analysis was conducted of a prospectively collected, clinician-led colorectal cancer database of private and public patients in Victoria, Australia from 2010-2017. Patient characteristics, surgical detail and histological outcomes together with patient follow-up were examined.

RESULTS: A total of 176 treatment episodes were analysed in the study period. Age range 22-88 years, 48% male. Pre-operative carcinoembryonic antigen tests were performed in 47% of cases, range 0.2-41.3 μg/L. Clinical follow-up was available in 86.4% of cases and ranged from 21 days to 6.7 years. Median lymph node harvest was 14 with malignant lymph nodes (including a mesenteric tumour deposit) detected in 14 patients (8%). Surgical entry included 8 robotic cases and 1 transanal total mesorectal excision. Follow-up data revealed 137 alive no recurrence, 6 alive with disease, 1 alive with second primary cancer and 7 deceased (other causes). Metastatic disease developed in 8 patients (4.5%), detection date range 0.7-4.7 years.

CONCLUSION: The appropriate management of residual disease and/or adverse histopathological features post colonoscopic polypectomy is challenging in many cases and concerns of 'over- treatment' are often raised. Our study revealed that malignant nodes were harvested in 8% of patients and may guide clinicians and patients in their choice of treatment.

13. INFLUENCE OF URETHRA CONTOURING ON NTCP MODELS PREDICTING URETHRAL STRICTURES IN PROSTATE HDR BRACHYTHERAPY

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AIM: HDR brachytherapy (HDRB) in combination with external beam radiotherapy (EBRT) is an established technique shown to achieve effective dose escalation in the treatment of prostate cancer. Despite its wide use there is still large variability between centres in the choice of dose prescriptions and dose limits to the organs at risk. This is particularly true for the urethra for which large variability also exists between contouring protocols.The aim of this work was to understand the influence of urethra contouring on urethral stricture NTCP model parameters.

MATERIAL AND METHODS: The Lyman-Kutcher-Burman (LKB) model was used in the study. DVHs, clinical and toxicity data were prospectively collected for a first cohort of 262 patients from a single institution (PD= 18Gy in 3, 19Gy in 2 and 17Gy and 2 fractions) and used to fit LKB model parameters with maximum likelihood. DVHs were corrected for equieffective dose in 2Gy fractions, $EQD2_{\alpha/\beta=5Gy}$. The urethra was contoured around the external diameter of a 22 Fr gauge three-way indwelling urinary catheter as a solid structure, from typically 1 cm below the apex to the bladder base. The end-point was stricture requiring urethrotomy within 4 years after RT completion, with an average rate of 12.6%. The model was internally validated using bootstrapping. Data from a second cohort of 187 patients from another institution treated as part of the TROG03.04 RADAR trial were then collected. PD was 19.5Gy in 3 fractions and the stricture rate was 8.6%. Both cohorts had identical EBRT doses.

For the second cohort urethras were initially contoured as the visible lumen of the urinary catheter (original) and, then for a subset of 100 patients, urethra contours were expanded 2mm in the AP and LR direction and limited in the SI direction to be similar to the first cohort's contours (expanded). Both structures' DVHs and associated clinical data were used to externally validate the LKB parameters obtained with the first cohort. Calibration was used to establish agreement between model estimated probabilities and observed stricture rates.

RESULTS: For the first cohort of 262 patients the risk of urethra stricture was modelled by means of a sigmoid function of EUD (LKB Model: TD50=70.7Gy, n=0.3 and m=0.37). Bootstrapping confirmed the parameters. The internal calibration is shown in Fig 1a. For the second cohort of 187 patients comparison between observed toxicity and NTCP predictions of the LKB Model with the original DVHs showed poor calibration (Fig 1b), while for the subset of patients with the expanded urethra the calibration was considerably improved (Fig 1c).

CONCLUSION: In the treatment of prostate cancer with HDRB there are still no general recommendations for urethral dose constraints. This work shows that to understand the relationship between dose and toxicity consensus for the outlining of the urethral volume is needed. This in turn has implications for the application of urethral complication prediction in extreme hypofractionation.

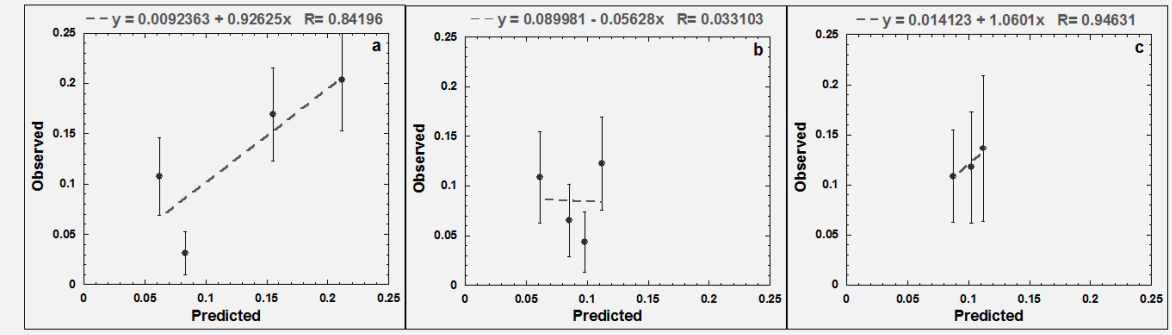

Figure 1: Calibration plots showing observed toxicity rates vs model estimated toxicity probabilities. For each curve the trend line and its equation are displayed. 68% confidence intervals are also shown.

14. CRANIOCERVICAL HEMANGIOPERICYTOMAS – LOCAL RECURRENCE & DISTANT METASTASES

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BACKGROUND: Haemangiopericytomas are rare mesenchymal tumours with propensity to recur locally and metastasise distantly. Gross total resection remains the cornerstone of management with post- operative radiotherapy a potential adjunct. Tumours located in deep regions pose complex management challenges as safe maximal excision may be limited by proximity to eloquent structures.

We report the unique case of a fifty-five-year-old male with local recurrence of a previously resected craniocervical haemangiopericytoma and new metastatic cerebellar deposits, and review management at this anatomically complex region.

Haemangiopericytomas are rare but important differentials for lesions at the craniocervical junction. Despite advances in neurosurgical techniques, surgical management remains complex as dissection endangers lower cranial nerves, vertebral arteries and brainstem. Traditional techniques include the anterior transoral and posterolateral approaches, although both provide restricted exposure to posterolateral and medial surfaces.

Alternative transcondylar and extended lateral approaches, combined with occipitocervical fusion, have allowed for increased radicality of surgery and reported improved survival rates. Redo resection would likely be complicated by the added difficulty of scar tissue and adherent dura. Emergent surgical resection of the cerebellar metastases to relieve obstructive hydrocephalus was performed in this case. The patient elected for radiotherapy to the craniocervical recurrence, together with adjuvant radiotherapy to the cerebellar resection cavities.

This is the first reported case to our knowledge of recurrent haemangiopericytoma at the craniocervical junction with intracranial metastases. Whilst radiotherapy remains an adjunct rather than substitute for gross total excision, cases of recurrence in eloquent locations may advocate for consideration of stereotactic radiosurgery as the primary treatment.

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15. USE OF THE HANSEN MEDICAL MAGELLAN VASCULAR ROBOT IN TRANS-ARTERIAL CHEMOEMBOLISATION OF LIVER TUMORS

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INTRODUCTION: TACE is offered as a first line treatment for patients suffering incurable inoperable HCC with preserved liver function or as a bridge to curative treatment. Technical success is dependent on the ability to selectively catheterise feeding vasculature. Failure to do so may be due to atherosclerotic disease, aberrant anatomy, previous interventions or extreme angles.

PURPOSE: The aim of the study was to retrospectively audit the procedural results of the use of the Hansen Magellan vascular robot at a single center for the treatment of primary liver tumours in patients with challenging arterial anatomy.

METHODS: Retrospective cohort of 6 patients. Patients were selected by experienced interventional radiologists. Patients that were deemed to have arterial anatomy challenging for conventional angiographic techniques on pre-operative imaging studies (CT triphasic liver protocol) or that had failed previous attempts to catheterize. Data collected included demographics, primary diagnosis and staging, target lesion details, procedural details, complications and side effects.

RESULTS: A total of 6 patients were treated by two experienced interventional radiologists at a single institution using the Magellan Hansen Vascular Robot (Hansen Medical, Mountain View, California). Selective catheterisation of target feeding vessels was achieved successfully in all 6 cases with an average fluoroscopy time of 36:50 minutes. Technical success rate was 100% and there was no dissection of catheterised vessels.

CONCLUSION: The Magellan Vascular robot system is a safe and feasible tool for use in TACE and may offer benefits in patients deemed to have challenging arterial anatomy.

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16. LYL1 IS REQUIRED FOR SELF-RENEWAL OF NUP98-HOXD13 (NHD13) THYMOCYTES, BUT ITS ABSENCE PROMOTES T-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA

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T-cell acute lymphoblastic leukaemia (T-ALL) can be classified into a number of subfamilies, including those that overexpress TAL1/LMO, the TLX1/3 and HOXA transcription factors. Whilst it has been previously shown in mouse models that TAL1/LMO transcription factors induce thymocyte self-renewal, whether this is the case for other transcription factor subclasses is currently unknown. To address this, NUP98-HOXD13 transgenic mice (NHD13-Tg), which overexpress HOXA transcription factors, were used as a model system to study thymocyte self-renewal and T-cell leukaemia.

NHD13 induces a differentiation block in T-cell development at the DN2 ($CD44^+/CD25^+/Kit^+$) stage that precedes T-ALL development in approximately 15% of NHD13-Tg mice. NHD13-Tg thymocytes were found to engraft the thymus of recipient mice in serial transplantation assays and blocked the import of thymic progenitors from the bone marrow in YFP cell lineage tracing assays, which demonstrates that NHD13-Tg thymocytes have self-renewal capacity. Transcriptome analysis showed that NHD13-Tg thymocytes exhibit a Stem-Cell like transcriptional program which closely resembled that induced by Lmo2 in the CD2-Lmo2 transgenic mouse, including Lmo2 itself, and the critical Lmo2 cofactor Lyl1.

Analysis of NHD13-Tg mice on the Lyl1-null background showed that Lyl1 was required for thymocyte self-renewal and expression of the Lmo2-like Stem Cell gene expression program but its absence did not affect NHD13-induced HOXA gene expression. Furthermore, thymic cellularity was not rescued in NHD13-Tg; $Lyl1^{-/-}$ mice, due to the maintenance of an aberrant DN3 ($CD44^-/CD25^+/Kit^+$) population and despite the inability NHD13-Tg; $Lyl1^{-/-}$ thymocytes to self-renew, the absence of Lyl1 in NHD13-Tg mice promoted the rapid onset of T-ALL.

These studies demonstrate that Lyl1 is essential for self-renewal of NHD13-Tg thymocytes and suggest that Lyl1 is central to a common oncogenic Lmo2/Lyl1 dependent pathway in T-ALL. However alternative pathways, which in this model are thought to involve HOXA genes, are sufficient to promote T-ALL.

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17. THE IMPACT OF RENAL IMPAIRMENT ON THE PERIOPERATIVE OUTCOMES OF COLORECTAL CANCER SURGERY PATIENTS

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Colorectal cancer is the second most common cancer in Australia with almost 17,000 new cases reported in 2017. We hypothesised that colorectal cancer patients with renal impairment would have poorer perioperative outcomes.

AIM: The aim of this study was to assess the impact of renal impairment on perioperative colorectal cancer surgery outcomes, as compared to a reference population without renal comorbidities, and to examine factors affecting perioperative risk.

METHODS: We conducted an analysis of a prospectively collected, clinician-led colorectal cancer database of Cabrini Hospital and The Alfred Hospital patients from 2010-2017. Patients with renal comorbidities were compared to patients with no renal comorbidities on a range of perioperative outcomes and statistical tests.

RESULTS: A total of 3162 patients were analysed over 3358 treatment episodes in the study period including 144 patients (145 episodes) with renal comorbidities. Follow up (available in 71% of patients) ranged from 3 days (inpatient death) to 7.5 years. Renal impairment contributed to significantly increased inpatient death (Odds Ratio (OR) 4.76, 95% Confidence interval (CI) 1.60-14.2, p=0.005), 30-day mortality (OR 5.18, 95% CI 1.93-13.88, p=0.0011) and medical complications (OR 2.23, 95% CI 1.38-3.62, p=0.001). There was no significant effect on surgical complications (p=0.304). Renal impairment contributed to increased death from all causes compared to patients with no renal impairment (OR 1.76, 95% CI 1.14-2.7, p=0.01).

CONCLUSION: In this study of a large number of private and public patients with follow up, renal impairment contributed to increased death overall and increased perioperative complications. Further analysis is underway to determine other perioperative risk factors that contribute to poor outcomes in colorectal cancer patients with renal impairment

18. DIPEPTIDYL PEPTIDASE 4 INHIBITOR SITAGLIPTIN REDUCES TUMOUR-ASSOCIATED METASTASES IN AN EPITHELIAL OVARIAN CANCER MOUSE MODEL

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Current methods used to treat epithelial ovarian cancer (EOC) often result in relapse and acquired chemo-resistance; therefore, novel therapies for EOC are urgently needed. Immunotherapy for the treatment of EOC is gaining traction, as the success of anti- tumour immune responses in this cancer is heavily dependent on tumour-infiltrating immune populations. Recent studies have suggested that the clinically approved dipeptidyl peptidase 4 (DPP4) inhibitor sitagliptin can activate the immune system, but this has not been demonstrated in an ovarian cancer context.

We evaluated the anti-tumour effects of sitagliptin *in vivo* using an ID8 ovarian cancer syngeneic mouse model. C57BL/6 mice were intraperitoneally inoculated with ID8 EOC cells, and treated with sitagliptin (oral, 25, 50 or 100mg/kg/body weight/day) 14 days following inoculation until endpoint (28 days). Flow cytometry was used to evaluate T cell, dendritic cell (DC), macrophage and myeloid-derived suppressor cell (MDSC) populations in the tumour, spleen, and in circulation. The specific activity of circulating DPP4 and tumour-associated DPP4 expression in the tumour was reduced following sitagliptin treatment.

We demonstrated that oral administration of sitagliptin reduced the quantity of tumour nodules in mice bearing ID8 tumours. Sitagliptin treatment increased tumour-infiltrating CD3+ total and CD3+CD4+FoxP3- effector T cells, and decreased Ki67+ proliferating CD3+CD4+CD25+FoxP3+ T regulatory cells and CD3+CD8+ cytotoxic T cell apoptosis. In addition, sitagliptin increased circulating DCs and total macrophages, increased activated macrophages in the spleen, and decreased tumour-associated MDSCs.

Taken together, these results suggest oral administration of sitagliptin may decrease EOC- associated metastases by altering the immune profile of mice bearing ID8 tumours and may have therapeutic potential for epithelial ovarian cancer.

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19. IMPLEMENTATION AND EVALUATION OF A NURSE-LED ATRIAL FIBRILLATION EDUCATION PROGRAM

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INTRODUCTION: Atrial fibrillation (AF) is the most common type of irregular heart rhythm and a significant cause of morbidity, mortality and reduced quality of life in patients who are symptomatic. AF is responsible for a significant societal financial burden both in terms of costs and burden on healthcare systems. Strategies aimed at improving patient outcomes and reducing the demand on healthcare systems need to be considered. One model of care that may improve management of patients with AF is 'nurse-led care'. Authors of previous studies have shown that nurse-led management interventions have resulted in improved patient outcomes and decreased hospital admissions.

AIM: To assess the safety and feasibility of a nurse-led education program for outpatients with paroxysmal AF.

METHODS: A nurse-led intervention incorporated an individualised treatment in collaboration with medical staff, an individualised education plan, verbal and written tailored educational material and a personalised 'AF management plan' that included instructions on when to present to hospital in the event of worsening symptoms. Safety outcome measures included adverse events, deaths and patient satisfaction. Feasibility outcome measures included protocol implementation success, complete data collection, satisfactory recruitment and screening processes, and patient acceptability of the intervention

RESULTS: Sixteen participants were recruited. Fifteen participants completed data collection. No adverse events or deaths were reported. Two new hospital presentations were identified in line with the nurse-led protocol. Patient satisfaction was very high. Feedback from participants was supportive, indicating that the majority were positively influenced by the program. Participants particularly valued the ability to have direct contact with the nurse to seek advice, answer questions and alleviate concerns. The protocol was implemented as specified, within the timeframe and budget.

CONCLUSION: The results suggest that a nurse-led AF education program is safe and feasible with positive patient outcomes. Further investigation is required to assess the effectiveness of the intervention.

20. SEX DIFFERENCES IN EXERCISE HAEMODYNAMICS IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFPEF) AND NON-CARDIAC DYSPNOEA (NCD)

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BACKGROUND: Women have a 2.8-fold greater lifetime risk of HFpEF1. Exercise intolerance is a key feature of HFpEF, and a rise in pulmonary capillary wedge pressure (PCWP) with exercise is the gold standard for HFpEF diagnosis2. PCWP normalized to workload and weight is an strong predictor of mortality in HFpEF3. Sex differences in exercise haemodynamics in HFpEF have not been determined.

METHODS: Patients referred for investigation of dyspnoea with exercise right heart catheterisation from 2008-18 were included, and classified as HFpEF with an ejection fraction (EF) ≥50% and a rest PCWP ≥15mmHg or exercise PCWP ≥25mmHg. Patients with NCD had an EF ≥50% and normal resting/exercise PCWP.

RESULTS: 91 HFpEF patients (63% female) and 37 NCD patients (57% female) were included. Women with HFpEF had a higher increment in PCWP with exercise (18.6±4.3 vs. 14.5±6.9mmHg, *p*=0.003). Women achieved a lower workload (39.5±33.9 vs. 55±43.7 W/kg, *p*=0.03), and accordingly the difference in PCWP increment adjusted for workload was more pronounced (36.3±35.3mmHg/W/kg in women, 20.7±21.5mmHg/W/kg in men, *p*=0.001), pictured.

This sex difference in PCWP adjusted for workload was not seen in NCD (11.5±11.7 vs. 8.3±7.99 mmHg/W/kg in women and men respectively, *p*=0.059). There were no sex differences in rest or exercise cardiac index, pulmonary artery (PA) pressure, O_2 consumption, or PA saturation.

CONCLUSION: In HFpEF, women have a markedly higher rise in PCWP with exercise than men, which points to a source of severe symptoms and possible phenotypic differences.

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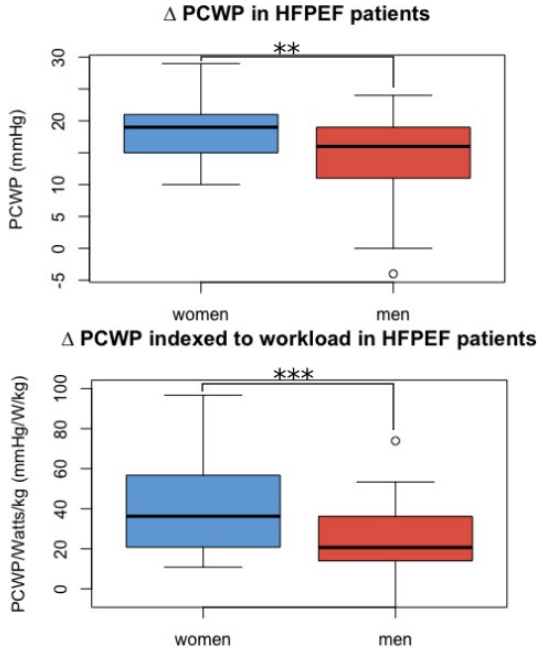

21. IMPACT OF EXTREME OBESITY ON CLINICAL OUTCOMES FOLLOWING PERCUTANEOUS CORONARY INTERVENTION: IS BIGGER BETTER?

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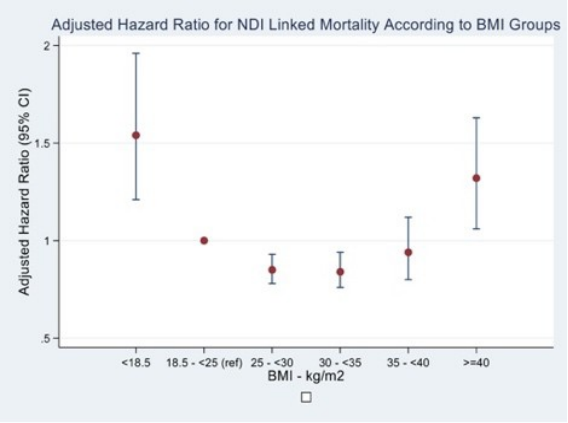
BACKGROUND: Over the last 2 decades, there has been an unprecedented rise in the proportion of overweight and obese individuals, particularly in developed countries including Australia. Previous studies have reported a protective effect of obesity compared to normal body mass index (BMI) in patients undergoing percutaneous coronary intervention (PCI). However, it is unclear whether this effect extends to the extremely obese.

AIM: To examine the impact of extreme obesity (BMI ≥40 kg/m2) on clinical outcomes following PCI in a large multi-centre registry.

METHODS: This retrospective cohort study included 25,645 patients who underwent PCI between 2005 and 2017 and were prospectively enrolled in the Melbourne Interventional Group registry. Patients were stratified by World Health Organization-defined BMI categories and compared. Of these, 24.6% had normal BMI (18.5 – 24.9 kg/m2), 0.9% were underweight (BMI <18.5 kg/m2) and 3.3% were extremely obese. The primary endpoint was National Death Index (NDI)-linked mortality. Mean time to NDI-linked mortality was 4.9±3.4 years.

RESULTS: As BMI increased, mean age decreased while the prevalence of diabetes increased (p<0.001). Those at the extremes of weight were more likely to be female (BMI <18.5 kg/m2: 39.7% female; BMI ≥40 kg/m2: 41.8% female). Overall NDI-linked mortality was highest for underweight patients (37.7%) and lowest for the moderately obese (12.2%). After adjustment for age, comorbidities including diabetes, chronic kidney disease, left ventricular systolic function, and presentation with cardiogenic shock, a U-shaped association was observed between BMI categories and adjusted hazard ratio for NDI-linked mortality. Overweight and mildly obese patients were at lowest risk while both underweight and extremely obese patients had higher mortality hazard.

CONCLUSION: An obesity paradox is still apparent in contemporary practice with elevated BMI up to 35 kg/m2 associated with reduced mortality after PCI. However, this effect appears not to extend to patients with extreme obesity.



22. GUT MICROBIOME AND ATHEROSCLEROTIC PLAQUE INSTABILITY: CAN A PROBIOTIC BE A FUTURE THERAPEUTIC AGENT IN TREATING CARDIOVASCULAR DISEASE?

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Myocardial infarction is the major cause of deaths worldwide. Gut bacteria can process choline (high content in red meat) and generate metabolite 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: Twenty-four Apolipoprotein E deficient mice were randomly divided into two groups, fed with a high fat diet containing either 0.4% choline or 3% choline) at 12 weeks of age, for 7 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 was performed by AGRF diversity profiling. After bacteria genomic DNA isolation, 16S rRNA were sequencing by targeting 27F-519R (V1-V3) and 341F-806R (V3-V4) on the Illumina MiSeq platform. Vessel segments of TS were histological process and plaques compositions of lipid, collagen, and intraplaque hemorrhage (marker of unstable plaques) were performed by 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 microbe showed that Fimicutes were down regulated in the high choline group ($p<0.05$, unpaired t-test). Within Phylum Fimicutes, only Clostridia (class) Clostridiales (order) were significantly downregulated. Interestingly, histological analysis of TS segments showed that TER-119 (Intraplaque hemorrhage) was significantly increased in the high choline group, indicating they are more unstable and prone to rupture ($p<0.05$, unpaired t-test). Nevertheless, CD68 (Foam cells) in the plaques were not affected by the concentration of choline.

CONCLUSION: Increase in the food intake of choline mobilises monocytes and granulocytes in the blood in the atherosclerosis mouse model. Reduction of Fimicutes may contribute to atherosclerotic plaque instability.

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23. POTENTIAL MECHANISMS UNDERLYING THE CARDIOVASCULAR BENEFITS OF SODIUM GLUCOSE COTRANSPORTER 2 INHIBITORS: A SYSTEMATIC REVIEW OF DATA FROM PRECLINICAL STUDIES

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There is growing evidence from phase III randomised clinical trials of the cardiovascular benefits of sodium glucose cotransporter 2 (SGLT2) inhibitors in patients with diabetes mellitus. It is hypothesized that these benefits are being mediated by mechanisms other than glucose control.

AIM: To data from preclinical studies regarding the direct cardioprotective effects of SGLT2 inhibitors.

METHODS: Medline, EMBASE, CINAHL and International Pharmaceutical Abstracts databases were searched for preclinical studies that examined the potential cardioprotective effects of SGLT2 inhibitors. Submission documents to the US Food and Drug Administration, European Medicines Agency and Japanese Pharmaceutical and Medical Devices Agency for the registration of SGLT2 inhibitors were also reviewed.

RESULTS: A total of 36 reports were included in the final analysis. The potential direct cardiovascular benefits of SGLT2 inhibitors include: vasodilation; augmentation of signal transduction and activation of transcription 3; inhibition of sodium hydrogen exchange; modulation of sympathetic tone; reduction of atherosclerosis; modulation of natriuretic peptides; and reduction of inflammation, oxidative stress, endoplasmic reticulum stress and cardiac glucose uptake via downregulation of SGLT1 expression.

CONCLUSION: There are a number of mechanisms by which SGLT2 inhibitors may exert cardiovascular benefits beyond glycaemic control.

24. THE USE OF EXTRA-CORPOREAL MEMBRANE OXYGENATION IN POST-CARDIOTOMY CARDIOGENIC SHOCK

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Post-cardiotomy cardiogenic shock (PCCS) is an infrequent occurrence reported from 3-5% (1). Where chemical support and intra-aortic balloon pump fail to resuscitate the patient, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is the next step to avert certain death.

AIM: to determine survival in post-cardiotomy ECMO, and identify adverse prognostic indicators (APIs) to ensure optimal selection of patients.

METHODS: A literature search identified 16 publications on post-cardiotomy ECMO via PUBMed and Ovid MEDline. Following this, an Australia-wide dataset of 387 patients (2012-2017) was acquired from the federal department of health, as was the cohort of post-cardiotomy ECMO patients from The Alfred Hospital (2008-2017). The data was retrospectively analysed, and survival to discharge and adverse prognostic indicators determined based upon procedure, age group, and use of intra-aortic balloon pump. Results: A literature review of 16 publications showed 0.5-3% of cardiac surgical cohorts needed ECMO for PCCS (2,3). Survival to discharge was reported in all studies and ranged from 23.7% - 41.8% (4,5). Survival at 1 year was reported in 7 of the studies and dropped to 16.5 - 37% (6,1). The most commonly reported API was age, described in 9 studies. In review of the Australia- wide database, survival to discharge was reportedly higher at 51.7%. Age also predicted survival, with only 33.3% of patients over 75 surviving compared to 68% of patients 15-49 years. Of the 67 Alfred patients, survival to discharge was 44.8%. Similarly, the average age of those patients who survived was lower (48.8 vs 55.8yo).

CONCLUSION: although ECMO post-cardiotomy is used infrequently, it averts certain death in a significant number of cases. Ongoing research may indicate APIs that may be modified to prevent poor outcome, or identified to plan for and attenuate disasters.

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25. INHIBITION OF VENTRICULAR REMODELING BY GINGERLS THROUGH ASK1/MAPK/NF-KAPPAB SIGNALLING PATHWAYS IN VITRO

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Cardiac hypertrophy and fibrosis are essential features in ventricular remodelling, in which apoptosis signal-regulating kinase 1 (ASK1) plays a critical role and is a promising therapeutic target for heart disease.

Molecular docking was used to identify active compounds from the Chinese medicine database. [6]-gingerol, [8]-gingerol, and [10]-gingerol, the major pharmacologically-active components of ginger, were identified to have the potential to bind to the protein kinase domain of ASK1 and prevent ventricular remodelling. Here, we investigated the involvement of ASK1 and its downstream signaling pathways, mitogen-activated protein kinase (MAPK) and nuclear factor kappaB (NF-kappaB), in the cardioprotective activity of gingerols using neonatal cardiac myocytes (NCM) and fibroblasts (NCF).

Results showed that stimulation with angiotensin II (Ang II) induced hypertrophy in NCM, collagen synthesis and proliferation in NCF. Treatment with the three gingerols attenuated the effect of Ang II in NCM in a dose-dependent manner, but only [8]-gingerol and [10]-gingerol dose-dependently inhibited Ang II stimulated collagen synthesis in NCF. Mechanistic pathway studies demonstrated the activation ASK1, JNK, P38, ERK and NF-kappaB by Ang II in NCM and NCF. Different gingerol appeared to inhibit different target within the ASK1/MAPK/NF-kappaB signalling cascade.

In summary, gingerols are potential cardioprotective agents in vitro, at least in part, via the inhibition of ASK1/MAPK/NF-kappaB signaling pathways.

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26. TRANSGENERATIONAL PREVENTION OF HEART FAILURE THROUGH MATERNAL INTAKE OF HIGH FIBRE

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Emerging evidence suggests dietary intake of fibre protects against the development of cardiovascular disease (CVD) through the production of gut microbial metabolites, but the intergenerational effect of fibre intake and gut microbiota composition has yet to be elucidated.

AIM: To determine if dietary intake of fibre during pregnancy can prevent the development of cardiac hypertrophy and heart failure through changes in the gut microbiota and metabolites using the angiotensin II (Ang II) model.

METHODS: C57BL/6 female mice were fed a no fibre or with high fibre during gestation. After weening, all offspring consumed a standard diet. At 6-weeks of age, minipumps containing saline or Ang II were implanted. Mice were followed for 4-weeks, at which point we determined cardiac weight, expression of key genes and gut microbiome composition.

RESULTS: Mums fed diets without or with high levels of fibre had a different gut microbiome composition (P=0.001). Pups born from mothers on high fibre diet had distinct gut microbial colonisation (P=0.001), irrespective of the presence of Ang II (P=0.013). Ang II pups whose mother had a high fibre diet had a significant decrease in heart to body weight ratio compared to those from no fibre mums (4.84 vs 5.43 mg/g, P=0.034). Ang II pups whose mother received a high fibre diet had lower levels of markers of fibrosis such as *Col1a1* (P=0.01), *Tgfb* (P=0.021) and *Ctgf* mRNA (P=0.005) and lower levels of *Nppb* mRNA, a marker of heart failure (P=0.002).

CONCLUSION: High fibre intake during pregnancy protected the offspring against the development of cardiac fibrosis, remodelling and hypertrophy in the heart compared to those born from mothers who consumed no fibre. Our findings support that the gut microbiota of the mothers was shaped by the intake of fibre during pregnancy and this had a lasting founding effect in the offsprings' microbiota.

27. IS THERE A DIFFERENCE IN PRECIPITANTS BETWEEN HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFPEF) AND HEART FAILURE WITH REDUCED EJECTION FRACTION (HFREF)?

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Heart failure is a disease of the elderly. Approximately half of heart failure admissions are associated with a preserved ejection fracture (HFPEF) and half with a reduced ejection fraction (HFREF). While clinically different, the two groups are thought to be indistinguishable at presentation.

AIM: To compare and contrast the precipitants for acute decompensated heart failure (ADHF) in patients with HFPEF and HFREF.

METHODS: This retrospective observational study utilised data from the Alfred Hospital's contribution to the 2015 and 2016 Victorian Cardiac Outcomes Registry Heart Failure Snapshot; a registry of ADHF admissions. Echocardiograms of participants with left ventricular ejection fraction (LVEF) of more than 50% were analysed. European Society of Cardiology (ESC) criteria for the diagnosis of HFPEF were applied. This group was then compared to admissions with an LVEF of less than 45% (HFREF).

RESULTS: 50 admissions had an LVEF of more than 50% but only 23 had ESC defined HFPEF. 53 admissions had HFREF. HFPEF patients were significantly older (81.7 years vs 61.9 years, $p<0.001$), more likely to be female ($p = 0.019$) and had more comorbidities recorded. There were no significant differences between precipitants of ADHF between the two groups however there was a trend to more HFPEF patients having ADHF precipitated by infection and arrhythmia. There was no difference in mortality or readmissions. CONCLUSION: The prevalence of heart failure with an LVEF > 50% matches that of larger studies however ESC defined HFPEF accounted for 20% of admissions. Precipitants of ADHF did not differ significantly between HFPEF and HFREF.

28. THE THERAPEUTIC ROLE OF LIPOXIN A4 AND BENZO-LIPOXIN AGAINST DIABETES- ASSOCIATED ARTHEROSCLEROSIS

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Cardiovascular (CV) diseases is a the leading cause of death worldwide with the risk of amplified in patients with diabetes, leading to an increase in incidence, size and complexity of atherosclerotic plaques. There remains a major unmet need for the development of new therapeutic strategies against diabetes-associated atherosclerosis (DAA). In this study we investigated whether Lipoxins are protective against atherosclerosis by attenuating inflammatory factors contributing to atherogenesis.

AIM: To investigate the therapeutic potential of Lipoxin A_4(LXA_4) and Benzo-LXA_4(B-LXA_4) as an intervention in an experimental model of DAA.

METHODS: Six-week-old male $ApoE^{-/-}$ mice were rendered diabetic by five daily intra-peritoneal (IP) injections of streptozotocin(55mg/kg). Controls received citrate buffer alone(n=23/gp). Blood glucose levels were measured to determine diabetes status. After 10 weeks, control and diabetic animals received twice weekly injections of either vehicle(0.02% ethanol), LXA_4(5µg/kg) or B-LXA_4(1.7µg/kg), a more stable analogue of LXA_4, from week 11 for a total of 6 weeks(n=16/gp). After 16 weeks, mice were culled and aortas collected to assess plaque deposition, gene expressions and immunohistochemistry.

RESULTS: Diabetic animals demonstrated increased levels of circulating blood glucose, serum glycated haemoglobin, as well as increased plaque deposition. These were accompanied by increased expressions of inflammatory and macrophage markers. Administration of LXA_4 and B- LXA_4 at 11-16 weeks significantly decreased thoracic plaque deposition(30% and 47% respectively), and significantly attenuated IL1b(~0.5fold). B-LXA_4, compared to LXA_4, significantly attenuated a number of macrophage markers(CD11b, CD204, ~0.6fold), and was more effective at reducing plaque area in the abdominal aorta and arch (~50%), as well as attenuating the expression of inflammatory cytokines(IL10, ICAM1, eNOS ~0.5 fold) and macrophage markers(Arg1, F4/80 ~0.4fold).

CONCLUSION: This study demonstrates the therapeutic potential of an endogenously produced molecule, LXA4, as novel anti-atherosclerotic and anti-inflammatory agent for the treatment of established atherosclerosis. The development of more stable and potent analogues such as B- LXA4 is likely to improve the outcome for patients clinically exhibiting established atherosclerosis.

29. MACHINE LEARNING MODELS SIGNIFICANTLY IMPROVE OUTCOME PREDICTION AFTER CARDIAC ARREST.

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INTRODUCTION: Cardiac arrest is associated with a high mortality. However, current illness severity scores are limited in regard to predictive accuracy. Pre-hospital data demonstrates the most significant prognostic accuracy for mortality, and no current models exist based on in-hospital variables.

OBJECTIVE: To use logistic regression and machine learning techniques develop and compare predictive models for in-hospital mortality after cardiac arrest developed from routine demographic, physiological and biochemical information available within 24 hours of admission to an Intensive Care Unit (ICU) but without specific pre-hospital data about aetiology or circumstances of the cardiac arrest, including no data on rhythm or time to CPR and ROSC.

METHODS: All patients between 2006 and 2015, who had experienced a cardiac arrest within 24 hours prior to admission to an ICU, were extracted from the Australia and New Zealand Intensive Care Society (ANZICS) Adult Patient Database. The primary outcome was mortality at the time of discharge from hospital. The models were trained on a dataset including age, lowest and highest physiologic variables during the first 24 hours, and key past medical history. Logistic regression and three machine learning approaches (gradient boosting machine (GBM), random forest (RF), deep learning (DL) and a stacked ensemble (SE)) were compared to the APACHE III score.

RESULTS: 9365 patients from 179 ICUs were analysed. Mean age was 62±16 years; 66% were male. Overall in-hospital mortality was 51.6%. The APACHE III-j score demonstrated reasonable discrimination and other logitisc regression techniques demonstrated reasonable discrimination (Area under receiver operator characteristic [AUROC] 0.74). Model discrimination was significantly improved using machine learning models (AUROC: GBM 0.855, RF 0.854, DL 0.836, SE 0.859).

CONCLUSIONS: In patients admitted to ICU following cardiac arrest, novel machine learning approaches significantly enhance predictive discrimination compared to classical logistic regression mortality prediction techniques, with a stacked ensemble approach proving most accurate. The impact of pre-hospital data may increase the accuracy of mortality prediction, and further efforts need to be made to enhance the explainability of such models to encourage translation to clinicalapplication.

30. FUNCTIONAL RECOVERY AND QUALITY OF LIFE AFTER IN-HOSPITAL CARDIAC ARREST – PRELIMINARY RESULTS

Australia and New Zealand Cardiac Arrest Outcome Determinants and ECMO suitability study (ANZ-CODE): A multi-centre prospective observational study of in-hospital cardiac arrests in Australia and New Zealand

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Frequency of in-hospital cardiac arrest (IHCA) in Australia and New Zealand ranges from 1.3–6.0 per 1000 admissions with an overall in-hospital mortality of 74.6%[1]. Little is known about long-term functional outcome and health-related quality of life (HRQoL) of survivors of IHCA.

AIM: To determine functional recovery and HRQoL of IHCA survivors at 6-months.

METHOD: A multi-centre prospective cohort study. Emergency calls were screened and data collected for all IHCA. Patients were contacted by telephone if they survived to 6-months post IHCA. Measurements included discharge destination, hospital readmission, return to work, functional status (modified Rankin Scale (mRS) and Barthel Index (BI)) and HRQoL (EQ5D-5L) at 6-months.

RESULTS: There were 52 IHCA across five sites between July-November 2017 (male 61.4%, median age 76.5 years (IQR 20.0)). 15 patients (28.8%) survived to hospital discharge and 14 (26.9%) survived to 6-months. 10 survivors consented to follow-up interview (71.4%). Three patients had subsequent hospital admissions. Median mRS and BI at 6-months were 3/6 (IQR 4.5) and 19/20 (IQR 6.5) respectively. In EQ5D-5L domains there were 'no problems' reported by 3 patients (33.3%) for mobility and self-care, 2 (22.2%) for usual activities, 1 (11.1%) for pain and 4 (44.4%) for anxiety/depression. Median EQ5D VAS score was 70/100 (IQR 30). Of the 4 patients working prior to IHCA, 2 (50%) had returned to work. Those who did not return to work reported this was due to health post IHCA.

CONCLUSION: Functional recovery and HRQoL at 6-months post IHCA is varied. Two thirds of patients report some level of functional disability and few patients report 'no problems' with HRQoL domains at 6-months. Only half of patients previously employed returned to work.

REFERENCES: 1. Fennessy G, Hilton A, Radford S, Bellomo R, Jones D. The epidemiology of in-hospital cardiac arrests in Australia and New Zealand. InternMedJ. 2016 Oct;46(10):1172-118.

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31. INDOXYL SULFATE AND P-CRESOL SULFATE INDUCE CARDIAC HYPERTROPHY AND CARDIORENAL FIBROSIS VIA THE APOPTOSIS SIGNAL REGULATING KINASE 1 PATHWAY

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Cardiorenal syndrome is a complex clinical disorder encompassing the concomitant dysfunction of both the heart and the kidneys, leading to a high rate of mortality with virtually no definitive and effective treatment at present. In this study, we investigated the adverse effects of non-dialyzable protein-bound uremic toxins, indoxyl sulfate (IS) and p-cresol sulfate (PCS), on cardiac hypertrophy and cardiorenal fibrosis *in vitro* and possible role of an oxidative stress-driven kinase, the apoptosis signal regulating kinase 1 (ASK1) in mediating such effects. IS and PCS induced cardiac hypertrophy in cardiac myocytes as well as collagen turnover in cardiac fibroblast, renal mesangial cells and proximal tubular cells as assessed by proline and leucine incorporation assay. These findings were accompanied by the upregulation of pro-hypertrophic (α-skeletal muscle actin and β-MHC) and pro- fibrotic genes (TGF-β1 and cTGF). Western blot showed the activation of ASK1 by IS and PCS, as well as ASK1 downstream protein kinases including p38 and ERK1/2 mitogen-activated protein kinases. ASK1 inhibitor abolished all of these effects without compromising cell viability as evidenced by 3-(4,5-dimethyl-2 thiazoyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay. In conclusion, ASK1 mediates cardiac hypertrophy and cardiorenal fibrosis induced by IS and PCS at the cellular level. Inhibition of the ASK1 pathway showcased therapeutic potential in reducing cardiac and renal adverse effects mediated by protein-bound uremic toxins *in vitro* that warrants further exploration for possible beneficial translatability in CRS disease models.

32. DUAL TARGETED THERANOSTIC DELIVERY OF MICRO-RNA-126 ARRESTS ABDOMINAL AORTIC ANEURYSM DEVELOPMENT

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Abdominal aortic aneurysm (AAA) is an often deadly disease without medical, non-invasive treatment options. The upregulation of vascular cell adhesion molecule-1 (VCAM-1) on aortic endothelium provides an early target epitope for a novel biotechnological theranostic approach.

AIM: To develop a novel theranostic approach toward AAA by utilizing a single-chain antibody targeted toward VCAM-1 and therapeutic microRNA-126 mimics coupled to echo- enhancing microbubbles (MBs).

METHOD AND RESULTS: MicroRNA-126 was used as a therapeutic agent, based on its capability to downregulate VCAM-1 expression in endothelial cells and thereby reduce leukocyte adhesion and exert anti-inflammatory effects. Ultrasound MBs were chosen as carriers allowing both molecular imaging as well as targeted therapy of AAA. MBs were coupled with a VCAM-1–targeted single-chain antibody ($scFv_{mVCAM-1}$) and a microRNA-126 mimic (M126) constituting theranostic MBs ($Targ^{MB}$-M_{126}). *In vitro* experiments using VCAM-1–expressing SVEC4-10 cells provided initial evidence that $Targ^{MB}$-M_{126} downregulates VCAM-1 expression following an ultrasonic burst. *In vivo* proof of successful targeting of $Targ^{MB}$- M_{126} to VCAM-1–expressing endothelial cells was obtained in an LPS-induced mouse model of vascular inflammation. *In vivo* validation of $Targ^{MB}$-M_{126} using an Angiotensin II–induced AAA mouse model successfully demonstrated decreased vascular inflammation & significant prevention of AAA, which can be directly visualized in 3D ultrasound imaging (Figure 1).
CONCLUSION: Overall, we describe a unique dual targeted, biotechnological, ultrasound-based theranostic approach with the potential for early diagnosis and a long sought-after medical therapy of AAA.

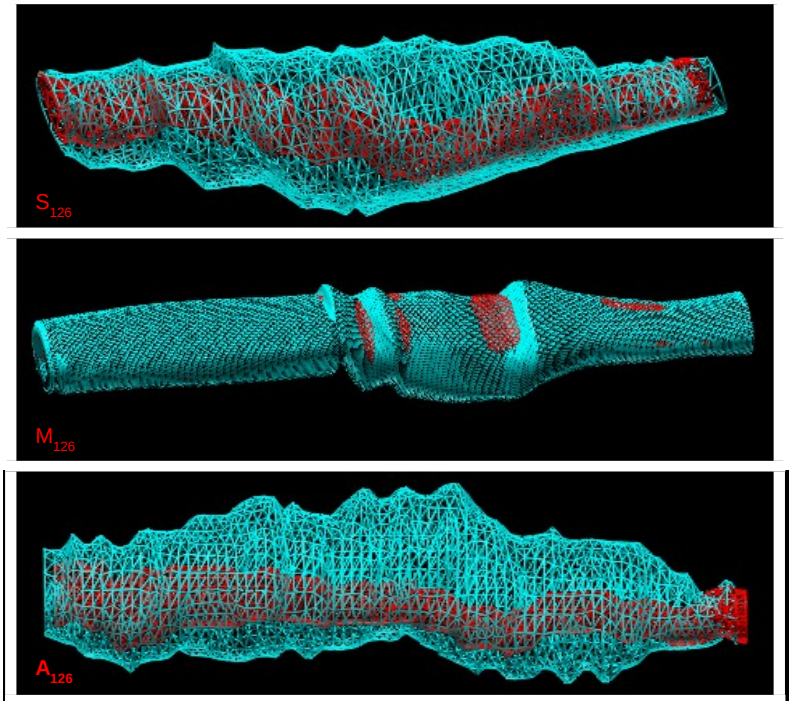

Figure 1: 3D molecular ultrasound reconstructions of mouse abdominal aorta shows vessel lumen (red), as well as massive areas of plaque build-up and aneurysm (blue), from animals treated with $Targ^{MB}$-A_{126}, $Targ^{MB}$-M126 or $Targ^{MB}$-S126.

33. ELEVATED PRESSURE PROMOTES ENDOMT-INDUCED FIBROSIS VIA A CAVEOLIN-1 DEPENDENT MECHANISM

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A major risk factor for cardiac fibrosis is high blood pressure which we have previously shown to induce endothelial activation *via* a caveolin-1 (cav-1) dependent mechanism. Endothelial-to-mesenchymal transition (EndoMT) is a key player in the development of cardiac fibrosis.

AIM: To examine whether increased pressure promotes EndoMT-induced fibrosis via a cav-1 dependent mechanism.

METHODS: Human umbilical vein endothelial cells (HUVECs) or cav-1 knockdown (cav-1 KD) cells were treated with TGFβ1 and TGFβ2 (10ng/mL), known inducers of EndoMT, or pressurised to 120 mmHg for up to 5 days. Cells were harvested and prepared for real-time PCR and flow cytometry analysis. Cell supernatants were prepared for MMP assessment via gelatin zymography. Two- week angiotensin II (AngII;490ng/kg/min) and noradrenaline (NA;3.8μg/kg/min) models of hypertension were used in wild-type and *Cav-1*$^{-/-}$ mice to confirm our findings *in vivo*. Cardiac hypertrophy and fibrosis were measured using both gene expression and Masson's Trichrome staining.

RESULTS: TGFβ1/2-treated HUVECs had increased expression of fibroblast genes, vimentin and alpha-smooth muscle actin (αSMA), and reductions in endothelial gene, CD31. A similar pattern was observed in HUVECs exposed to a hypertensive pressure (120mmHg), suggesting that exposure to increased pressure promotes EndoMT. This was accompanied by an increase in both MMP2 and MMP9 activity, consistent with the premise that pressure induces the breakdown of collagen type IV, essential for the progression of EndoMT. Interestingly, cav-1 KD cells were protected from these pressure-induced changes. In AngII and NA mouse models of hypertension, we found that *Cav-1*$^{-/-}$ mice compared to wild-type mice were protected from perivascular fibrosis and cardiac hypertrophy and failed to increase vimentin and αSMA gene expression.

CONCLUSION: Hypertension induces EndoMT via a cav-1 dependent mechanism and may be responsible for the end-organ fibrosis observed in the context of high blood pressure. This may provide a novel therapeutic target to prevent pressure-induced fibrotic disorders.

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34. CHARACTERISTICS AND CLINICAL OUTCOMES IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION COMPARED TO HEART FAILURE WITH REDUCED EJECTION FRACTION: INSIGHTS FROM THE VCOR HEART FAILURE MODULE

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BACKGROUND: With an ageing population, the prevalence of heart failure in Australia is anticipated to place an increasing resource and economic burden on the healthcare system. Distinguishing patients as having heart failure with preserved ejection fraction (HFpEF) or reduced ejection fraction (HFrEF) is important in optimising their management. We analysed the characteristics and clinical outcomes of HFpEF patients compared to those with HFrEF, to achieve a better understanding of how heart failure type influences the treatment and outcomes of these patients.

METHOD: Data were sourced from the Victorian Cardiac Outcomes Registry- Heart Failure (VCOR-HF) Snapshot module of 1357 patients admitted with heart failure from 2014-2017, over 1 consecutive month in each year, across 16 Victorian hospitals. Comprehensive details on baseline characteristics and management were collected. Outcomes included 30-day readmission and mortality.

RESULTS: Patients with HFpEF were more likely to be female and older. They were also more likely to have diabetes, hypertension, COPD and chronic kidney disease. Patients with HFrEF were more likely to have ischaemic heart disease with a history of previous myocardial infarction, percutaneous coronary intervention and cardiac bypass surgery. 30-day all-cause mortality was higher in the group with HFrEF (10.2% vs. 6.2%), whereas 30-day readmission rates were higher in the HFpEF (29.1% vs. 22.1%) group.

CONCLUSION: The VCOR-HF Snapshot highlights distinct patterns for patient characteristics and short-term outcomes among HFpEF and HFrEF groups. Measures designed to improve heart failure outcomes and readmissions that are specifically tailored to heart failure type will be increasingly important in the future.

35. IMPAIRED LEFT ATRIAL STRAIN PREDICTS ABNORMAL EXERCISE HAEMODYNAMICS IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

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BACKGROUND – Elevated left atrial (LA) pressure, particularly during exercise, is associated with both symptomatic status and survival in patients with heart failure with preserved ejection fraction (HFpEF). The mechanical properties of the LA are abnormal in HFpEF however their contribution to exercise haemodynamics in HFpEF are unknown.

METHODS – Simultaneous echocardiography and right heart catheterization was performed in 71 subjects with LVEF≥50% referred for assessment of exertional dyspnoea. According to the hemodynamic evaluation, 49 patients were diagnosed with HFpEF (pulmonary capillary wedge pressure (PCWP) ≥15mmHg at rest and/or ≥25mmHg at maximal exertion) and 22 as Non-Cardiac Dyspnoea (NCD). The apical 2- and 4-chamber views were used for 2-dimensional speckle tracking analysis of the LA, blinded to other data.

RESULTS – HFpEF was characterized by impaired LA reservoir (24.3±9.6 vs 36.7±8.4%, P<0.001) and pump strain (-11.5±3.2 vs - 17.0±3.4 %, P<0.001); and increased LA stiffness (0.8±0.7 vs 0.2±0.1 mmHg/%, P<0.001). Reservoir and pump strain correlated with exercise PCWP (r=-0.64 and r=0.72, P<0.001), and remained independent predictors after adjusting for LV mass index, LA volume index, mean E/e' and systolic blood pressure (B=-0.66 and B=1.41, P<0.001). LA stiffness was strongly related to brain natriuretic peptide levels (r=0.73, P<0.001; B=173.0 P<0.001). Reservoir strain at a cutoff of ≤33% predicted invasively verified HFpEF diagnosis with 88% sensitivity and 77% specificity, which in our cohort provided a net reclassification improvement of 15% in comparison to the 2016 ESC criteria for the non-invasive diagnosis of HFpEF.

CONCLUSIONS – Impaired LA reservoir and pump function and increased stiffness are associated with abnormal exercise haemodynamics in HFpEF. These markers provide diagnostic utility together with a potential approach for studying disease progression and treatment responses.

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36. RESTRICTIVE VERSUS LIBERAL FLUID THERAPY FOR MAJOR ABDOMINAL SURGERY

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AIM: To investigate the effectiveness of fluid restriction (vs. liberal).

METHODS: In a pragmatic, international, trial, we randomly assigned at-risk patients undergoing major abdominal surgery to a restrictive or liberal IV fluid regimen during and up to 24 hours after surgery. The primary outcome was disability-free survival through to 1 year after surgery. Secondary outcomes included 30-day acute kidney injury (AKI), a composite of septic complications, surgical site infection or death, and 90-day renal replacement therapy.

RESULTS: We enrolled 3,000 patients in 47 hospitals and 7 countries. During and up to 24 hours after surgery, 1,493 patients in the restrictive group received a median (IQR) 3.7 (2.9 to 4.9) liters compared with 6.1 (5.0 to 7.4) liters in 1,490 patients in the liberal group (P<0.001). Disability-free survival at 1 year was 81.9% in the restrictive fluid group and 82.3% in the liberal fluid group (HR 1.05, [95% CI, 0.88 to 1.24], P=0.61). The rate of AKI was 8.6% in the restrictive group and 5.0% in the liberal group RR 1.71 (95% CI, 1.29 to 2.27); P<0.001. The rate of septic complications or death was 21.8% in the restrictive group and 19.8% in the liberal group (P=0.19). Rates of surgical site infection (16.5% versus 13.6%, P=0.024) and renal replacement therapy (0.9% versus 0.3%, P=0.048) were higher in the restrictive group.

CONCLUSIONS: In patients having major abdominal surgery, a restrictive fluid regimen did not improve disability-free survival but was associated with higher rates of AKI, surgical site infection and renal replacement therapy.

37. HAEMODYNAMIC CHARACTERISTICS IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFPEF) AND NON-CARDIAC DYSPNOEA (NCD)

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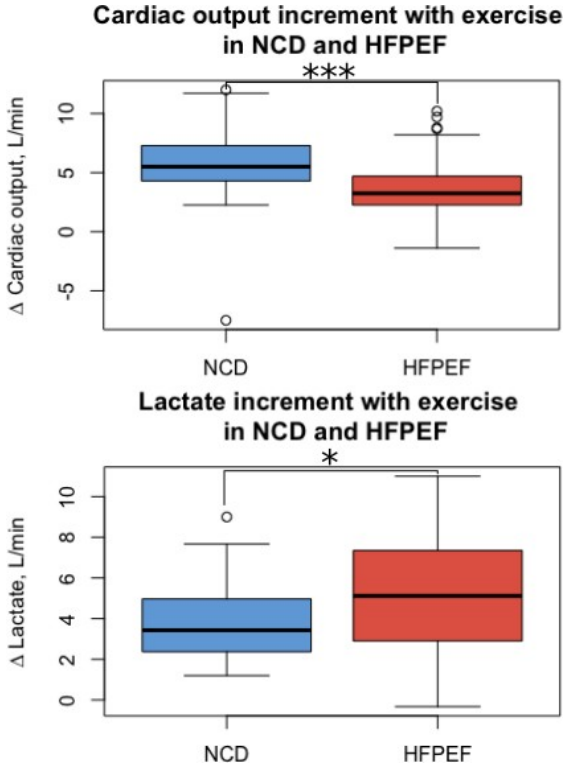
INTRODUCTION: Exercise intolerance is a cardinal feature of HFPEF. The underlying mechanism of this is multi-factorial. Differences in haemodynamic indices between HFPEF and NCD may highlight key contributors to exercise intolerance in HFPEF.

METHODS: Patients referred for investigation of dyspnoea with exercise right heart catheterisation from 2008-18 were reviewed retrospectively. HFPEF was defined as an ejection fraction (EF) ≥50% and a rest pulmonary capillary wedge pressure (PCWP) ≥15mmHg or exercise PCWP ≥25mmHg. Patients with NCD had an EF ≥50% and normal resting/exercise PCWP. Haemodynamic parameters, oxygen and mixed venous saturation and lactate were recorded at rest and peak exercise, and the difference calculated and expressed as Δvalues.

RESULTS: There were 91 HFPEF and 37 NCD patients. Patients with NCD achieved a higher workload (67W vs. 45W, *p*=0.002), had a higher baseline and Δ cardiac output (ΔCO, 5.6±3.4 vs. 3.7±2.3L/min, *p*<0.001). HFPEF patients had a higher rest and exercise PCWP (ΔPCWP 17±6 vs. 9±4mmHg, *p*<0.001) and mean pulmonary artery pressure (ΔPAm, 21 vs. 16mmHg, *p*=0.008), and a higher lactate level indexed to workload (5.2±2.9 vs. 3.9±2.1mmol/L, p=0.045).

CONCLUSIONS: Patients with HFPEF show worse functional capacity as indicated by lower achieved workload, driven by a combination of lower CO, higher PCWP, and higher lactate compared to NCD patients. The higher lactate indexed to workload may indicate dysfunctional peripheral oxygen handling



38. DURABILITY OF LEFT VENTRICULAR UNLOADING IN LVAD THERAPY RELATES TO PROGRESSIVE INCREASES IN PUMP SPEED

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Left ventricular assist devices (LVADs) elicit reverse remodelling (RR) by promoting left ventricular (LV) unloading. Insufficient LV unloading in LVAD therapy has been shown to result in poorer outcomes. We hypothesized that titration of device speed in the outpatient follow-up period may influence the degree of LV unloading achieved.

METHODS: Data from echocardiography and right heart catheterisations (RHC) were retrospectively collected for 76 patients who underwent CF-LVAD implantation at Alfred Health since 2010. Five time points were identified: prior to implant, during the initial 14 days post-LVAD implant, then at 1, 3 and 6 months post-implant. Indices collected included LV end-diastolic diameter (LVEDD), fractional shortening (FS), left atrial volume (LAV), pulmonary capillary wedge pressure (PCWP) and device speed (RPM). Patients in whom device speed increased between the time of hospital discharge and 6 months (ΔRPM>0%, Group A, n=35) were compared to those in whom device speed remained unchanged or reduced (ΔRPM ≤0%, Group B, n=41). Optimal LV unloading was defined as achievement of LVEDD<65mm.

RESULTS: At 6 months, LVEDD was significantly lower in Group A patients in whom device speed was increased compared with Group B (59±10mm vs 67±10mm, p=0.001). Significant correlation was demonstrated between ΔRPM and LVEDD (r= -.367, p<0.001). A greater proportion of Group A patients maintained optimal LV unloading at 6 months compared with Group B (65.7% vs 39.0%, p=0.02). At 6 months, Group A patients demonstrated greater change in LAV (-71±50mL vs -37±47mL, p=0.02) and lower PCWP (11±3 vs 16±11mmHg, p<0.001). Fractional shortening was similar between both groups at 6 months (13±7 vs11±8%, p=0.38).

CONCLUSION: LVAD recipients whose pump speeds are progressively increased in the outpatient follow-up period are more likely to maintain maximal LV unloading, which may be of prognostic significance.

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39. EFFICACY STUDY OF A NOVEL PROTOTYPE INHIBITOR TO RETARD KIDNEY DISEASE IN MODELS OF DIABETES.

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Diabetic nephropathy is the major cause of end-stage renal disease worldwide, and remains suboptimally treated medically. A large body of compelling data from our group have demonstrated that CDA1/CDA1BP1 interaction is a promising target to retard diabetic nephropathy. We have developed a prototype inhibitor, CHA-061, to target this novel axis. This study focuses on the assessment of CHA-061 for its efficacy to attenuate parameters relevant to renal fibrosis in two models of diabetes. The first model is an insulin deficient model using streptozotocin (STZ)-induced diabetes in ApoE KO mice, a model relevant to type 1 diabetes. The second is a type 2 diabetes model using db/db mice which initially become obese and subsequently diabetic as a result of the leptin receptor mutation.

Diabetic mice were treated in a delayed intervention protocol where treatment was withheld for the first 10 weeks of diabetes in order to allow diabetes-induced kidney disease to be established. Then, both non-diabetic and diabetic mice were randomly allocated to receive either vehicle or CHA-061 treatment (10 mg/kg IP injections twice a week) for 10 weeks. The analysis of kidney tissues showed that, in the vehicle treated ApoE KO mice, diabetes was associated with >2-fold increase in gene expression of sclerotic molecules such as collagens I and III as well as proinflammatory genes such as TNFα and MCP1.

Immunohistochemical staining of collagen III was increased >10-fold and the glomerulosclerosis index (GSI) as assessed by PAS staining was increased >2-fold in diabetic ApoE KO mice. These parameters were significantly attenuated in CHA-061 treated diabetic ApoE KO mice. Similarly, CDA1 expression levels were increased ~2-fold in diabetic db/db mice accompanied by >2-fold increase in gene expression of sclerotic molecules such as CTGF, fibronectin, collagens I, III and IV when compared to the non-diabetic dbh mice.

CHA-061 treatment reduced these parameters in the diabetic db/db mice to levels similar to those in the non-diabetic controls. These results were consistent with our previous target validation data using CDA1 KO and CDA1BP1 KO mouse strains. Taken together, the current study has demonstrated the efficacy and feasibility to pharmacologically target the novel CDA1/CDA1BP1 axis to retard nephropathy in both type 1 and type 2 diabetes by targeting not only fibrotic but also proinflammatory pathways.

40. PHOSPHOINOSITIDE 3-K**INASE P110A GENE DEL**IVERY LIMITS CARDIAC REMODELLING AND INFLAMMATION IN A PRE-CLINICAL MODEL OF TYPE 2 DIABETES

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INTRODUCTION. Diabetic cardiomyopathy in both type 1 (T1D) and type 2 diabetes (T2D) is characterised by cardiac inflammation, remodelling and dysfunction, with diastolic dysfunction preceding systolic dysfunction. Phosphoinositide 3-kinase (PI3K)-p110α is cardioprotective in type 1 diabetes but its effectiveness in the more prevalent T2D is unknown.

AIM. To test the hypothesis that PI3K gene therapy rescues diabetic cardiomyopathy in a preclinical model of T2D. Method. T2D was induced in 6wk-old male mice with low dose streptozotocin (55mg/kg/day i.p. for 3 days) combined with high-fat diet for 24wks. After 18wks of diabetes, diastolic dysfunction was confirmed by echocardiography. A single i.v. injection of recombinant adeno- associated virus (rAAV6)-caPI3K ($2x10^{11}$vg) or null vector was then administered, and mice were followed for a further 8wks (n=8- 12/group).

RESULTS. Diabetes-induced increases in cardiac inflammatory markers tumor necrosis factor-α and NF-B, which was not observed in rAAV6-caPI3K-treated T2D mice (↓53±11%, ↓15±6% vs null-treated-T2D, respectively; both P<0.05). Cardiac interstitial and perivascular fibrosis induced by T2D were also significantly reduced (to baseline levels) in rAAV6-caPI3K-treated T2D mice (↓67±16%, ↓49±17% vs null-treated-T2D, respectively; both P<0.05). rAAV6-caPI3K also reduced expression of cardiac pro- fibrotic genes in T2D, including connective tissue growth factor, transforming growth factor-β and tissue inhibitor of metalloproteinase-2 (reduced by 49±16%, 43±10% and 45±13% vs null-treated-T2D, respectively, all P<0.05). These cardioprotective actions of PI3K gene therapy were accompanied by improvements in LV diastolic (isovolumic relaxation time, ↓12±5% vs null-treated-T2D and e'/a', ↑44±10% vs null-treated-T2D; both P<0.05) and systolic function (fractional shortening: ↑31±8% vs null-treated-T2D, P<0.05).

CONCLUSION. This study is the first to demonstrate that PI3K gene delivery rescues T2D cardiomyopathy & limits the associated cardiac remodelling and inflammation. Thus, suggesting a robust therapeutic approach for the treatment of diabetic cardiomyopathy.

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

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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.

AIM: 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 homeostas

42. IS NOX-5 EXPRESSION IN CIRCULATING PERIPHERAL BLOOD MONOA POTENTIAL BIOMARKER FOR DIABETES ASSOCIATED CARDIOVASCULAR DISEASE?

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Background and Aims: Cardiovascular disease, with the clinical manifestations of myocardial infarction, strokes as well as peripheral vascular disease is known to be accelerated by diabetes contributing to premature mortality and morbidity. Current treatment strategies fail to prevent vascular complications in diabetes. Thus, novel more effective treatments and better diagnostic tools are urgently needed. NADPH-oxidases (NOX) are known to be potent sources of oxidative stress and play a central role in diabetes associated cardiovascular disease. The aim of this study was to determine whether, the most recently discovered human NADPH oxidase, Nox-5 expression, in the PBMCs is a potential biomarker for diabetic cardiovascular disease.

Material and Methods: We collected human endarterectomy, buffy coat white blood cells as well as whole blood from diabetic and non-diabetic patients. In our human endarterectomy samples immunohistochemical analysis demonstrated a significant increase in Nox-5 expression in diabetic patients compared to controls. In collaboration with the Alfred and Baker biobanks (Ethics#24/07) we subsequently collected buffy coat samples from diabetic and non-diabetic patients, extracted the resulting RNA and measured Nox-5 expression in the white blood cells at the gene level by RT-PCR. Nox-5 expression was found to be elevated in diabetic patients with cardiovascular disease when compared to non-diabetic patients with cardiovascular disease ($p<0.05$). In collaboration with the Alfred Heart Centre (Ethics#237/17), we collected whole blood from control and diabetic patients undergoing an angiogram at the Alfred Heart Centre. The patients were consented by the study doctors to donate 10mls of whole blood during their procedure. Peripheral blood mononuclear cells (PBMCs) were isolated from the blood and Nox-5 expression was measured by flow cytometric analysis. Our preliminary data demonstrates that Nox-5 expression in the PBMCs was highest in diabetic patients with cardiovascular disease compared to non- diabetic patients ($p<0.05$).

Conclusion: In conclusion, our data demonstrates, that Nox-5 may indeed be a potential biomarker for the identification of diabetic patients with high risk of developing cardiovascular disease.

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43. INHIBITION OF COMPLEMENT C5A RECEPTOR 1 REDUCES RENAL INFLAMMATION AND ATTENUATES DIABETIC KIDNEY DISEASE

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BACKGROUND: Complement C5a binds to its receptor, C5aR1, and initiates a series of proinflammatory responses. Our pilot studies have shown that C5a/C5aR1 signalling is activated in human and experimental diabetes kidney disease (DKD). However, the relative importance of this pathway in the pathogenesis of DKD is still unknown.

AIM: The aim of this study was to determine if inhibition of C5aR1 is therapeutically relevant in DKD.

METHODS: Two approaches were used to inhibit C5aR1 in the setting of experimental diabetes: (i) mice with a genetic deletion of C5aR1 (global knockout) or (ii) pharmacological inhibition of C5aR1 using a highly selective cyclic peptide antagonist, PMX53.

RESULTS: We found that lack of (study i), or blockade of C5aR1 (study ii) was associated with an attenuation of albuminuria [study (i), 154±31 μg/24hr vs 60±8 μg/24hr, $p<0.001$; study (ii), 83±18 μg/24hr vs 30±9 μg/24hr, $p<0.05$] in streptozotocin-induced diabetic mice. Furthermore, oxidative stress marker, 8-isoprostane, and urinary C5a were reduced in diabetic C5aR1 knockout mice ($p<0.05$) and in diabetic mice treated with PMX53 ($p<0.05$). Inhibition of C5aR1 by PMX53 also attenuated glomerulosclerosis ($p<0.05$). Importantly, in the diabetic C5aR1 knockout, there was a reduction in macrophage infiltration in the kidney ($p<0.05$), concomitant with an increase in anti-inflammatory FoxP3+ regulatory T cells (Tregs; $p<0.05$). Similarly, diabetic mice treated with PMX53 had increased Tregs ($p<0.05$) and a reduction in glomerular IgG (marker of immune complexes) deposition ($p<0.05$).

CONCLUSION: The current study demonstrates that inhibition of C5aR1 is associated with an improvement in renal function and structural changes associated with diabetes in mice, possibly through the resolution of inflammation in the kidney. Our results confirm that C5a-C5aR1 signalling plays an important role in the pathogenesis of DKD and inhibition of this pathway may have significant therapeutic potential for patients with DKD.

44. ENDOSCOPIC INTRAPYLORIC BOTULINUM TOXIN INJECTION AS A TREATMENT OF GASTROPARESIS POST LUNG TRANSPLANTATION

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Introduction: Gastroparesis is a recognised complication of lung transplantation. Intrapyloric botulinum toxin injection (IPBI) is the most common endoscopic treatment for refractory gastroparesis. However current literature reports variable success rate and its use remains controversial.

Aim: To determine the short term outcomes of patients with gastroparesis post lung transplantation treated with endoscopic IPBI.

Method: Retrospective review of medical records in a single institution, of patients with gastroparesis after lung transplant who underwent IPBI, from April 2014 to May 2016. Primary outcome evaluated was response to treatment at 1-2 weeks post procedure (immediate), at 4-8 weeks (short term), and at 4-6 months. Response to treatment was defined as subjective improvement in patients' symptoms or reduction in prokinetic agent use.

Results: 17 patients with gastroparesis post lung transplantation had IPBI (100 units botulinum toxin). Median time from lung transplant to IBPI was 74 days, with 3 patients treated within 30 days. Immediately post procedure, 88.2% had a positive response to treatment. However at short-term follow up, 47.1% continued to gain benefit from the procedure. Only 23.5% retained benefit from the procedure at 4-6 months. 5 patients had repeat IPBI and 2 patients underwent pyloroplasty. On multivariate analysis, age more than 50 years old, male sex, and the use of only one prokinetic agent were identify as statistically significant factors for favourable outcome post IPBI.

Conclusion: Endoscopic intrapyloric botulinum toxin injection may be an effective treatment in the shortterm period for refractory gastroparesis in lung transplant patients up to 4-8 weeks.

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45. IS THERE A DIFFERENCE IN ADALIMUMAB DRUG LEVELS ACCORDING TO PEN VS SYRINGE USE - AN INTERNATIONAL, MULTICENTRE RETROSPECTIVE ANALYSIS

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Introduction: Preliminary research suggests adalimumab (ADA) drug levels in Crohn's disease (CD) may be higher in syringe compared to pen users.

Aim: To compare drug levels associated with the use of pen and syringe delivery in patients receiving ADA therapy for CD.

Methods: Retrospective observational study of therapeutic drug monitoring (TDM) in adult CD patients receiving 40mg ADA fortnightly across five centres. The first recorded drug level, markers of disease activity including Harvey Bradshaw Index (HBI), C- reactive protein (CRP) and faecal calprotectin (FCP), and patient/disease demographics were collected. Drug levels >4.9µg/ml were considered therapeutic.

Results: 218 patients were included – 52% male, mean age 39yrs. Mean FCP was 283µg/g and CRP 10.2mg/L at TDM. Pens were used by 64% of the cohort. Syringe users had a higher albumin, lower HBI and higher rates of concomitant immunomodulation than pen users (40 vs. 38g/L p=0.016; 2.2 vs. 3.4 p=0.017; 71 vs. 54% p=0.014). No significant differences in CRP or FCP, duration or patient demographics between delivery device were observed. Considering all patients, there was no difference in drug levels in pen vs. syringe (5.3 vs 5.2µg/ml, p=0.442). On subgroup analysis by centre, syringe users at Alfred Health had significantly higher drug levels than pen users (6.1 vs. 4.5µg/ml p=0.039) and a greater proportion were therapeutic (75 vs. 44% p=0.045). In contrast, a higher proportion of pen users from CHU Saint-Étienne had therapeutic ADA level (79 vs. 42% p=0.027), yet no significant difference in absolute drug level (7.9 vs. 4.5µg/ml p=0.119). No differences between delivery device were seen at the remaining sites.

Conclusion: Optimising the efficacy of monoclonal antibodies is applicable to a range of medical specialities. In Crohn's disease, drug delivery device does not appear to affect ADA drug levels. Nevertheless, given site-specific differences between pen and syringe, prospective trials are required.

46. CHARACTERISATION OF A HAEMOCOMPATIBLE DUAL IN-LINE RECIPROCATING MICROPUMP AND MIXER FOR ON-CHIP ASSESSMENT OF EXPERIMENTAL ANTI-PLATELET AGENTS

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Microfluidic technologies offer unique possibilities for improvements in clinical platelet diagnostics. However, the use of blood with such systems presents significant challenges, particularly due to biomarker loss and biofouling due to platelet aggregation. The impact of advancements in microfluidic automation, such as micropumps and microvalves, must be carefully considered in the development of haemocompatible devices.

AIM: This study aims to explore the development and characterisation of a haemocompatible elastomeric microvalve that can act as a dual pump-mixer for antiplatelet drugs, and to determine the design considerations for microscale active mixing in whole blood.

METHODS: Through application of novel injection-moulding fabrication methods, we fabricated v-shaped and straight valve-gated, pneumatically-actuated reciprocating micropumps. Analysis of platelet-like particle motion through Micro-Particle Image Velocimetry and Computational Fluid Dynamic analysis was used to determine the optimal pumping geometry from a shear and platelet distribution perspective.

Platelet-sensitive biomarker loss was assessed via ELISA measurement of VWF and Fibrinogen adsorption. Biofouling due to platelet aggregation was assessed through monitoring epifluorescence when $DIOC_6$ labelled whole blood was perfused through pump manifolds. Platelet activation was assessed through FACS analysis of PAC-1 binding, P-Selectin expression and Phosphatidyl Serine exposure.

RESULTS: We demonstrate an in-line micropump which may be used in pumping or mixing applications requiring haemocompatibility with regards to platelets. We demonstrate a valving iteration that minimises platelet reactivity, biomarker loss or biofouling, while maintaining capacity as an in-line pump-mixer.

CONCLUSION: This study describes the development and characterisation of an inline elastomeric microfluidic micromixer which may be utilised in applications requiring haemocompatibility, such as in high-throughput anti-platelet drug screening systems.

47. OUTCOMES FROM PEGFILGRASTIM USE IN ADULT ACUTE MYELOID LEUKAEMIA (AML) AND ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL)

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Granulocyte colony-stimulating factors (G-CSFs), such as pegfilgrastim, stimulate neutrophil production post-chemotherapy and may reduce incidence and duration of neutropenia, thereby reducing infection risk. However, evidence and recommendations on pegfilgrastim use in acute leukaemia are inconsistent.

AIM: To explore associations between pegfilgrastim administration and neutropenia in acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL), and examine effects of pegfilgrastim timing of administration with respect to neutrophil nadir.

METHODS: A retrospective analysis of forty-eight AML patients undergoing consolidation chemotherapy and eighteen ALL patients treated with Hyper-CVAD protocol, admitted to The Alfred Hospital from 1st January 2014 to 31st July 2017, was conducted. Outcomes included neutropenia duration, incidence of febrile neutropenia, infection and mucositis; length of stay (LOS) and readmission rates. AML and ALL patients were analysed separately.

RESULTS: A reduction in median duration of neutropenia was identified for patients administered pegfilgrastim compared to those who were not in both AML (11.8 vs 15.1 days, p=0.01) and ALL cohorts (6.4 vs 11.8 days, p<0.001). For AML patients there were no significant differences in incidence of febrile neutropenia, infection or mucositis; there was a reduction in LOS (19 vs 25 days, p=0.01).

For the ALL cohort significant reductions were observed for incidence of febrile neutropenia (41 vs 85%, p=0.01), infection (23 vs 61%, p=0.01), and LOS in the A-cycle of Hyper-CVAD treatment (14 vs 26 days, p=0.004). A shorter neutropenia duration was observed when pegfilgrastim was administered when neutrophils were greater than 1x10^9/L for both AML (9 vs 13 days, p=0.026) and ALL (5 vs 8 days, p=0.015).

CONCLUSION: There was a significant reduction in neutropenia duration in AML and ALL patients who received pegfilgrastim, and febrile neutropenia and infection incidence in ALL patients. In addition, duration of neutropenia was shorter when pegfilgrastim was administered when neutrophils were greater than 1x10^9/L

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48. HHEX PROMOTES LYMPHOID PROGENITOR SURVIVAL INDEPENDENTLY OF STAT5 AND CDKN2A

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The transcription factor Hhex (Haematopoietically-expressed homeobox gene) is critical for development of lymphoid lineages beyond the common lymphoid progenitor. In addition, Hhex has subtler roles in Haematopoietic Stem Cell (HSC) self-renewal and emergency haematopoiesis, where Hhex was shown to mediate its effects on HSCs via repression of the *Cdkn2a* tumour suppressor locus (encoding $p16^{Ink4a}$ and $p19^{Arf}$). Moreover, the failure of lymphoid development in the absence of Hhex is characterised by apoptosis of lymphoid progenitors and defective Stat5b signalling.
AIM: To investigate the role of Hhex in lymphopoiesis in relation to anti-apoptotic protein Bcl2, Stat5b signalling and Cdkn2a.
METHODS: We generated mice in which both Hhex and Cdkn2a were absent, as well as mice lacking Hhex, but also expressing transgenic Bcl2 or constitutively active Stat5b. These mice were analysed *in vitro, in vivo* at steady state and in a chimeric transplant setting using flow cytometry to determine whether lymphopoiesis could be rescued in the absence of Hhex.
RESULTS: Loss of Cdkn2a failed to rescue B-cell development caused by the absence of Hhex. However, expression of Bcl2 rescued B-cell development in the steady state as well as restoring the development of T-, B- and Natural Killer cell lineages during *in vitro* differentiation and *in vivo* transplantation experiments. In contrast, constitutively active Stat5b was unable to restore lymphoid development *in vitro* or *in vivo* in the absence of Hhex. Further analysis of Hhex-null, Bcl2-transgenic B-cells demonstrated that they were capable of proliferation, indicating that these rescued B-cells were functional.
CONCLUSION: These results indicate that Bcl2 expression, but not Stat5b signalling or loss of Cdkn2a, can overcome the lymphoid deficiencies observed in the absence of Hhex, suggesting that the primary role of this transcription factor is to promote survival of lymphoid progenitors during early lymphoid development.

49. DEEP LEARNING BASED IMAGE ANALYSIS OF INVASIVE MOLD DISEASES IN CHEST COMPUTED TOMOGRAPHY SCANS AMONG HAEMATOLOGY-ONCOLOGY PATIENTS

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Chest Computed Tomography (CT) dominates the initial diagnostic workup in patients with suspected Invasive Mold Disease (IMD). Improving the efficiency and rigor of radiologic diagnosis is important for clinical practice, trials and radiologist workflow..

AIM: To develop image analysis of IMD from chest CT using a neural network.

METHODS: Haematology-oncology patients with IMD were identified in 2 iterations: in iteration 1, from previous studies and in iteration 2, by screening chest CT reports from our data warehouse using natural language processing (NLP) followed by medical verification of IMD.

A fully convolutional neural network (CNN) was trained with CT images hand labelled by 3 radiologists using pre-specified criteria. In iteration 2, annotation of training data was accelerated by radiologists editing images initially annotated by the network.

RESULTS: We identified 158 patients with 174 episodes of IMD, of which 29% were probable/proven. Number of patients with corresponding axial CT slices, increased between iterations from 72/307 to 158/11,532, with NLP augmenting data acquisition by over 3600%. Area under the receiver operating curve in iterations 1 and 2 increased from 93.0% to 99.3%, indicating system learning. For a range of thresholds, sensitivity (Sn)/specificity (Sp) were (%): (Sn 98.3, Sp 94.1), (Sn 99.0, Sp 92.2) and (Sn 99.9, Sp 79.2).

CONCLUSION: Deep learning using a CNN achieved strong performance for a challenging and diverse condition. A platform technology integrating NLP and image recognition could support radiologist decision support and electronic IMD surveillance, addressing important needs of a rare disease.

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50. PLATELETS AFTER LONG-TERM SPLENECTOMY: DEFICIENCY OF KEY PLATELET-SPECIFIC SURFACE RECEPTORS AND PLATELET ACTIVATION SUGGEST A ROLE IN INCREASED THROMBOGENICITY

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Aim The mechanisms underlying increased thromboembolic risk after long-term splenectomy are poorly understood. We evaluated the potential role of platelets by analysing surface expression of key platelet-specific receptors glycoprotein (GP)Ibα, GPVI and αIIb3 and a platelet activation marker, P-selectin.

Methods Whole blood from same-day healthy controls (n=15) or splenectomy (n=30) was centrifuged to obtain platelet-rich-plasma, stained with phycoerythrin (PE)-labelled antibodies against GPIbα (PE-AK2), GPVI (PE-1G5), αIIb (PE-CD41a), CD9 (PE-CD9; control), or P-selectin (PE-CD62P), and analysed using a FACSCalibur. Stored plasma was analysed for soluble GPVI (sGPVI) by ELISA.

Results Splenectomy cases showed significantly decreased platelet surface expression of GPIbα ($p<0.0001$) and GPVI ($p=0.0154$) compared to healthy controls. There was no significant difference in relative surface expression of αIIb ($p=0.1681$). P-selectin was significantly elevated in splenectomy cf. control platelets ($p<0.0001$). Evaluation of sGPVI suggests decreased surface GPVI expression is not related to increased shedding.

Conclusion These results support a role for hyper-activated platelets in thromboembolism post-splenectomy, and identify platelet-specific markers related to these changes. Results here enable future studies to determine if such measurable changes correlate with the clinical thromboembolic dysfunction, & may indicate potential therapeutic targets for prevention of thrombosis.

51. THE CRITICAL ROLE OF CD45/SFK AXIS IN CELL MIGRATION IN MULTIPLE MYELOMA

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CD45 (*PTPRC*) is a receptor-like protein tyrosine phosphatase ubiquitously expressed on haemopoietic cells that mediates B cell receptor signaling through Src family kinases (SFK). In multiple myeloma (MM) loss of CD45 expression has been correlated with earlier disease progression and inferior treatment outcomes. Our previous *in vitro* studies demonstrated a 'metastatic' phenotype for CD45 negative MM, but the underlying mechanism(s) remain unknown. SFK activation has been reported in different metastatic malignancies.

AIM: To investigate the potential role of CD45/SFK in the 'metastatic' phenotype for CD45 negative MM.

METHODS: CRISPR/Cas9-mediated PTPRC knockout (KO) in a human myeloma cell line, OCI-MY1, was used to investigate the role of CD45/SFK. Phenotypic and transcriptional changes were identified by immunoblotting, modified Boyden chamber assays and RNA sequencing. SFK-specific inhibitor, Saracatinib, and siRNAs were used to validate the role of SFK in migration.

RESULTS: The inhibitory phosphorylation on Lyn p-Y507 (the predominate member of SFK in MM) was significantly enhanced in the absence of CD45 phosphatase activity in the OCI-MY1 CD45 KO cells, leading to the subsequent inactivation at Y416. The KO cells demonstrated a significant reduction in homing capacity towards bone marrow stromal cells, down to 11.5% (p-value<0.0001) compared with the WT cells. Saracatinib-treated WT cells showed 50% (p-value<0.05) reduction in the homing capacity. Also, silencing Lyn and Fyn expression with siRNAs in WT cells demonstrated similar effects (76%, p-value<0.01 and 55%, p-value<0.001 respectively), confirming the reduction in homing potential of CD45 KO cells was due to their lower level of SFK activity. RNA sequencing identified differentially expressed migration-related genes in the CD45 KO cell. Validation of these data is in progress.

CONCLUSION: The loss of CD45 diminishes the homing capacity towards bone marrow by inactivating SFK activity. Further evaluation will identify molecular mechanisms and pathways regulated by CD45/SFK axis.

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52. MACROPINOCYTOSIS: AN IMPORTANT ROUTE OF TUMOR NUTRIENT UPTAKE IN KRAS-MUTATED MYELOMA CELLS

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Aim: Sustained cancer cell growth requires up-regulation of nutrient acquisition mechanisms. Novel approaches can identify "tumor fuel", the way it is obtained and then altered for cellular usage. This study investigated the role of macropinocytosis as a protein uptake mechanism in myeloma cells.

Method: Macropinosomes were visualized using confocal microscopy in KRAS-mutated and WT human myeloma cells utilising TMR-dextran and 5-[N-ethyl-N-isopropyl] amiloride (EIPA) as a marker and specific inhibitor of macropinocytosis, respectively. Internalization of labelled albumin and its co-localization with TMR-dextran were evaluated in parallel. Degradation of macropinocytic albumin was evaluated by dual labelling of cells with TMR-dextran and DQ-BSA. Cell sensitivity to glutamine deprivation was examined with an ATP-based viability test. To evaluate possible correlation of macropinocytosis to cell phenotype, macropinocytosis in WT-KRAS TK1 (intra-medullary) and WT-KRAS TK2 (leukaemic) cells contemporaneously derived from the same patient was studied.

Result: KRAS-mutated KMS28-PE, KMS18 and MM1S cells displayed higher levels of macropinocytosis compared to WT-KRAS KMS34, KMS12-BM and TK1 cells. This was inhibited by EIPA. Macropinocytosis led to the internalization of albumin which subsequently underwent proteolytic degradation. In sub-physiological concentrations of glutamine the viability of WT-KRAS cells was reduced when compared with KRAS-mutated cells that not only remained viable but could continue to slowly proliferate over a period of 7 days (p<0.05). Albumin rescued the partially compromised growth of KRAS-mutated cells at sub-physiological glutamine concentrations and this effect was abrogated by EIPA. Interestingly, the leukaemic TK2 cells but not the marrow-derived TK1 cells demonstrated high levels of macropinocytosis comparable to mutated-KRAS cells.

Conclusion: Macropinocytosis is a mode of protein uptake in KRAS-mutated and leukaemic-phase myeloma cells that maintains cellular viability in the context of nutrient deprivation. We hypothesise that enhanced macropinocytosis may promote a more 'metastatic' phenotype and that pharmacological inhibition of macropinocytosis may represent a novel therapeutic approach for myeloma.

53. MATURING DATA FROM THE AUSTRALIA AND NEW ZEALAND MYELOMA AND RELATED DISEASES REGISTRY

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Background: Multiple myeloma (MM) is associated with a high community burden of disease. The Australia and New Zealand (ANZ) Myeloma and Related Diseases Registry was established in 2012 to explore epidemiology and practice variation.

Methods: Registry data were assessed for patients from Jan 2013 to Oct 2016. Survival analysis was used in time to survival and disease progression.

Results: Of 1422 patients registered, 68% had MM, 61% were male and mean age at diagnosis was 66y, with 35% over 70y. Of MM patients, 34% were high risk, and CRAB was identified in 67%: 55% had bone lesions, 23% anaemia and 8% renal impairment. Of patients with ECOG status, 22% were ≥ grade 2, and 30% with ISS had ISS=3. Of 738 MM patients with bone marrow biopsy data, 610 had flow cytometry data (not performed in 328, 54%); 557 had cytogenetics data (not performed in 238, 41%); 579 had FISH data (not performed in 207, 36%) reflecting access to treatments and tests.

First-line chemotherapy: 87% received bortezomib-based therapy, 11% an immunomodulatory drug, 1% both. First-line response: overall response rate (ORR) (≥PR) 84%; bortezomib RR 88%.

Autologous stem cell transplant (ASCT) was performed in 70% of patients ≤70y. Only 6 patients >70y had ASCT. In 65% of cases with ASCT not planned, the rationale was age. Bortezomib-based first-line chemotherapy was used in 83% of patients not for ASCT.

Second-line chemotherapy: 36% received bortezomib-based therapy, 69% an immunomodulatory drug; 16% both. Second-line response: ORR 65%, bortezomib RR 81%.

Median time to disease progression: 29.5 months. Median times from diagnosis to treatment and ASCT were 20.5 days (9-36) and 6.4 months (5.2-8.1) respectively.

Conclusion: 'Real world' myeloma data are scarce. In ANZ most patients receive bortezomib-based first-line therapy and immunomodulatory drugs for second-line. Registry data can inform future clinical management and research.

54. INHIBITION OF PRMT5 EFFECTS MALIGNANT ERYTHROID DIFFERENTIATION AND SURVIVAL OF JAK2V617F MUTANT PRECURSORS IN MYELOPROLIFERATIVE NEOPLASMS

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BACKGROUND: Myeloproliferative neoplasms (MPN) are a diverse group of hematopoietic stem cell disorders. Discovery of genes mutated in most MPN like MPL, CALR and Jak2, brought hope that targeting these lesions would transform the MPN therapeutic landscape, however this has failed to eventuate. PRMT5 was initially identified as a JAK-binding protein. Its enzymatic function catalyses the symmetric di-methylation of arginines on a variety of substrates, including histones and proteins of the splicing apparatus.

AIM AND STRATEGIES: Proof of principle of the therapeutic effectiveness of an in house inhibitor of PRMT5 (CTx034, IC50=5nM) in Jak2V617F driven MPN by using an in vivo model of MPN and in human primary samples.

RESULTS: Using a murine model of Jak2V617F MPN in a competitive transplant assay, we showed that inhibition of PRMT5 led to a normalization of Jak2-mutant erythropoiesis with reduced spleen size and loss of immature erythroblasts. Progenitor assays of bone marrow cells from patients showed that JAK2-mutant erythropoiesis was approximately 5-fold more sensitive to CTx034 than normal erythropoiesis. Gene set enrichment analysis of RNA-seq data from CD34 cells treated with CTx034 revealed an expression profile similar to loss of ribosomal function. Follow-up experiments showed an imbalance of ribosomal subunits and reduced numbers of active polysomes. Moreover, RNA pulldowns showed decreased RNA binding capacity of PABP1 (poly(A) binding protein 1) thereby preventing the correct formation of the initiation of translation complex. Both effects led to a 30% decrease in protein translation in primary human CD34 cells.

CONCLUSION: Our findings reveal that inhibition of PRMT5 leads to impaired ribosomal function and translation with a profound effect on malignant erythroid differentiation and survival. The erythroid specificity of CTx034 might be explained by the fact that erythroid precursors have an uncommonly high proliferation rate and therefore a higher demand for ribosome biogenesis and protein production.

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55. A MODEL TO STUDY THE EFFECTS OF ENFORCED PRMT5 EXPRESSION IN THE BLOOD SYSTEM AND LEUKAEMIA

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Acute Myeloid Leukaemia (AML) is the most common blood cancer and presents with the worst 5-year survival outcomes. Protein Arginine Methyltransferase 5 (PRMT5) is thought to be overexpressed in AML. However, whether this overexpression is a driver of leukaemia or simply a reflection of a leukaemic state, is still unknown.

AIM: To generate a model that will allow us to examine the effects of PRMT5 overexpression in haematopoiesis and leukaemia.
METHODS: Immunohistochemistry was performed on bone marrow smears from healthy patients and patients with AML to assess the levels of PRMT5 protein. To generate an *in vitro* model of enforced PRMT5 overexpression, a retrovirus with a fluorescent reporter was generated that contained the sequence for a FLAG-tagged PRMT5 protein. This virus was used to infect an AML cell line, and Western blot, FACS and qRT-PCR were conducted to assess the levels of PRMT5 protein and RNA in the infected cells.
RESULTS: Immunohistochemistry confirms that bone marrow smears from patients with AML show a higher level of PRMT5 protein than control patients. In our *in vitro* PRMT5 overexpressing cell line, Western blot analysis revealed that PRMT5 was overexpressed, and FACS confirmed that there was 4.38 (SD 0.48) fold increase in the level of PRMT5 protein as compared to control cells ($p < 0.05$, unpaired t-test). PRMT5 mRNA was also increased in the overexpressing cells line, associated with a 31.36 (SD 3.76) fold increase in mRNA levels as compared to control ($p<0.01$, unpaired t-test).
CONCLUSION: Our retroviral construct effectively causes an overexpression in PRMT5 RNA and protein levels *in vitro*. We will use this system to generate an *in vivo* model of PRMT5 overexpression by transplanting infected fetal liver cells into recipient mice. This will allow us to examine what effect enforced PRMT5 expression has on haematopoiesis, and leukaemia development.

56. THE EMT TRANSCRIPTION FACTOR ZEB1 REGULATES MYELOID DEVELOPMENT AND ACTS SYNERGISTICALLY WITH ZEB2 IN HEMATOPOIETIC STEM CELLS DIFFERENTIATION

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INTRODUCTION: The Zinc-finger E-box binding (ZEB) family of transcriptional regulators consists of two structurally related proteins: Zeb1 and Zeb2. Besides their roles in epithelial-to-mesenchymal transition (EMT) processes during embryogenesis and tumour progression, there is accumulating evidence that both proteins are over-expressed and involved in acute myeloid leukaemia. Here we examined the roles of Zeb1 in hematopoietic development and its potential effect in leukaemia development using conditional gain- and loss-of-function models.

METHODS: Conditional Zeb1 gain-of-function or Zeb1 loss-of-function mice were crossed with Tie2-Cre (Cre enzyme expressed in endothelial cells and their progeny), Vav-iCre (Cre enzyme in hematopoietic cells) or tamoxifen-inducible Cre-ERT2 line. All the strains were backcrossed to a C57Bl/6 genetic background for at least 6 generations.

RESULTS: While over-expression of Zeb1 has led to an increase in myeloid lineage especially monocytes, Zeb1 loss-of-function model indicated that there were differentiation defects in myeloid populations. A significant decrease of myeloid cells including neutrophils and monocytes were observed in mice reconstituted with Zeb2-deficient bone marrow cells. Since Zeb2 conditional knock-out mice have been shown to develop myeloproliferative disorder, we will keep monitoring the aging mice to see whether Zeb1 deletion will lead to hematopoietic transformation such as Sezary Syndrome.

Given the fact that Zeb1 acts in a quite different manner from Zeb2 in hematopoietic differentiation, we then investigated whether there was a functional synergy or antagonism between the two. In tamoxifen-inducible Zeb1 and Zeb2 double knock-out mice, flow cytometric analysis revealed a dramatic effect in hematopoietic stem cells differentiation. The consequences of the double deletion on AML maintenance and progression will be further investigated using oncogenic MLL-AF9 and MLL-ENL models.

CONCLUSIONS: These results reveal that, different from Zeb2, Zeb1 may act as a positive regulator for myeloid development. Given the fact that Zeb1 controls MLL-AF9 AML cell migration and invasion, Zeb1 and its downstream target genes might be excellent targets for novel and improved therapies in MLL fusion protein-driven AML.

57. INTEGRATION OF CLINICAL QUALITY REGISTRY INFORMATION INTO ALFRED HEALTH'S CLINICAL GOVERNANCE FRAMEWORK: A SHARED JOURNEY

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Clinical quality registries (CQRs) collect high quality data regarding a specific disease/condition to monitor patterns of disease and treatment, benchmark quality of care, and reduce variation in quality and outcomes of care.

AIM: To maximise the value of Alfred Health (AH) CQR participation by integrating CQR reporting within the AH clinical governance framework.
METHODS: AH CQR participation was identified via contact with AH Ethics committee, registry websites, word of mouth, and received reports. Over 12 months, one-on-one meetings with AH CQR lead investigators/clinicians enabled the capture and tabulation of information regarding CQR purpose, data collection, governance, and reporting frameworks. CQR reports providing benchmarked outcome results were prioritised for organisational clinical governance reporting. Methods to engage clinicians in ongoing sharing of CQR outcomes with the clinical governance unit (CGU) were explored.
RESULTS: A comprehensive picture of AH CQR participation, and an annual CQR reporting schedule resulted. Seventy-five clinical registries or external audits (regular site-level clinical outcome results) were identified, with twenty-two reports providing benchmarked data. Key factors impacting organisational tracking included variation in registry type, maturity, and reporting frameworks. CQR reports varied from 7-page quarterly site reports to over 300-page public annual reports. Outside of narrative-style executive summaries, few reports provided an "at-a-glance" overview of key findings to facilitate organisational reporting. Ongoing clinician engagement underpinned effective clinical governance reporting due to complex clinical content and risk-adjustment variation. Time constraint and workload concerns required careful consideration in local reporting framework development.
CONCLUSION: AH clinical registry participation provides high-quality information for clinicians delivering clinical care. Standardised CQR reporting of key messages would facilitate more effective CQR finding integration into health service clinical governance frameworks and make it easier for health service executives and Boards to review CQR outputs and how they can inform health service quality improvement. Local clinician engagement and support are fundamental to effective organisational CQR report use.

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58. INCIDENCE, PREVALENCE AND FACTORS CONTRIBUTING TO BRAIN INJURY IN THE FAMILY VIOLENCE CONTEXT: A SYSTEMATIC REVIEW

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Brain injury among victims and perpetrators of family violence is an increasing international health concern. Brain injury can occur as a result of family violence or as a pre-disposing factor which can contribute to the perpetration of family violence. International research into the nexus of brain injury and family violence is sparse. Prevalence statistics of brain injury for those exposed to family violence, are not available. Challenges to obtaining accurate statistics on these phenomena include; under-reporting of family violence, and victims not being mandatorily screened.

AIM: To investigate the current literature regarding prevalence, incidence and contributing factors of brain injury within a family violence context.
METHODS: A systematic search of CINAHL, MEDLINE and PsychINFO databases was undertaken with the search limited to: English, published between 2000 and 2017. Search strategy incorporated appropriate customised key words and MeSH terms and Boolean operators, tailored for each database.
RESULTS: Initially 707 studies were identified with 66 meeting inclusion criteria. Data were extracted to identify context, incidence and prevalence and contributing factors. The comprehensive search resulted in no population wide studies being found and the participant groups investigated were vulnerable populations and not representative of the general population. Thematic analysis revealed biological factors: age of parent/baby, gender (e.g. male infants and twins more likely to sustain a brain injury through family violence with young mothers); behavioural factors: alcohol and drug use; social factors: childhood abuse, hostile living environments, previous trauma; financial pressures, employment status, housing availability; and environmental factors (natural disasters).
CONCLUSION: Limited research exists examining the prevalence and/or incidence of brain injury in the context of family violence. Future investigation into the nexus between brain injury and family violence is required however, this is complex due to the inconsistency of definitions, assessment tools and research methods used throughout the world.

59. DEFINING A STANDARD SET OF QUALITY INDICATORS FOR BREAST DEVICE SURGERY – TOWARDS GLOBAL BENCHMARKING.

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Breast device registries provide a platform for monitoring breast devices encompassing breast implants, tissue expanders and dermal matrices, and the quality of care and patient outcomes for breast device surgery. Defining a standard set of quality indicators and risk factors, will enable consistency and adjustment for case-mix in benchmarking quality of care across breast implant registries globally.

OBJECTIVE: To develop a set of quality indicators to enable assessment and reporting of quality of care for breast device surgery which can be applied globally.

METHODS: Potential quality indicators were identified and a scoping review undertaken. Consensus on the final list of quality indicators was obtained using a modified Delphi approach. This process involved a series of online surveys, and teleconferences over six months.

The Delphi panel included participants from various countries. Participants included a panel with representation from surgical specialty groups including breast and general surgeons, plastic and reconstructive surgeons, cosmetic surgeons, a breast-care nurse, a consumer, a devices regulator (Therapeutic Goods Administration) and a biostatistician. A total of 12 candidate indicators were proposed: Intraoperative Antibiotic wash, Intraoperative Antiseptic wash, Preoperative antibiotics, Nipple Shields, Surgical plane, Volume of implant, Funnels, Immediate vs delayed reconstruction, Time to revision, Reoperation due to complications, Patient satisfaction, and Volume of activity.

RESULTS: Three of the 12 proposed candidate quality indicators were endorsed by the panel: preoperative intravenous antibiotics, reoperation due to complication, and patient reported outcome measures.

CONCLUSIONS: The three endorsed quality indicator measures will enable breast device registries to standardize benchmarking of care internationally for patients undergoing breast device surgery. Uniform reporting practices enable registries to ensure continual safety and consistency in the quality of care and improvement in patient outcomes.

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60. UNDERSTANDING END-OF-LIFE CARE AT THE ALFRED HOSPITAL

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Providing optimal end-of-life care in acute hospital settings is challenging and data describing current practices in Australian acute hospitals is limited.

AIM: To explore the end-of-life practices at Alfred Health.

METHODS: A retrospective, descriptive, observational study was undertaken and ethics approval granted. Patients who died at the Alfred were identified for audit from hospital administrative data between 1st July 2015 and 30th June 2016. Inpatients that died at least 4 hours after admission were eligible. A total of 200 deceased patient records were selected at random. Data were entered into an online collection tool and included demographic data, information pertaining to advanced care and resuscitation plans, life sustaining treatments, whether or not clinicians recognised that the patient was dying and the type, if any, of the palliative approach to patient care.

RESULTS: Most patients (72%) were aged 60 years and over. Most (69%) were admitted from home, which was higher if admitted to ICU (77%). 16% of patients were from a residential aged care facility but if they died on the ward at 4-48 hours this rose to 38%. In the vast majority (88%), the patient was recognised to be dying but time between recognition and death was short at 20 hours. A small number (14%) had an advance care plan. Almost all patients (88%) had a documented resuscitation plan during their stay but duration of time from first documentation to death was short at 1.53 days. Less than half (37%) of patients were referred to palliative care and for those who died in ICU only 1%. ICU utilisation was high at 51% and 36% died in ICU.

CONCLUSION: The late recognition of dying exposes patients to invasive interventions such as ICU and limits utilisation of specialist palliative care potentially leading to poor quality end-of-life care.

61. A DESCRIPTIVE ANALYSIS OF SYRINGE VENDING MACHINE USE IN SOUTH-EAST MELBOURNE

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Syringe vending machines (SVMs) provide a secondary distribution point of sterile injecting equipment for persons who inject drugs (PWID). This study describes data collected between December 2015 and August 2016 from a recently installed SVM in South-East Melbourne, which aims to inform future implementation and provide corrective measures to better meet the needs of PWID.

METHOD: Age, gender and postcode are recorded by the individual via keypad prior to product distribution, with product, timestamp, and machine operation status recorded concurrently by the machine. A 40-second exclusion period was used to prevent event (a single fit pack distributed) duplication.

RESULTS: Two thirds of use occurred outside NSP operating hours (9am-5pm). Under-30 age categories accounted for 68% of events, with 15-20 year-olds the single largest group (20%). 'Other' gender accounted for 10% of events; proportions were similar for women (46%) and men (44%). The machines distributed 1,841 free fit packs (two fits), 954 fit packs with water ($2, two fits), accounting for 5590 needles and syringes, and 71 steroid packs. The machines were 'sold-out' 15% of times and jammed less than 1%.

CONCLUSION: This descriptive analysis provides insight into a sub-population of PWID who have not been previously described by Australian epidemiological studies of PWID. Importantly, age, gender and time accessed. However, needle and syringe availability requires investigation to decrease sold-out status, which may include more frequent stocking of machines. Further evaluation of machine data can provide useful metrics for future machine optimisation in Melbourne.

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62. INTEGRATIVE REVIEW: ENGAGING PATIENTS, FAMILY AND HEALTH PROFESSIONALS IN COMMUNICATION DURING TRANSITIONS OF CARE

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Aims. To determine the current evidence and gaps in knowledge around patient and family engagement in communication with health professionals during transitions of care to, within and from acute care settings.

Background. Transitions of care are recognised as times of increased risk for a range of adverse events. Without an agreed understanding of how to promote the engagement of patients in transitions of care, approaches adopted to support patient safety may not be effective.

Design. An integrative mixed method review was conducted.

Data Sources. Between 2003 to 2017, a systematic search of bibliographic databases was conducted, including the Cochrane

Central Register of Controlled Trials (CENTRAL), Web of Science™, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline, PsycInfo, EMBASE and Sociological Abstracts.

Review Methods. Inclusion criteria were established, and identified studies were screened for relevance. Two reviewers extracted data independently, and the methodological quality of the studies was independently assessed using the Mixed Methods Appraisal Tool (MMAT) Version 2011. Overall quality scores are provided for each study.

Results. Four themes emerged: 1) Partnering in care; 2) Augmenting communication at transitions; 3) Impeding information exchange; and 4) Outcomes of communication during transitions.

Conclusion. While attitudes towards engaging patients and family members in transition communication in acute settings are generally positive, current practices are variable and structural supports for this practice are not always present.

63. MECHANISMS OF FAILURE IN BASE OF THUMB IMPLANT ARTHROPLASTY: A SYSTEMATIC REVIEW

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Base of thumb osteoarthritis (OA) is a common condition in the Caucasian population. Up to one third of post-menopausal women have radiological changes and one quarter of these women have pain. Many types of implant arthroplasty are available for treatment of base of thumb OA, however most are associated with complications and high rates of failure.

AIM: The objective of the current systematic review was to identify the complications leading to implant failure in basal thumb arthritis

METHODS: The systematic review was performed according to the Preferred Reporting Items for Systematic reviews and Meta- Analyses (PRISMA) guidelines. The identified implants were grouped by design concept in to 5 groups: Total joint replacement, Hemiarthroplasty, Interposition with No, Partial and total trapezial resection. The number of reported complications were combined for each implant design group and overall by simple addition. Implant-years were calculated by multiplying number of arthroplasties in each study by the study mean length of follow up. The rate of each complication was calculated for each implant design group, and an overall rate as a proportion of the number of cases with each complication divided by the total number of Implant-years for each design group. A 10-year rate of complication was calculated.

RESULTS: A total 125 articles were included post full text review. 4 articles were level I, 2 level II, 21 level III, 98 level IV. A total of 5363 arthroplasties in 5313 patients were identified. 83% were done on females, and 57% on the dominant hand. The mean age of the patients ranged from 51 to 71 years, and the mean length of follow up of the studies ranged from 4 to 196 months (16 years). A total of 51 separate implant types for base of thumb arthritis were identified; 18 total joint replacements, 6 Hemiarthroplasty, 12 interposition with partial trapezial resection, 13 interposition with total trapezial replacement, and 2 interposition with no trapezial resection.

11 implant related complications were identified which lead to at least revision of one implant. The overall 10-year revision rate for all implants combined from most common to least common: Aseptic loosening (7.96%), Dislocation (6.40%), Persistent pain (3.86%), Subluxation (1.27%), Fracture of implant (1.35%), Peri-prosthetic fracture (0.76%), Foreign body reaction (1.59%), Infection (0.68%), Osteolysis (0.56%), Implant subsidence (0.44%), and Periprosthetic ossification (0.12%)

CONCLUSION: A range of complications can lead to implant failure in implant arthroplasty for base of thumb arthritis. Designs found to be susceptible to aseptic loosening, dislocation, persisting pain and using materials inducing foreign body reaction need to be used with caution. The evidence supporting the use of implant arthroplasty can be strengthened by means of prospective studies with longer term follow up.

64. A MULTI-FACETED BURN OUT PREVENTION PROGRAM (TREAT) IS FEASIBLE AND WELL ACCEPTED BY HEALTHCARE WORKERS IN A LARGE METROPOLITAN HEALTH SERVICE

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Background: Occupational stress is associated with burn out which causes adverse physical and psychological outcomes. Burn out is common in healthcare. Burn out in healthcare is reduced by staff interventions, including exercise, meditation and dietary change, and organisational interventions, including favourable rostering and workload allocation and providing staff support. Health services should facilitate these approaches.

Methods: AlfredHealth is a major health service employing over 8000 staff. Therapeutic Relaxation and Enhanced Awareness Training (TREAT) is a program for reducing burn out through self-awareness, self-compassion, resilience and engagement, provided to AlfredHealth staff. TREAT uses mindfulness, yoga, education and other self-care tools. TREAT is multi-modal with seven-week programs, one-off sessions supporting leadership / team events, brief focus sessions prior to ward rounding and a mobile meditation app. The app has guided mindfulness meditations focusing on health care situations, including brief work place meditations and longer meditations for outside the work place. Evaluation has been by anonymous surveys and mobile app utilisation data.

Results: 1052 staff undertook TREAT between 2015 and 2017. 100% of survey respondents found TREAT was beneficial in the workplace. 97% wanted to participate in further sessions. The majority felt better able to cope with stress and to handle conflict at work. 93% reported TREAT improved the experience of working for AlfredHealth. 93% believe that other health services should offer similar programs.

The mobile app was released in January 2017. At March 2018 there were 5300 downloads, with 150 active weekly users and 74% returning users.

The online survey results showed: 100% would recommend the app to friends or colleagues 95% reported improved well-being and 79% reported better coping at work

Conclusion: TREAT is feasible with high staff participation, high approval ratings and significant levels of self-reported positive personal change. Further study is required to determine whether this reduces burn out.

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65. A NEW MODEL OF CARE FOR HEART FAILURE IN-PATIENTS TO REDUCE VARIATION

Ingrid Hopper[1], Kellie Easton[1], Illona Bader[1], James Campbell[2], Peter Bergin[1], David Kaye[1]

[1]Alfred Heart Centre, Alfred Hospital; [2]Alfred Redesigning Care, Alfred Hospital.

The Alfred is a tertiary 638 bed hospital admitting approximately 1500 patients with heart failure (HF) each year under general medicine (GEN MED), cardiology–general (CAGE), and cardiology–advanced heart failure (CAHF). There was no standardised model of care, resulting in variation in the delivery of guideline recommended care for heart failure patients.

AIM: To maximize the time HF patients spend well in the community by delivering best practice guidelines to reduce variation in care and improve overall outcomes.
METHODS: We engaged stakeholders from all units involved with delivery of care to HF patients. Small group discussions identified perceived problems, and “acute” and “ambulatory” working groups were established. A project steering committee was established with executive sponsorship. Mapping, hospital ICD-10 codes, and VCOR Heart Failure Snapshot data from May 2016 provided a detailed audit of care of HF patients. Staff knowledge was surveyed, patient experience unit involved.
RESULTS: The quality improvement intervention launched in February 2017 comprised an electronic *HF care bundle* which established the standard of care, a 4-page education pack “Important information for patients” was created to standardise HF education, *a Transitional safety net* was established through blanket referral of all patients with HF to HARP, with a phone call at 72 hours after discharge to assess risk of readmission and home visit if needed. A *nurse-pharmacist early review clinic* was established for CAGE patients to reduce variation in wait times to see patients within 10 days of discharge.Improvements in process measures were seen in the 2017 Heart Failure Snapshot (prescribing of heart failure medications, referral to HARP, delivery of patient education, timely follow up). Annual HF readmission rates were compared using the students’ t-test. Preliminary results indicate no significant reduction in readmission rates (2016:19.7% vs 2017:18.7%, p=NS) and no significant change in bed days per patients (2016: 8.4 days vs 2017: 8.7 days, p=NS).
CONCLUSION: Implementation of this model of care for heart failure improved delivery of guideline mandated heart failure care but did not reduce readmissions.

66. CONSULTING THE ORACLE: USING THE DELPHI TECHNIQUE TO OBTAIN CONSENSUS ON MAKING MEDICAL EMERGENCY TEAM (MET) STAND-DOWN DECISIONS

Natalie Kondos[1,2], Associate Professor Helen Forbes[1,2], Professor Jonathan Barrett[3] and Professor Tracey Bucknall[1,2].

Organisation/department: [1]Alfred Health, [2]Deakin University, School of Nursing and Midwifery, [3]Epworth HealthCare

A stand-down decision is the decision of the medical emergency team (MET) to cease a medical emergency response once the immediate patient crisis has been resolved. The patient must be perceived to have had all unmet needs attended, been stabilized medically or have a clear plan in place inclusive of altered medical emergency review criteria or limitation of treatment orders.

AIM: The primary aim of this study was to describe MET call stand-down decision-making and the influences on decision making practice.

METHODS: A Delphi design was used to develop consensus on the MET stand-down decision. This method uses a consensus building approach by undertaking a series of questionnaires with multiple iterations, with the previous questionnaire results informing the next questionnaire. Data was obtained from a panel of 10 experts in the field of patient deterioration and MET responses. This group of experts was determined by their current vocational involvement in rapid response systems and through their contribution to peer-reviewed publications in high quality journals on the topic matter.

RESULTS: The major stand-down decision themes collected from the expert panellists were: that patient stability has been achieved; a management plan to treat or mitigate further risk of deterioration inclusive of limit of treatment orders has been documented and verbally communicated to relevant staff; an escalation plan for management of further deterioration has been documented and verbally communicated to relevant staff; and that ward capability and staff capacity has been considered with respect to being able to provide ongoing care to the patient in the post emergency response period.

CONCLUSION: By determining the decision-making elements for optimal stand-down decisions we can develop a checklist for stand-down decision making within the context of a MET, with the overarching aim of optimising this practice to prevent and mitigate the risk of future patient deterioration.

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67. CONSULTING THE ORACLE: USING THE DELPHI TECHNIQUE TO OBTAIN CONSENSUS ON MAKING MEDICAL EMERGENCY TEAM (MET) STAND-DOWN DECISIONS

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CONCLUSION: By determining the decision-making elements for optimal stand-down decisions we can develop a checklist for stand-down decision making within the context of a MET, with the overarching aim of optimising this practice to prevent and mitigate the risk of future patient deterioration.

68. CLINICAL AGGRESSION IN A LARGE HEALTH SERVICE IS NOT JUST AN ED PROBLEM

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[1]Pre-hospital Emergency Care Australia and New Zealand (PEC-ANZ); [2]Department of Epidemiology and Preventive Medicine, Monash University; [3]Psychiatry, Alfred Health; [4]General Medicine, Alfred Health; [5]Aged Care, Alfred Health.

'Code grey' is the security response to clinical aggression in the hospital setting. Code grey episodes present a risk of assault to healthcare providers, and may place a significant burden on resources in a non-acute hospital space.

AIM: To describe the frequency of in-patient clinical aggression as part of an organisational review characterising the epidemiology, management and resource utilisation associated with code grey episodes.

METHODS: A retrospective audit was conducted of all in-patient code grey episodes occurring between 1 January and 31 December 2015, across three Alfred Health hospitals. Patients were identified from security records and clinical incident reports. Variables collected included socio-demographics, risk factors and resource utilization. The frequency of staff assault, physical (limb) and mechanical restraint, rapid tranquilisation (parenteral drugs for sedation) and patient attendant (nursing staff) were analysed based on data extracted from the security log, administrative database and medical notes.

RESULTS: There were 1644 code grey episodes in 658 patients. The number of episodes per patient admission ranged from 1 – 43 (median 1). Patients were 68% male with a median age of 55 years (range 16-98 years). Risk factors of interest included psychiatric diagnosis (48%), dementia or cognitive impairment (21%), acquired brain injury (20%), smoking (46%), alcohol abuse (42%) and illicit drugs (28%). Staff assault was recorded in 14% of episodes. Patient management included physical restraint (37%), mechanical restraint (15%) and rapid tranquilisation (28%), with two or more forms of restraint required in 25% of cases. Patient attendant presence rose from 38% during episodes to 52% after episodes.

CONCLUSION: Clinical aggression is challenging in its complexity and case mix. The prevalence of assault was high, and the most common form of restraint was physical restraint. While half of code grey episodes were followed by a patient attendant, the therapeutic value of this resource allocation requires consideration.

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69. A QUALITATIVE ANALYSIS ON THE PERCEIVED BARRIERS AND ENABLERS TO FALLS PREVENTION IMPLEMENTATION IN THE ACUTE HOSPITAL SETTING

Aisha Emilirosy Roekman[1], Dr Darshini Ayton[1], Dr Renata Morello[1], Associate Professor Anna Barker[1], Associate Professor Caroline Brand[1], Professor Keith Hill[2]

[1]Health Service Research Unit, Division of Health Services, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; [2]School of Physiotherapy, Curtin University, Western Australia, Australia.

Studies examining the effectiveness of falls prevention programs have been the focus of research attention as falls remain the most common adverse event in the hospital settings. However, there is limited research exploring the barriers and enablers to the implementation of falls prevention programs. 6-PACK was a nurse-led falls prevention program implemented in six hospitals in Australia. The 6-PACK RCT was the world's largest falls prevention trial. Unfortunately, the trial results demonstrated that 6-PACK did not reduce in-hospital falls. To understand the contextual factors impacting on the trial results, this study collected qualitative data from senior hospital staff and nurses post-implementation of 6-PACK program.

AIM: To explore the perceived barriers, enablers, and sustainability factors to implementation of the 6-PACK program.

METHODS: Seven focus groups with nurses and 13 interviews with hospital senior staff. Data analysis was guided by the COM-B framework. This framework includes capability, opportunity, and motivation factors that interact to create behaviour change.

RESULTS: Small hospital rooms, belief that falls were inevitable, privacy issues during bathroom supervision, insufficient staffing levels, lack of resources to implement 6-PACK strategies, ineffectiveness of 6-PACK facilities, and staff juggling multiple projects were identified as barriers to 6-PACK implementation. Enabling factors included: one-on-one education during ward round, senior staff leadership and support, nurses' positive attitudes towards 6-PACK, provision of audit-feedback-reminder, and staff held accountable for program implementation. In order to sustain the program, the hospitals must continue ward-champion role as project leader, introduce 6-PACK to future nursing staff, provide on-going audit and feedback, encourage staff involvement in 6-PACK implementation, and adopt 6-PACK for hospital-wide implementation.

CONCLUSION: This study identifies the perceived barriers, enablers, and sustainability factors to falls prevention program implementation from the perspective of hospital staff. These results can be used in the design future falls prevention programs and implementation strategies.

70. ACUTE COLONIC PSEUDO-OBSTRUCTION LEADING TO PERFORATION: A CASE-CONTROL STUDY.

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An apparent 'cluster' of cases of acute colonic pseudo-obstruction (ACPO) complicated by colonic perforation within our institution led us to explore whether there was a causal link between ACPO complicated by perforation and a number of known aetiological factors, including a potentially new cause, tapentadol.

METHODS: The study was a retrospective, case-control study. ICD-10-AM coding was used to identify 8 adult patients with ACPO and subsequent perforation between August 2014 and March 2017. ACPO was confirmed as cause of perforation through evaluation of CT scans to exclude other potential causes. Four controls were identified for each case and matched based on age, sex, admission date, admission unit.

RESULTS: A total of 40 patients were identified (eight cases and 32 controls). Mean age for cases and controls were 63.7yrs (SD 15.0) and 62.1yrs (SD 11.3), (p=0.634). There was a significantly higher incidence of alcohol use among cases (p=0.031) but similar incidence of hypertension, diabetes and COPD. The mean duration of opioid use was longer for cases, 7.6 days (SD, 1.6) compared with controls, 5.0 days (SD, 3.1) days, (p=0.023). The total median opioid use (OME) 975mg [IQR, 780mg - 1256mg] versus 324mg [IQR, 71mg - 681mg], (p=0.407) was not significantly different. Tapentadol use did not differ significantly between cases (50%) and controls (32%), (p=0.338). There were no significant differences in electrolyte imbalance, laxative use or need for inotropic support.

CONCLUSION: We found an association between ACPO complicated by bowel perforation, high background ethanol requirement, longer duration of and total opioid use, but not specifically with use of tapentadol. There is a need to combine contemporary data from multiple sites exploring links to complicated ACPO with our data to confirm our associations.

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71. REPORT OF A QUALITY IMPROVEMENT INITIATIVE TO IMPROVE COMPLETENESS OF LUNG CANCER MULTIDISCIPLINARY MEETING PRESENTATION

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Despite guideline recommendation and evidence of patient benefit through MDM presentation there is still significant concern that too few patients are being presented to the MDM with published presentation rates suggesting as few as 33-60% of new cases are presented prior to treatment (6, 20, 21).

Background: We sought to evaluate the extent to which patients were presented to the Lung Cancer MDM within an Australian metropolitan university teaching hospital and sought to develop a Quality Initiative (QI) designed to evaluate system process with the objective of increasing the proportion of cases presented to the MDM. Methods: We performed a quality improvement redesign process using standard QI tools measuring MDM attendance on a 6-month pre-implementation period (PreI) compared to a 6 month post implementation (PostI) period.

Results: 76 new lung cancer subjects were observed in the PreI with mean age 72 years and 66% were presented to the MDM. 53 of 66 (80%) of subjects in the PostI period.

Conclusion: This service redesign QI initiative increased MDM attendance substantially for this cohort and demands further sustainability evaluation.

72. HIP FRACTURE CARE AT THE ALFRED

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The Australian and New Zealand Hip Fracture Registry (ANZHFR) is a clinical registry that allows access to data to improve performance and optimise outcomes of people with hip fractures. Currently, Alfred Health does not contribute to the ANZHFR.

AIM: We aimed to describe the characteristics and processes around hip fracture care at The Alfred and assess the feasibility of the orthogeriatric service to contribute data to the ANZHFR.

METHODS: We performed a retrospective chart review of all patients with a hip fracture admitted to The Alfred from 1st August to 1st November 2016 and manually extracted ANZHFR data and additional data regarding patient-related outcome measures.Demographic, injury event and hospital-based outcomes were collected as was the time taken to collect each patient's ANZHFR minimum dataset.

RESULTS: A total of 54 patients (mean age 85 years, 41% male) were admitted in three months. Pre-fracture, 67% lived at home and 61% were independent in performing personal activities of daily living. Intracapsular fractures occurred in 33% and 59% were per/intertrochanteric. The median time to surgery was 28 hours and the most common surgery performed was a sliding hip screw (52%). The median length of stay in The Alfred was 8 days and 54% were discharged to Caulfield Hospital. In this sub-acute facility, the median length of stay was 25 days. A total of 21 patients (39%) had an Alfred admission in the 12 months following hip fracture. The median time spent at home in the 12 months post fracture was 346 days. The median time to collect the ANZHFR minimum dataset was 14 minutes.

CONCLUSION: The Alfred's experience of hip fracture care is similar to that described nationally in the ANZHFR. It is feasible for the orthogeriatric service to contribute data to the ANZHFR and is likely to be simpler to complete contemporaneously.

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73. IMPLEMENTATION OF A NURSE –LED MODEL OF CARE TO TREAT PEOPLE WHO INJECT DRUGS (PWID) FOR HCV IN THE COMMUNITY

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Background: The Hepatitis C Treatment and Prevention (TAP) Study evaluates the effectiveness of an Nurse-led, outreach model to improve hepatitis C treatment uptake by current People Who Inject Drugs (PWID) and their injecting networks.

Method: PWID are recruited by Nurses from a study van in various locations in Melbourne. Primary participants invite their injecting networks to become secondary participants. Referrals come through the SuperMIX cohort, or as self-referrals. Participants are randomly allocated to immediate or deferred treatment with sofosbuvir/velpatasvir. Nurses perform pre-treatment assessments (including elastography) and offer treatment to eligible participants. Follow-up is for 18 months to monitor treatment outcomes, re- infection or resistance to therapy. Social and behavioural data are collected at each visit.

Results: 316 PWID have been screened, comprising 163 Primary and 153 Secondary participants. 112 have started and 72 have completed treatment. Some treated participants report an increased sense of well-being and changing their injecting practices to "stay clean". Many have stated that they value the chance to get treatment through the study, as they normally don't engage with other health care services. Referral to tertiary health services has been facilitated for those needing treatment outside the study criteria with some degree of success. Eighty-eight participants are screening failures. Mental health issues, homelessness and incarceration impact negatively on being able to attend study visits. Mobile phone numbers change frequently. Finding suitable locations for the van has proven problematic and is dependent on the goodwill of Local Councils and businesses.

Conclusion: While homelessness and mental health issues may be obstacles to accessing HCV treatment, we have shown that a Nurse-led outreach model provides the platform for treatment for many PWID. Its' success relies heavily on existing relationships and continued rapport building, but also on the support of local authorities, businesses and PWID themselves.

74. FUNGAL AI: BREAKING THE MOLD OF THE TRADITIONAL ANTIMICROBIAL STEWARDSHIP PARADIGM USING ARTIFICIAL INTELLIGENCE

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Introduction: Evaluation of antifungal stewardship (AFS) is hampered by a lack of patient level data on invasive mold disease (IMD) in hospitals. The aim of this study was to characterise the epidemiology of IMD & to explore metrics of relevance to AFS.

Methods: We identified haematology-oncology and haemopoietic stem cell transplant (HSCT) patients with IMD at Alfred Health from January 2010 to August 2016, by screening chest computed tomography (CT) reports with natural language processing followed by expert medical review. Host, microbiological and antifungal drug characteristics were manually extracted.

Results: There were 156 IMD-episodes in 144 patients being probable/proven in 37%. *Aspergillus* species accounted for 49% of probable/proven IMDs. Underlying disease was acute myeloid leukaemia (56%), acute lymphoblastic leukaemia (ALL, 15%), lymphoma (8.3%), multiple myeloma (8.3%), myelodysplastic syndrome (3.8%), chronic lymphocytic leukaemia/small lymphocytic lymphoma (3.2%), and post-HSCT (33%). Poor prognosis disease (refractory/progressive, relapse) underpinned 42% of IMD- episodes. Breakthrough IMD despite antifungal prophylaxis (AFP) occurred in 89 (58%) episodes. Among 67 IMD-episodes lacking AFP, 37% occurred post-HSCT with 64% occurring >100 days post-allogeneic HSCT (median 364 days). 9 episodes without prophylaxis occurred in patients with graft versus host disease. In 15 IMD-episodes among pre-transplant ALL patients, one patient did not receive prophylaxis and 14 represented breakthrough IMD, associated with intermittent liposomal amphotericin prophylaxis in 10 episodes (71%).

Conclusion: IMD surveillance facilitated by technology can strengthen AFS, yielding detailed patient-level data across all haematology patients, identifying gaps in practice and defining new risk groups who may benefit from preventative strategies.

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75. TARGETING LIPID RAFTS TO MITIGATE CARDIOMETABOLIC CO-MORBIDITIES IN HIV DISEASE

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HIV-infected patients have an increased risk of cardiometabolic diseases even when ARV treatment makes virus undetectable. We hypothesized that HIV protein Nef-containing exosomes released from infected cells could be a key contributor to pathogenesis of these comorbidities by increasing abundance of lipid rafts in bystander cells. To test this hypothesis we investigated the effects of Nef- containing exosomes on cholesterol efflux, cholesterol transporter ABCA1 and lipid rafts in macrophages. We also examined possible reversal of the effect with treatments reducing lipid rafts, ApoA-I Binding Protein (AIBP) and ABCA1 agonist peptide (AAP).

METHODS: RAW 264.7murine macrophages were treated with either GFP- or Nef-containing exosomes. When reversal was tested, the cells were also treated with ApoA-I/AIBP complex or AAP. Abundance of total & cell-surface ABCA1 was measured by western blot and cholesterol efflux assay was carried out to determine the efflux capacity of the treated cells. Lipid rafts were quantitated by confocal microscopy. The effect of AIBP on replication of HIV was tested in human macrophages.

RESULTS: Nef-containing exosomes decreased total amount of ABCA1 and decreased the cholesterol efflux capacity. Lipid rafts were increased in cells treated with Nef- compared to GFP-containing exosomes. Treatment with ApoA-I/AIBP and AAP partially reversed the effects on ABCA1 abundance and showed a tendency to increase the efflux. ApoA-I and ApoA-I/AIBP reduced the abundance of lipid rafts in the Nef-treated cells. Treatment with AIBP reduced virus replication in vitro.

CONCLUSION: Nef-containing exosomes reduce ABCA1 and cholesterol efflux thus increasing the abundance of lipid rafts in macrophages. This may lead to accumulation of cholesterol and inflammation contributing to the increased risk of cardiovascular diseases in the HIV patients. Our experiments demonstrated that AIBP and AAP may reverse this changes and even mitigate HIV replication.

76. DIFFERING PATTERNS OF PROTECTIVE ASSOCIATIONS FOR ANTIBODIES TO SURFACE ANTIGENS OF P. FALCIPARUM-INFECTED ERYTHROCYTES AND MEROZITES IN IMMUNITY AGAINST MALARIA IN CHILDREN

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Acquired antibodies play an important role in immunity to *P. falciparum* malaria and are typically directed towards surface antigens expressed by blood-stage parasites, such as merozoites and infected erythrocytes (IEs). The importance of specific IE surface antigens as immune targets remains unclear, especially in populations outside Africa, and a lack of tools has hampered the study of individual antigens.

AIM: We evaluated antibodies & protective associations in two cohorts of older & younger children in Papua New Guinea (PNG).

METHODS: We used genetically-modified *P. falciparum* with reduced PfEMP1 expression to evaluate the importance of IE surface antigens and a *P. falciparum* isolate with a virulent phenotype defined by expression of specific PfEMP1 variants.

RESULTS: We found that PfEMP1 was the dominant target of antibodies to the IE surface, with limited reactivity to other antigens. Antibodies were associated with increasing age and active parasitemia, and were higher among children exposed to a higher force- of-infection which was determined using molecular detection and genotyping. Antibodies to IE surface antigens were consistently associated with reduced risk of malaria in both younger and older children's cohorts. However, protective associations for antibodies to merozoite surface antigens was only observed in older children.

CONCLUSION: Our findings suggest that antibodies to IE surface antigens, particularly PfEMP1 variants linked with virulent phenotypes, play an earlier role in acquired immunity to malaria, whereas greater exposure is required to develop protective antibodies to merozoite antigens. These findings have implications for vaccine design, and serosurveillance of malaria transmission and immunity, especially in the current era of declining malaria transmission.

77. IMMUNE MODULATORY EFFECTS OF VAGINAL MICROBIOTA ORGANIC ACID METABOLITES ON ECTOCERVICAL EPITHELIAL CELLS

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Bacterial vaginosis (BV), a dysbiotic and pro-inflammatory condition, increases the risk of women acquiring HIV compared to eubiotic non-inflammatory lactobacillus-dominated microbiota. Lactic acid (LA), a vaginal microbiota organic acid metabolite (VMB) present at 110 mM pH 3.8 during eubiosis elicits anti-inflammatory effects on cervicovaginal epithelial cells. During BV, LA is dramatically depleted and short chain fatty acids (SCFAs), succinic acid (SA) and vaginal pH are elevated. SCFAs elicit pro- inflammatory responses from PBMCs. Here we assessed the immune modulatory effects of VMB combinations mimicking eubiosis and dysbiosis on ectocervical epithelial cells and the inflammation inhibitory mechanism of LA.

METHODS: Ectocervical cells (Ect1/E6E7) cells cultured in transwells were treated with VMB combinations to mimic eubiosis or BV in the absence or presence of TLR agonists to simulate pathogen challenge. Cytokines in the supernatant were quantified using a Luminex assay. Mechanism by which LA inhibits pro-inflammatory responses elicited by a TLR agonist and TNFα was determined by measuring NF-kB P65 and IkB by Western blot.

RESULTS: Similar to LA alone, VMB representing eubiosis elicited an 8.5 fold production of the anti-inflammatory cytokine IL-1RA and significantly dampened the production of pro-inflammatory cytokines and chemokines (IL-8, IL-6, IP-10, TNF, RANTES, MIP3) elicited by TLR stimulation. In contrast, VMB representing BV had no effect on the production of pro- or anti-inflammatory mediators from Ect1 cells. In the presence of TLR agonist stimulation, BV VMB neither promoted nor significantly dampened pro-inflammatory cytokine and chemokine responses. TNFα and TLR-agonist treatment of Ect1 cells resulted in NF-B P65 phosphorylation coinciding with degradation of IB, which was abolished in the presence of LA. These data indicate that LA inhibits pro-inflammatory effects through the NF-B signalling.

CONCLUSIONS: The eubiotic VMB combination elicits anti-inflammatory effects through LA, which inhibits inflammation through the NF-B signalling pathway. VMB representing BV conditions did not elicit immune modulatory effects on cervicovaginal epithelial cells. These data are consistent with the non-inflammatory and pro-inflammatory milieu associated with eubiosis and BV, respectively.

78. THE IMPACT OF RECURRENT CMV DISEASE ON LONG-TERM SURVIVAL IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) remains a significant contributor to morbidity and mortality following solid organ transplantation (SOT). While relapse after treatment completion can occur in up to 30% of patients, the effect of this on mortality is not clear. The aim of this study was to explore the impact of recurrent CMV disease on long-term survival in SOT recipients.

Methods: We performed a retrospective cohort study of SOT recipients who completed treatment for an episode of CMV disease. Data on potential confounders were collected from the time of treatment completion. Censoring occurred at death, loss to follow-up or 10 years. Univariable and multivariable hazard ratios (HR) were calculated using a Cox model, treating relapse as time-varying.

Results: 79 kidney, 52 heart, 34 liver and 5 liver-kidney recipients were included. 62/170 died, at a median of 3.8 years (interquartile range [IQR] 0.8-6.6 years). Median follow-up amongst the 108 survivors was 7.4 years (IQR 3.7-10 years) although 22 (13%) were censored before 3 years. CMV relapse occurred in 49/170 (29%), 67% within 6 months. Overall mortality amongst those who relapsed was 39% (19/49) versus 36% (43/121) in those who remained relapse-free. On univariable analysis, CMV relapse was not associated with a significantly increased risk of death (unadjusted HR 1.59, 95% CI 0.92-2.75, p=0.10). After controlling for age and transplanted organ type, findings were similar (adjusted HR 1.68, 95% CI 0.93-3.04, p=0.09).

Conclusion: Mortality rates following CMV remain high even in the valganciclovir era. We did not identify a significant relationship between the development of recurrent CMV disease and death. However the complex nature of these patients, multiple layers of potential confounding and limited statistical power of our cohort make detection of small effects difficult. Future prospective studies evaluating the clinical efficacy of strategies to reduce recurrence are needed to further assess this relationship.

79. VANCOMYCIN AND CEFTRIAXONE PRESCRIBING: ANALYSIS OF THE AUSTRALIAN SURGICAL NATIONAL ANTIMICROBIAL PRESCRIBING SURVEY (SNAPS) DATASET

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Current Australian data highlights guideline non-concordant prescribing of surgical antimicrobial prophylaxis (SAP)[1], in particular for broader spectrum antimicrobials such as vancomycin and ceftriaxone.[2] Vancomycin is a broad Gram-positive spectrum antimicrobial that is only recommended for SAP under defined circumstances. [3] Ceftriaxone is a broad-spectrum antibiotic covering both Gram-positive and Gram-negative infections and is not recommended for SAP for any defined circumstances as per current Australian guidelines. [3]

AIM: To use the Australian SNAPS dataset 2016-17 to describe current SAP prescribing practices for vancomycin and ceftriaxone.

METHODS: Data was collected in accordance with the standardised SNAPS guidelines via registered auditors of the SNAPS online portal. Auditors predominately employed a retrospective methodology; including point prevalence (consecutive and random) and directed surveys i.e. targeted surgical units and wards. Descriptive analyses of the SNAPS 2016 were performed with analysis of the 2017 dataset pending completion on November 30th 2017.

RESULTS: The 2016 SNAPS dataset included a total of 3189 antimicrobial doses prescribed for procedural prophylaxis. From this, ceftriaxone and vancomycin represent the 4th and 5th most commonly prescribed procedural antimicrobials (3.5% and 2.5% respectively) and both demonstrated high rates of inappropriateness (92.0% and 72.2% respectively).

In terms of the 1515 post-procedural antimicrobial doses; ceftriaxone and vancomycin accounted for 2.2% and 1.8% respectively of all antimicrobials and demonstrated high rates of inappropriateness (91% and 74% respectively).

CONCLUSIONS: Pending analysis of the 2017 data set will provide further insight to current practice and allow for further analysis of the surgical procedural groups involved and the presence of risk factors. The prescription of vancomycin and ceftriaxone for SAP is generally not indicated or appropriate. Further research to identify trends of such prescribing behaviour is warranted to inform the development of tailored interventions for the optimisation of SAP and subsequent patient care and safety.

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80. INVESTIGATING FUNCTIONAL ANTIBODY MECHANISMS AGAINST MALARIA IN NATURALLY-ACQUIRED AND VACCINE-INDUCED IMMUNITY

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Plasmodium falciparum malaria is a substantial cause of global morbidity and mortality, and the development of a highly efficacious vaccine would significantly aid malaria elimination. RTS,S is the leading malaria vaccine candidate, and is based on major surface antigen expressed on the sporozoite developmental stage, termed circumsporozoite protein (CSP). In clinical trials, RTS,S was partially efficacious against malaria, and protection had some association with anti-CSP antibodies. However, it is unclear how antibodies function to confer protection. This hinders our ability to evaluate RTS,S and develop strategies to enhance vaccine- induced immunity and efficacy, or to develop more efficacious next generation vaccines.

AIM: To determine whether human antibodies to CSP and sporozoites function by activating complement proteins, and if this activity can be naturally-acquired or induced by RTS,S-immunisation.

METHODS: We investigated whether anti-CSP antibodies fix complement protein, C1q, and the functional consequences of antibody-complement interactions against *P. falciparum* sporozoites, *in vitro*. We then examined the acquisition of C1q-fixing antibodies in children naturally-exposed to malaria from Papa New Guinea (PNG, N=206), and in children vaccinated with RTS,S from Mozambique (phase II clinical trial, N=100).

RESULTS: Firstly, we demonstrated that antibodies can fix C1q, and sporozoites were susceptible to antibody-complement attack which consequently inhibited parasite motility and lead to cell death. Functional C1q-fixing antibodies could be naturally-acquired in children from PNG, and those with high levels had a significantly reduced risk of developing clinical malaria. We then evaluated the immunogenicity of RTS,S. Vaccination strongly induced C1q-fixing antibodies, although this was variable among children, mostly due to differences in IgG subclasses and epitope-specificity. Furthermore, functional antibodies substantially declined during the follow-up period, which may also reflect the waning of vaccine efficacy.

CONCLUSION: We identified antibody-complement interactions as a mechanism of human immunity to malaria, and demonstrate that functional antibodies can be induced by leading vaccine candidate.

81. DISCOVERY OF NEW DRUG CLASSES FOR HIV TREATMENT AND PREVENTION: EXPLORING NOVEL REVERSE TRANSCRIPTASE ALLOSTERIC SITES

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HIV-1 reverse transcriptase (RT) inhibitors form the major backbone of antiretroviral therapy (ART) for HIV treatment and prevention programs[1]. To fast-track elimination, WHO recommends a massive scale up of ART. However, increasing disease burden, drug resistance, as well as long term ART toxicity and intolerance, threaten these efforts with an eventual exhaustion of drug options predicted[2].

Despite these challenges, there is little in the way of new drug classes in the discovery pipeline, apart from those within pre-existing classes that are susceptible to cross-resistance[3]. This gap warrants an intensified search for new and better drug classes[3]. To this end, we have initiated a fragment-based drug discovery (FBDD) program targeting HIV-1 RT to identify inhibitory small molecular weight (MW<250 Da) compounds (i.e. “fragments”). HIV-1 RT is an ideal target for FBDD since it’s a conformationally flexible enzyme that is critical for viral replication[4] and a validated drug target[5]. Fragments can be strategically elaborated into larger, higher affinity inhibitors[4], while simultaneously probing novel druggable pockets for drug design.

Here we used a combination of biophysical (SPR, X-ray crystallography) and biochemical functional (RT activity inhibition) assays to screen and characterise compound libraries for novel RT inhibitory fragments and new druggable allosteric sites.

Our screen identified three hits that inhibited the polymerase activity of both wild-type and non-nucleoside RT inhibitor (NNRTI)-resistant HIV-1 RT in the micromolar range, with two of these exhibiting distinctive mechanisms compared to clinically available anti-HIV-1 drugs[6]. To advance hit-lead optimisation based on these parental scaffolds, we have established a preliminary structural activity relationship (SAR) profile based on ~ 240 functional isomers spanning the three parental fragment scaffolds. We have identified several hits with ~50-200-fold greater potency relative to the parent compounds, where SAR and molecular modelling have guided on-going organic synthesis of high potency lead molecules using medicinal chemistry.

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82. DEVELOPING STRATEGIES TO IMAGE HIV IN VIVO: COMBINING THE SARCOPHAGINE CHELATOR MECOSAR TO 3BNC117 DOES NOT AFFECT HIVE BINDING OR NEUTRALISATION

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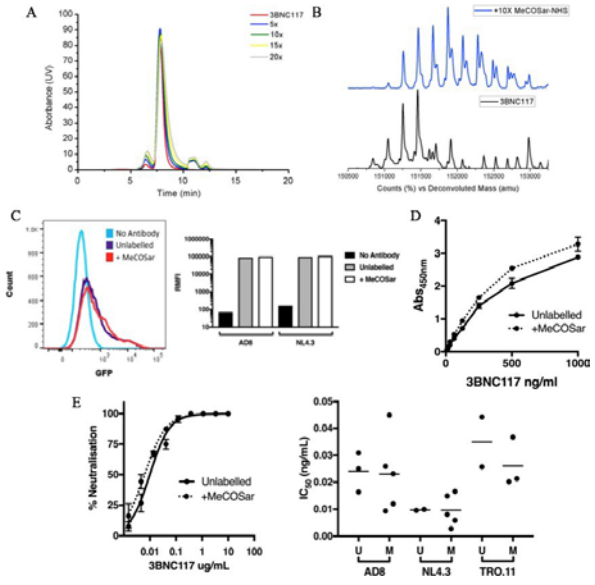
Background: Non-invasive methods to detect and quantify HIV persistence in tissue and assess cure- focused interventions in HIV-infected individuals on antiretroviral therapy (ART) are needed. Infusing radiolabelled broadly neutralising antibodies (bNAbs) targeting HIV envelope (Env) then scanning with positron emission tomography (PET) identified affected tissues sites in a macaque model. Prior to a clinical trial bNAb binding to its Env target with the addition of a next generation bifunctional chelator needs to be confirmed *in vitro*.
Methods: The bNAb 3BNC117 was reacted with different molar ratios (5x, 10x, 15x, 20x) of the sarcophagine copper chelator MeCOSar-NHS and the resulting conjugates were assessed by size exclusion chromatography (SEC) and liquid chromatography-mass spectrometry (LC- MS) and the optimal molar ratio selected. Unlabelled and MeCOSar-modified 3BNC117 were then assessed for neutralisation capability of reporter viruses pseudotyped with 3 subtype B Env strains in JC53 cells, and assessed for binding using 2 assays: 1) ELISA to immobilised Env (gp140) and 2) to Env presented on the surface of human embryonic kidney cells transfected with an Env expression plasmid. The 50% inhibitory concentration, colorimetric absorbance and flow cytometry were used to compare unlabeled and MeCOSar- modified 3BNC117 to the 3 assays respectively
Results: Different molar ratios of MeCOSar bound to 3BNC117 yielded SEC with similar elution profiles to IgG and unmodified 3BNC117. The predominant peak for unmodified 3BNC117 mass on LC-MS was 151467 Dalton (Da) and when combined with 10x molar ratio clearly demonstrated the addition of 1, 2 and 3 MeCOSar (410 Da each) per 3BNC117. 10x molar ratio was then selected to assess HIV binding and neutralization. Unlabeled and MeCOSar- modified 3BNC117 had comparable levels of binding to immobilized gp140; binding to Env expressed on the surface of 293T cells; and neutralisation of reporter viruses pseudotyped with 3 different Envs. (Figure)Conclusions: The copper chelator MeCOSar conjugates to 3BNC117 and does not interfere with binding to HIV Env or neutralisation *in vitro.* MeCOSar is appropriate to combine with 3BNC117 and is known to tightly bind the radioisotope copper-64. This construct is ideally suited to continue development for use in a clinical trial using PET to detect HIV persistence on ART.



See Figure: Modification of 3BNC117 using a 10x molar ratio MeCOSar does not interfere with 3BNC117 neutralisation or binding *in vitro.* A SEC of unlabeled and MeCOSar modified 3BNC117; B) LC-MS of unlabeled (bottom) and modified 3BNC117 bound with either one, two or three MeCOSar chelators attached (top); C) Flow cytometry of transfected cells expressing cell surface Env bound to unlabeled or Mecosar modified 3BNC117; D) Env ELISA assay; E) Neutralisation assay (U=unlabeled, M=MeCOSar

83. MICROBIAL BIOFILM FORMATION AND MIGRATION ON VENTRICULAR ASSIST DEVICE DRIVELINES: IMPLICATIONS FOR INFECTION.

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Driveline infections remain an Achilles heel of ventricular assist devices (VADs). Microbial biofilm formation on drivelines is the root cause of driveline infections, potentially leading to more invasive infections involving the pump and bloodstream.
AIM: To characterise biofilm formation and microbial migration along contemporary drivelines using in vitro models representing clinically relevant environmental conditions, and along the various driveline components, with high-resolution imaging and biofilm quantification.
METHODS: Novel *in vitro* biofilm assays were developed to assess early microbial adherence and biofilm maturation on HVAD drivelines (HeartWare-USA) at the skin driveline exit site (drip-flow biofilm reactor) and within the subcutaneous tract (tunnel-based interstitial biofilm assay). The most clinically relevant pathogens were assessed (*Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans*) & surface chemistry of the driveline was analysed.
RESULTS: All pathogens adhered to and formed biofilms on the smooth and velour sections of the drivelines in the drip-flow biofilm assay. *P. aeruginosa* and *C. albicans* showed a larger biomass compared to *S. epidermidis* and *S. aureus* ($P<0.05$). The presence of a driveline tunnel mimicking the subcutaneous tract facilitated *S. epidermidis* and *S. aureus* biofilm formation on drivelines, increasing their cell counts by 500-10,000 times, and mediated the migration of *S. epidermidis*, *S. aureus* and *C. albicans* but not *P. aeruginosa*. Scanning electron microscopy and detailed surface chemistry analyses identified that silicone glue and the intricate and complex network formed by the driveline velour, appeared to promote microbial attachment and biofilm formation, especially of *P. aeruginosa* and *C. albicans*.
CONCLUSION: Our work highlights the predilection of different pathogens to different driveline sections and the importance of the subcutaneous tunnel as a key driver of persistent driveline infection. These data provide crucial insights for the development of novel strategies to prevent one of the most troublesome complications of VADs.

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84. KEEPING YOUR COOL: A SIMPLE, REUSABLE NECK COOLING DEVICE IMPROVES SURGEON COMFORT AND REDUCES LEVELS OF PERSPIRATION: A RANDOMISED CONTROL TRIAL

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Background: Infection in orthopaedic surgery can be catastrophic. Increased perspiration from theatre staff has been associated with higher rates of wound contamination. Wearing lead safety gowns, which is often done during surgery to allow the use of image intensifier, may result in heavy perspiration.
Aim: We aimed to determine feasibility of wearing a neck cooling device during surgery and whether it reduced surgeons' perspiration levels and decreased the negative impact on surgeons' comfort levels during orthopaedic procedures requiring the use of lead gowns.
Method: A pilot randomised control trial was conducted. Surgeons were randomised to either wearing the neck cooling device (intervention) or not wearing the device (control). Procedure duration, theatre temperature, humidity and perceived technical difficulty of operation were recorded. After the procedure, surgeons completed a questionnaire documenting how the temperature and humidity had a negative effect on their comfort and perceived level of perspiration. Multilevel mixed effects linear regression with random effects, adjusting for potential confounders was performed. Alfred Ethics Committee approved the study.
Results: 29 cases (44.6%) were randomised to the intervention group, and 36 to the control group. Adjusting for operating room temperature and perceived difficulty of surgery, the neck cooler reduced surgeons' level of discomfort by 1.9 points (95%CI:1.1 to 2.8,$p<0.001$), as well improved on their self reported perspiration by approximately 1.9 points (95%CI:1.0 to 2.8,$p=0.04$).
Conclusions: Wearing a neck cooling device during surgery is feasible and reduces perceived levels of perspiration and decreases the negative impact temperature and humidity has on a surgeons' comfort levels.

85. OPPORTUNITIES TO PROVIDE INFLUENZA VACCINATION TO GENERAL MEDICAL UNIT INPATIENTS

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Acute hospitalisation presents an opportunity for annual inactivated influenza vaccination (IIV). Many General Medical Unit (GMU) inpatients have indications for IIV (as determined by Australian National Immunisation Program criteria).

AIM: To determine IIV rates prior to hospitalisation and elucidate opportunities to provide IIV during GMU admission

METHODS: From July to September, during the 2017 influenza season, 200 randomly selected consenting adult patients admitted to a The Alfred's GMU, with indications for IIV, were included in this cross-sectional study.

IIV rates pre-admission were determined from general practitioners' records. Eligibility to receive IIV in hospital was determined in the unvaccinated cohort. Patients with contraindications, precautions and barriers to IIV were deemed ineligible. Subsequent IIV post-discharge, hospital readmissions and mortality over a 3-month period were analysed.

RESULTS: Of 200 patients (50.5% male; median IQR age 79 [72-87] years), 134 (67%) had IIV prior to hospitalisation. Of 66 unvaccinated patients, 46 (69.7%; 23% of total) were eligible for IIV during admission. 20 (30.3%, 10% of total) were considered ineligible; the most common barrier being cognitive impairment precluding consent for IIV. If the consent process were overcome, the eligibility rate improved to 81.8% (or 27% of total). Among unvaccinated patients eligible for in-hospital IIV, only 1 (2.2%) was vaccinated during hospitalisation and 1 (2.2%) recommended for IIV upon discharge. No patients received IIV in the community post- discharge, during the follow-up period. No statistically significant differences were noted in hospital readmission or mortality rates between unvaccinated and vaccinated cohorts.

CONCLUSION: This study highlights an important opportunity to provide IIV to inpatients with indications, with over a quarter being unvaccinated &eligible during the peak of the influenza season. Similar studies should extend to elucidate IIV indications & rates across other inpatient units & ultimately guide a hospital-wide policy to routinely identify & vaccinate eligible patients.

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86. ASSOCIATION BETWEEN MORTALITY AND ARTERIAL CARBON DIOXIDE LEVELS IN PATIENTS REQUIRING VENO-ARTERIAL EXTRACORPORAL MEMBRANE OXYGENATION.

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OBJECTIVE: Veno-arterial extracorporeal membrane oxygenation (ECMO) in patients with severe circulatory failure aims to reverse inadequate perfusion and shock. A relationship between arterial carbon dioxide ($PaCO_2$) and mortality is recognised for intensive care and cardiac arrest patients. In ECMO and circulatory failure this however has not been studied. We aimed to investigate the relationship of initial $PaCO_2$ levels and mortality in patients undergoing ECMO for cardiac arrest and refractory cardiogenic shock.

DESIGN, SETTING AND PATIENTS: Retrospective cohort analysis of adult patients placed on veno- arterial ECMO, recorded on the international Extracorporeal Life Support Organisation (ELSO) database from 2003-2014. Patients were categorised into 5 cohorts according to their $PaCO_2$ before initiation of ECMO. Univariable analyses were undertaken to compare survivors to those who died. Multivariable logistic regression analysis was used to adjust for confounding factors and investigate the relationship between $PaCO_2$ and mortality, in all patients and in two pre-specified subgroups: ECMO during cardio-pulmonary resuscitation (ECPR) and refractory cardiogenic shock (non-ECPR) group.

RESULTS: 7372 patients were identified, 5624 in the non-ECPR group and 1748 in the ECPR group with a mortality of 58.0% and 70.7% respectively. In the whole cohort, a U-shaped relationship between pre-ECMO $PaCO_2$ levels and hospital mortality was demonstrated. In the ECPR group hypercarbia ($PaCO_2$ > 60mmHg) was associated with an increase in mortality in the ECPR group (odds ratio [OR], 2.15; 95% confidence interval [CI], 1.36 to 3.41, p=0.001) whereas in the non-ECPR group hypocarbia ($PaCO_2$ < 30mmHg) was associated with increased mortality (OR, 1.37; 95% CI, 1.11 to 1.70, p=0.004).

CONCLUSION: Abnormal initial $PaCO_2$ levels in this cohort of veno-arterial ECMO patients were independently associated with increased mortality. Differences between ECPR and non-ECPR patients warrant further investigations to differentiate mere reflection of pathophysiology from potential therapeutic $PaCO_2$ targets.

87. ACUTE SKELETAL MUSCLE WASTING AND RELATION TO PHYSICAL FUNCTION IN PATIENTS REQUIRING EXTRACORPOREAL MEMBRANE OXYGENATION

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Severe muscle weakness is common in patients requiring extracorporeal membrane oxygenation (ECMO), but early identification is challenging. Muscle ultrasound is emerging as a promising tool to assist in the early diagnosis of skeletal muscle injury.

AIMS: 1) to quantify the change in quadriceps muscle size and quality (echogenicity) from day 1 to day 10 using ultrasound in patients requiring ECMO, 2) determine the relationship between ultrasound measures, muscle strength and highest mobility level.
METHODS: Prospective cohort study involving serial ultrasound measurement of the quadriceps muscle performed at day 1 (within 48hours of ECMO commencement), days 10 and 20. Muscle strength and highest mobility level were assessed at days 10 and 20 using the Medical Research Council sum-score (MRC), hand-held dynamometry (HHD) and the ICU mobility scale (IMS).

RESULTS: Twenty-five patients (age 49±14 years, 44% male) received ECMO. There was a significant reduction (-19%, $p<0.001$) in rectus femoris cross-sectional area by day 10. Echogenicity did not change over time. There was a negative correlation between echogenicity and MRC at day 10 ($r=-0.66$) and HHD at day 20 ($r=-0.81$). At day 20, there was a moderate correlation between total muscle thickness and IMS ($rho=0.59$) and MRC ($rho=0.56$).

CONCLUSION: In patients requiring ECMO there was marked wasting of the quadriceps muscle over the first 10 days. Ultrasound measures (muscle size and echogenicity) were associated with measures of muscle strength and highest mobility level.

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88. CENTRAL VENOUS ACCESS BY A CLINICAL NURSE CONSULTANT IN INTENSIVE CARE: A PILOT STUDY.

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The increasing number and acuity of critically ill patients has led to re-evaluation of traditional models of healthcare delivery, in particular, the insertion of central venous access devices (CVAD) by medical staff only. In February 2017, a new Clinical Nurse Consultant (CNC) role was created, allowing the insertion of central venous catheters (CVC), peripherally inserted central catheters (PICC), haemodialysis catheters (Vascaths), and intra-arterial lines (IAL) by a suitably trained and credentialed nursing specialist.

AIM: To evaluate the implementation and utility of a dedicated CVAD CNC in the Intensive Care Unit (ICU).

METHODS: The CVAD CNC was required to complete a rigorous training package, including an intensive online and didactic education program (quality and risk management, infection prevention, anatomy and physiology, use of real-time ultrasound guidance), and the supervised successful insertion of a minimum of 10 CVADs (per anatomical site), as assessed by an attending ICU Consultant. All complications were recorded prospectively.

RESULTS: To date, the CVAD CNC has inserted more than 275 CVADs and IALs in the ICU. These include 79 internal jugular, 10 subclavian, and 48 femoral CVCs or vascaths, 114 PICCs, 24 IALs and supervised 58 JMOs' CVADs. There have been no reported complications to date. This equates to over 90-hours of procedural patient-contact that has not required direct medical staff involvement (traditional model). Other key outcomes include:

1. Reducing the number of blocked lumens through various initiatives; labeling, flushes, daily auditing and education.
2. Reinforcing aseptic techniques, protocols and guidelines.
3. Reducing infection rates (central line associated blood-stream infections).

CONCLUSIONS: The introduction of a CVAD CNC in the ICU has resulted in a significant number of lines being inserted, in a timely and efficient manner, without medical practitioner involvement. No complications were reported. This model of care can be considered for application in other clinical areas.

89. PREDICTORS OF MORTALITY FOLLOWING EXTRACORPOREAL CARDIOPULMONARY RESUSCITATION

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Extracorporeal membrane oxygenation (ECMO) is a promising adjunct to cardiopulmonary resuscitation (CPR) in refractory cardiac arrest (CA). Factors associated with outcome are incompletely characterized.

AIM: To identify pre-ECMO factors associated with in-hospital mortality following Extracorporeal-CPR (E-CPR).

METHODS: All patients admitted to Alfred hospital following E-CPR, from January 2012 to April 2017, were included in the study. Chart review was performed for CPR, ECMO and outcomes data. Primary outcome was in-hospital mortality. Secondary outcomes were survival with favorable neurologic outcome, days on ECMO, cause specific mortality and ICU length of stay. Univariable and multivariable logistic regression was performed to identify factors associated with in-hospital mortality. Statistical analyses were performed using STATA 11.2 (StataCorp, Tx). The study was approved by the local human research ethics committee.

RESULTS: During the study period, 75 patients received E-CPR. Median age was 59 years, 61 (81%) were male, 38 (51%) had out-of- hospital CA, and 43 (57%) had an initial shockable rhythm. Median (IQR) time from arrest to ECMO was 91 (56-129) minutes for non-survivors and 51 (37-84) minutes for survivors (p=0.02). Twenty-six (39%) patients were successfully separated from ECMO with 23 (31%) surviving to hospital discharge and 22 (29%) with a cerebral performance category score of 1 or 2. In multivariable analysis, significant predictors of in-hospital mortality were ongoing CPR at time of ECMO initiation (OR=13.69, 95% CI 2.09-89.66; p<0.01) and arrest to ECMO cannulation time (OR = 3.1, 95% CI 1.19-8.53; p=0.02).

CONCLUSIONS: Following E-CPR, the factors most strongly associated with mortality were ongoing CPR at the time of ECMO initiation and arrest to ECMO cannulation time. Interventions aimed at reducing time to ECMO initiation may lead to improved outcomes.

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90. EARLY HYPEROXIA IN PATIENTS WITH TRAUMATIC BRAIN INJURY ADMITTED TO INTENSIVE CARE IN AUSTRALIA AND NEW ZEALAND: A RETROSPECTIVE MULTICENTER COHORT STUDY.

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AIM: Early hyperoxia may be an independent risk factor for mortality in critically ill traumatic brain injury (TBI) patients, although current data are inconclusive. Accordingly, we conducted a retrospective cohort study to determine the association between systemic oxygenation and in-hospital mortality, in critically ill mechanically ventilated TBI patients.

METHODS: Data were extracted from the Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Adult Patient Database (ANZICS-APD). All adult TBI patients receiving mechanical ventilation in 129 ICUs between 2000 and 2016 were included in analysis. The following data were extracted: demographics, illness severity scores, physiological and laboratory measurements, institutional characteristics, and vital status at discharge. In-hospital mortality was used as the primary study outcome. The primary exposure variable was the 'worst' partial arterial pressure of oxygen (PaO_2) recorded during the first 24-hours in ICU; hyperoxia was defined as > 299 mmHg. Adjustment for illness severity utilized multivariable logistic regression, the results of which are reported as the odds ratio (OR) 95% CI.

RESULTS: Data concerning 24,148 ventilated TBI patients were extracted. By category of worst PaO_2, crude in-hospital mortality ranged from 27.1% (PaO2 40-49 mmHg) to 13.3% (PaO2 140-159 mmHg). When adjusted for patient and institutional characteristics, the only PaO2 category associated with a significantly greater risk of death was < 40 mmHg [OR 1.52, 1.03-2.25]. 3,117 (12.9%) patients were hyperoxic during the first 24-hours in ICU, with a crude in-hospital mortality rate of 17.8%. No association was evident in between hyperoxia and mortality in adjusted analysis [OR 0.97 (0.86-1.11)].

CONCLUSIONS: In this large multicenter cohort of TBI patients, hyperoxia in the first 24 hours after ICU admission was not independently associated with greater in-hospital mortality. Hypoxia remains associated with greater in-hospital mortality risk, and should be avoided where possible.

91. RELATIVE AND ABSOLUTE LEVELS OF CD64 AND NEUTROPHIL ELASTASE HAVE POTENTIAL FOR THE DIAGNOSIS OF SEPSIS

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Introduction: Improved biomarkers are required for the detection of sepsis, both in laboratory settings and at the point of care (POC). Upregulation of surface CD64 expression (the neutrophil CD64 index, nCD64i) has been extensively studied as a sepsis biomarker with around 80% sensitivity, but is not amenable to use at POC. We hypothesised that simultaneous measurement of neutrophil CD64 and a neutrophil-specific protein in whole blood could yield a surrogate of the nCD64i that might be feasible for development of a POC test. To test this hypothesis, we evaluated the relative levels of total CD64 and neutrophil elastase in whole blood of healthy controls and patients with clinically diagnosed sepsis.

Methods: We are recruiting adult ICU patients (n=50) with clinically suspected sepsis (Alfred ICU) and healthy individuals (n=50). Levels of a selected neutrophil specific marker, neutrophil elastase (NE), and neutrophil activation marker (CD64) are measured by commercial sandwich ELISA kits. Samples were also tested using the Leuko64™ assay (Trillium Diagnostics) (surface CD64), and total (surface and intracellular) expression of CD64 was confirmed by flow cytometry staining, and microscopy.

Results: A strong correlation between total (whole blood) CD64 and NE was observed in healthy individuals (n=30, R^2=0.7, p<0.0001), even without depletion of monocytes. We established assay cutoffs (mean+ 2SD) for CD64 and NE as well as a "Gating" strategy for healthy levels of CD64/NE for the samples with very low neutrophil count. The commercial Leuko64 kit (surface staining by flow) was positive in 20/25 patients. Conversely, total CD64 was highly elevated in most sepsis patients (23/25 positive, p<0.0001 compared to healthy controls), and was elevated compared to the healthy CD64/NE ratio in the remaining two patients (total 25/25 positive, p=0.052 compared to Leuko64). Flow cytometry using intracellular staining showed that a significant proportion of neutrophil CD64 was intracellular in patients negative by Leuko64.

Conclusion: We observed high correlation of CD64 and NE in controls, compared with the presence of elevated amounts of total CD64 (including intracellular CD64) and/or NE in whole blood of sepsis patients. Our results suggest that measurement of both total CD64 and NE levels in whole blood has promise as an improved candidate biomarker for diagnosis of sepsis.

92. THE EPIDEMIOLOGY OF EARLY VASOPRSSOR THERAPY FOR PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH SEPTIC SHOCK.

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AIM: It is unclear how vasopressors (VP) are currently used in the early treatment of septic shock. Accordingly, we aimed to describe the epidemiology of VP use in patients presenting to the emergency department (ED) with septic shock. In addition, we aimed to explore the association between time to VP initiation and 90-day mortality.

METHODS: Post hoc analysis of the Australasian Resuscitation In Sepsis Evaluation (ARISE) trial of early goal directed therapy (EGDT). ARISE was a multicenter, randomized controlled trial in 51 EDs, mostly in Australia and New Zealand, comparing EGDT to usual care in patients with septic shock.

RESULTS: 1,130 of 1,588 patients (71%) in ARISE received VP at any point. The median [IQR] time from ED presentation to commencing VP was 4.5 [2.8, 7.1] hours, and 37% did so prior to central venous access. Norepinephrine was the most common first-line agent (83%). The mean (SD) volume of IV fluid administered prior to commencing VP was 3,361 (1,573) mL. Increasing age and volume of IV fluid therapy were associated with a lower likelihood of commencing VP early (within 4-hours of ED presentation), while increasing Acute Physiology and Chronic Health Evaluation (APACHE) II score was associated with a higher likelihood, $P<0.001$ respectively. In those who subsequently died within 90 days, the sub-hazard ratio (95%CI) for commencing VP was 1.7 (1.44, 1.92), $P<0.001$ unadjusted and 1.6 (1.33, 1.89), $P<0.001$, adjusted for age, APACHE II score, EGDT group, plasma lactate, IV fluid prior to VP infusion, study institution, and site of infection.

CONCLUSIONS: VP support is commonly provided to septic shock patients in the ED, with 50% of the ARISE cohort commencing this within 4.5-hours of presentation. A significant proportion received VP prior to central venous access. Earlier initiation of VP was associated with greater 90-day mortality.

93. A PHASE 1 STUDY OF A NOVEL BIDIRECTIONAL PERFUSION CANNULA IN PATIENTS UNDERGOING FEMORAL CANNULATION FOR CARDIAC SURGERY

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OBJECTIVE: Leg ischaemia is a serious complication of femoral artery cannulation. The primary aim of this study was to assess the safety and efficacy of a novel bidirectional femoral arterial cannula (Sorin Group USA), that provides both antegrade and retrograde flow, in patients undergoing peripheral cannulation for cardiopulmonary bypass during cardiac surgery.

METHODS: Patients undergoing routine cardiac surgery requiring femoral artery cannulation for cardiopulmonary bypass were identified preoperatively. Informed written consent was obtained in all cases. Bidirectional cannula insertion used either a surgical cut-down and wire through needle approach or a percutaneous technique. Flow in the superficial femoral artery was assessed using Doppler ultrasound after commencement of cardiopulmonary bypass. Lower limb perfusion was assessed using reflectance near-infrared spectroscopy to measure regional oxygen saturations in the cannulated limb during cardiopulmonary bypass.

RESULTS: Fifteen patients (median age=61.3 years, range= 26-79 years, 10 males, 5 females) underwent femoral arterial cannulation using the novel bidirectional femoral cannula between August 2016 and May 2017. Fourteen cannulae were inserted directly into the femoral artery via a surgical cut-down and wire through needle technique. One bi-directional cannula was inserted using a percutaneous insertion technique. The median duration of cardiopulmonary bypass was 129 minutes (range = 53-228 minutes). The cannula was inserted and positioned without difficulty in 14 of 15 patients. Incorrect sizing and arterial spasm prevented correct cannula positioning in one patient. Antegrade flow in the superficial artery was observed on Doppler ultrasound in 12 of 12 patients in which this was performed. Continuous stable distal perfusion was demonstrated in the cannulated limb in 14 of 15 patients. No procedural complications occurred in the immediate or convalescent postoperative period.

CONCLUSIONS: This study demonstrated that in patients undergoing femoral arterial cannulation for cardiopulmonary bypass during cardiac surgery, the use of a novel bi-directional cannula is safe and easy to insert and provides stable distal perfusion of the cannulated limb. Use of the device should largely obviate the need to insert a separate downstream perfusion cannula or use other techniques to protect against lower limb ischaemia. Further research on a larger scale and in different patient populations is now warranted.

94. EXPLORING THE PREVALENCE AND IMPACT OF BEHAVIOURS OF CONCERN AND WHETHER A PSYCHIATRIC BEHAVIOUR OF CONCERN TEAM IMPROVES SAFETY

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Aggression, absconding, deliberate self-harm and sexual harm are four behaviours of concern (BOC) that often occur on adult psychiatric inpatient units. Preventing these can lessen distress and increase safety.

AIM: To understand which patients engage in BOC's and how they are managed and whether a Psychiatric Behaviour of Concern (Psy-BOC) team contributed to preventing BOC's and restrictive intervention (e.g. seclusion) use.
METHODS: A mixed method design was utilised, including:
1. A retrospective audit to measure the nature, response and outcomes from the specified BOC's and compare their frequency and use of seclusion in the 6-months following (Feb–July 2017) and preceding (Aug 2016–Jan 2017) Psy-BOC commencement.
2. Group discussions to explore staff experience of BOC's and the Psy-BOC team.
RESULTS: Over 12-months, 433 BOC episodes occurred (82% aggression, 14% absconding, 8% deliberate self-harm and 5% sexual harm) involving 179 (18.2%) patients. Patients with BOC's were more likely to be male, have schizoaffective disorder, and had a hospital length of stay of more than double the average. Many used illicit substances, were homeless, single and unemployed. Staff feedback highlighted that a containing environment without sufficient space and therapeutic options, knowing the patient and effective teamwork, and patient complexity and beliefs about care impacted safety. Following Psy-BOC implementation there were 23-50% fewer BOC's, attempted aggression towards staff significantly reduced ($p<0.001$), and seclusion episodes reduced by 65%. Some staff thought Psy-BOC had improved safety through improving escalation, access to multidisciplinary expertise, and modelling how to de- escalate, whereas others were unclear about how Psy-BOC operated and continued to feel unsafe.
CONCLUSION: Aggression and other BOC's occur frequently in inpatient psychiatry and a Psy-BOC team may contribute to reducing their occurrence and restrictive intervention use. Vulnerable feelings expressed by some nurses highlight the need to further refine Psy-BOC and continue to improve BOC prevention.

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95. TIBOLONE TREATMENT FOR DEPRESSION IN PERIMENOPAUSAL WOMEN.

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Many women with no past psychiatric history experience severe mood symptoms for the first time in their life during the menopausal transition, with debilitating long-term consequences. Women with a history of depression can experience a relapse or worsening of symptoms during the menopause transition. Traditional antidepressants, SSRIs or SNRIs are commonly prescribed as the first line response. However, such treatment has shown only small improvements with side effects. Hormone therapies directly targeting the perimenopausal fluctuations in reproductive hormonal systems such as tibolone, have significant potential to treat perimenopausal depression.

AIM: Our study investigated the use of adjunctive tibolone, selective tissue estrogenic activity regulator, to treat de-novo or relapsing depression occurring in the perimenopausal period.

METHODS: Women with perimenopausal depressive symptoms were invited to participate in a double-blind, 12 week randomised control trial with two arms: tibolone (2.5mg oral/day) or oral placebo. Forty-three women met inclusion/exclusion criteria; 22 were randomized to tibolone and 21 were randomized to oral placebo. Symptoms were measured with the 'Montgomery- Asberg Depression Rating Scale' (MADRS) as the primary outcome measure. Latent growth curve analysis was used to assess the MADRS scores change over time.

RESULTS: Participants in the tibolone group demonstrated a significant improvement in depression scores, as compared to the placebo group, without any significant side effects.

CONCLUSION: The use of hormone therapies such as tibolone provide exciting innovations for the treatment of perimenopausal depression.

96. YOUTH PEER SUPPORT IN MENTAL HEALTH: MAKING A DIFFERENCE AND CHANGING PRACTICE

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headspace Youth Early Psychosis Program (hYEPP) is implementing a range of innovative programs to assist recovery in young people experiencing First Episode Psychosis (FEP) or at Ultra High Risk (UHR). Among these programs is the employment of paid youth peer support workers as members of the multi-disciplinary care team, representing a significant change in practice for the service, in line with both national and state policy on recovery in mental health.

AIM: This formative research and evaluation project examined the process of implementing a Youth Peer Support Program (YoPS) at hYEPP to examine the barriers and enablers to effective implementation as well as to examine outcomes for young people of having youth peer support during their recovery journey.

METHODS: We collected both survey and interview data from staff regarding beliefs around peer work and attitudes to service change, as well as routinely collected quantitative outcomes data from young people.

RESULTS: The implementation of paid Youth Peer Support services into a clinical mental health setting raises challenges for clinical staff as well as the peer workers themselves, however support from management, flexibility and a trial and error approach enabled effective implementation to occur. Issues which need to be addressed during implementation include: clear understanding of roles and boundaries; integration with clinical teams; defined referral processes; high level management support; and a willingness to embrace change.

CONCLUSION: Establishing youth peer support in a clinical setting is challenging but ultimately achievable given appropriate high level support and a flexible and willing workforce.

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97. MEMANTINE: A NOVEL DRUG FOR BORDERLINE PERSONALITY DISORDER

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Objective: Borderline personality disorder (BPD) is a complex, severe, and highly stigmatised psychiatric illness. Several lines of evidence highlight the causal link between chronic stress, glucocorticoid response to stress, and glutamatergic overactivity as a key event in the pathophysiology of BPD. Therefore, molecular mechanisms capable of regulating glutamate excitotoxicity represent novel and potentially promising treatment targets.

Memantine-HCl is a voltage-dependent N-methyl-D-aspartate (NMDA) receptor 'channel blocker' that selectively blocks pathological glutamate over-activity. The aim of the current study was to determine if memantine can improve BPD symptoms.

Methods: An 8 week double-blind placebo controlled trial of adjunctive memantine was conducted. Sixteen participants received oral placebo while 17 participants received 10mg daily oral memantine for 7 days, with subsequent titration to 20mg daily oral memantine. Eligibility criteria included men and women aged between 16- 65 years, with a diagnosis of BPD according to the Diagnostic Interview for Borderline patients. Primary outcome measures included the Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD) assessed fortnightly. Secondary measures included an adverse effect questionnaire, administered fortnightly to assess adverse events known to be related to memantine use.

Results: According to intention-to-treat, latent growth curve analyses, a significant change in total score of ZAN- BPD symptom severity was observed in the memantine group at 20mg/daily across time, compared to placebo (p=0.02). No adverse events were significantly more frequent among participants receiving active memantine than among those receiving placebo.

Conclusion: Memantine at a 20mg daily dose is a well-tolerated drug that can improve BPD symptomatology and may be a promising novel therapeutic for its treatment. Further studies are needed to explore the efficacy of memantine versus placebo, as well as in comparison to other potential treatments for BPD.

98. THE ROLE OF AN ENDOCRINOLOGIST IN A WOMEN'S MENTAL HEALTH CLINIC.

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The Monash Alfred Women's Mental Health Clinic (WMHC) provides tertiary level consultations for women experiencing mental ill health and related hormonal issues. Patients are seen by a psychiatrist and endocrinologist, either together or sequentially. Women with Premenstrual Dysphoric Disorder (PMDD), Perimenopausal Depression, depression related to exogenous contraception, Polycystic Ovary Syndrome (PCOS) and other conditions are provided with detailed, integrated psychoneuroendocrine management plans. Endocrine treatment strategies include oestrogen and progestogen treatment for premenstrual and perimenopausal mood disorders; management of thyroid abnormalities, comprehensive approaches for PCOS, plus treatment of metabolic consequences of psychotropic medications.
AIM: To investigate the impact of an integrated psychoneuroendocrine management plan on women seeking treatment at the WMHC.
METHODS: Data were collected from sequential new patients in the first year of this endocrinologist attending WMHC. Included are demographic details, clinical diagnoses, integrated psychiatric and endocrine history, physical examination, anthropomorphic data and laboratory investigations. Quantitative and qualitative methods were used to analyse this data plus patient feedback data.
RESULTS: Data from 78 sequential new patients were analysed. The age range was 17 to 72 years. Diagnoses include: Perimenopausal mood and anxiety disorders (31%) and PMDD (28%). Early life trauma in 44% of women resulted in complex Post Traumatic Stress Disorder. Fifty-seven per cent of patients are obese with BMI >30, exacerbated by the side effects of psychotropic medication. PCOS also develops as a consequence of obesity and early life trauma and is present in 15 % of patients. Patient feedback for the joint specialty approach taken in the Clinic has been excellent (87% excellent rating).
CONCLUSION: Combining endocrinology and psychiatry expertise provides a holistic approach for women with mental illnesses. This exciting new clinical model promises to improve mental health outcomes for many women.

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99. ANTISACCADE AND MEMORY-GUIDED SACCADE PERFORMANCE ACROSS THE SCHIZOPHRENIA SEVERITY CONTINUUM

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Saccadic (ocular motor) deficits are one of the most replicated findings in schizophrenia. However, less research has been conducted investigating the entire severity continuum. Research suggests that the personality characteristics and symptoms observed in schizophrenia lie on a continuum with subclinical symptoms, known as schizotypy, observed in the non-clinical population. As saccadic deficits are a cognitive hallmark of schizophrenia, it is believed that saccadic deficit may be associated with higher schizotypy.
AIM: To replicate previous findings of impairments in antisaccade and memory-guided saccade performance in schizophrenia and to investigate the relationship between saccade performance and schizotypy.
METHODS: 105 adults (35 patients with schizophrenia/schizoaffective disorder and 70 healthy controls) completed the antisaccade and memory-guided saccade tasks. Schizotypy was assessed using the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE). Controls were divided equally into low and high schizotypy groups based on total O-LIFE score. MANOVAs were conducted to observe differences in eye movement performance between low schizotypy individuals, high schizotypy individuals and patients.
RESULTS: There was a significant difference between patients and controls for all O-LIFE factors, as well as antisaccade and memory- guided saccade error rate and latency ($p<0.001$). When comparing low schizotypy, high schizotypy and patient groups, the MANOVA revealed significant differences for antisaccade and memory-guided saccade latency and a non-significant trend for antisaccade gain. While post-hoc analyses revealed that the significant differences were only between low schizotypy and patient groups ($p<0.001$), high schizotypy individuals performed worse than low schizotypy individuals but better than patients with schizophrenia, as expected. CONCLUSION: This study replicated previous findings of impaired saccade performance in schizophrenia. Preliminary findings indicate that antisaccade and memory-guided performance may be associated with higher schizotypy. The findings support the use of schizotypy as a model for schizophrenia and also support the theory of schizotypy and a broader schizophrenia continuum.

100. SYSTEMATIC REVIEW AND META-ANALYSIS OF BASAL CORTISOL LEVELS IN BORDERLINE PERSONALITY DISORDER

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Objective: Borderline personality disorder (BPD) is a prevalent, complex, and serious mental disorder involving multiple symptoms and maladaptive behavior. The underlying psychobiological mechanisms involved are not yet fully understood, but increasing evidence indicates that changes in hypothalamic- pituitary-adrenal axis (HPA) activity may contribute to BPD, and can be measured by cortisol levels.
Whilst various studies have demonstrated elevated levels of cortisol in BPD sufferers, others have presented opposite findings. Inconsistent findings may be attributable to use of comorbidity, collection and measurement methods, gender, and sample size. Considering these discrepancies, the aim of this systematic review and meta-analysis was to assess available studies in the scientific literature examining basal cortisol levels in patients diagnosed with BPD compared to non-psychiatric controls.
Methods: We conducted a systematic literature review with descriptions of primary studies as well as meta-analysis of studies with a control group. Meta-analysis was performed using Comprehensive Meta- analysis software (CMA version 2). The effect size (Hedges' g) was calculated with random-effect model.
Results: A systematic literature search identified studies (*N* = 545; 276 BPD and 269 non-psychiatric controls) that met the eligibility criteria from a total of 1960 unique records initially examined.Twelve studies fulfilled the inclusion criteria for meta-analysis. The standardised mean difference (Hedges' g) of basal cortisol level between BPD and control groups was -0.32 (pooled data from 12 studies; 95% confidence interval -0.56 to -0.06, p = 0.01), indicating significantly lower mean cortisol level for the BPD group.
Conclusion: These findings confirm reduced levels of basal cortisol levels are associated with BPD and suggest HPA axis dysregulation is implicated in the disorder. Further research is necessary to understand the biological factors contributing to the syndrome.

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101. IDENTIFYING BIOMARKERS FOR DRUG-INDUCED ADVERSE CUTANEOUS REACTIONS: A PROOF OF CONCEPT STUDY

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Antiepileptic drugs (AEDs) are the mainstay of treatment for epileptic seizures but they are associated with skin reactions that range from mild to potentially fatal reactions, such as Stevens Johnson syndrome (SJS). Genetic variants can modify risk but these biomarkers are neither necessary nor sufficient. The identification of more effective biomarkers is an active area of research.
AIM: To evaluate the utility of RNA-based markers for pretreatment screening.
METHODS*:* Transcriptomic analyses were undertaken using two platforms: the RNA molecular barcoding technology NanoString nCounter®, considered an appropriate technology for a screening tool, and whole genome RNA sequencing as a gold standard technology for discovery transcriptomics. The EdgeR software was used to assess differential expression for both platforms. Differential expression was assessed using an nCounter panel of 579 immunology-related genes in peripheral blood mononuclear cells from patients who had experienced drug-induced severe (SJS) rash (n=7) and mild rash (n=6), drug naïve controls (n=6), and drug-tolerant controls (n=9). RNA-seq was undertaken for a subset of these cases and tolerant controls (n=4/group).
RESULTS: The 10 most dysregulated genes identified by nCounter were compared with the RNA-seq results and showed strong concordance in fold change for SJS vs. drug-tolerant (Pearson r = 0.93, p = $7.32e^{-5}$) and SJS vs. mild rash (r = 0.95, p=$2.60e^{-5}$). Further, five of the top 10 differential expressed genes identified by nCounter in the SJS vs. mild comparison (IL1B, IL1A, CCL20, CCL7 and PTGS2) were also among the top 10 differentially expressed genes in the RNA-Seq experiment which included over 30,000 genes and non-coding transcripts.
CONCLUSION: This pilot study using complementary technologies provides proof of concept that individuals who develop different types of rash following drug exposure have different transcriptomic profiles and that expression profiles obtained post resolution of symptoms can delineate susceptible and drug-tolerant patients.

102. EVALUATION OF A PHARMACIST-LED WARFARIN DOSING SERVICE IN THE INPATIENT STROKE POPULATION

Olga Bagiotas, Eleanor van Dyk, Erica Tong, Gary Yip, Hadley Bortz, Susan Poole, Michael Dooley

AIM: To evaluate whether pharmacist-led warfarin dosing effectively achieves and/or maintains INR control equivalent to that of medical staff dosing in stroke patients

METHOD: A retrospective pre- and post-intervention study was conducted in the stroke inpatient unit at Alfred Health. The pre-intervention consisted of patients initiated, restarted or continued on warfarin from December 2015 to June 2016 with dosing managed by medical staff. The post-intervention group consisted of patients initiated, restarted or continued on warfarin from December 2016 to June 2017 with dosing managed by credentialed clinical pharmacists. In both the pre- and post-intervention arms there were two groups analysed (Group 1: newly initiated/restarted patients; Group 2: continuing patients) with two distinct primary outcomes (Group 1: time to achieve therapeutic international normalized ratio (INR); Group 2: time spent in therapeutic INR range).

RESULTS: Thirty-five patients received warfarin therapy during the study period. Twenty patients commenced or were restarted warfarin therapy (twelve pre-intervention, eight post- intervention), however 14 patients were excluded due to discharge prior to reaching therapeutic INR. Fifteen were continued on warfarin (five pre-intervention, ten post intervention). For newly initiated/restarted patients, the mean number of days to achieve two consecutive therapeutic INRs was 8 days for the pre-intervention group (n=3) and 6 days for the post-intervention group (n=3) (p=0.398). For patients continuing warfarin, the mean percentage of INR levels in therapeutic range was 65.1% in pre-intervention group (n=5) compared to 67.7% in the pharmacist led group (n=10) (p=0.903). There were no differences in mortality or hospital readmission rates between pre- and post-intervention patients.

CONCLUSION: The pharmacist-led warfarin dosing service effectively achieved and maintained INR control and appears to be a safe and feasible alternative to medical staff dosing.

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103. AGED RATS GIVEN A TRAUMATIC BRAIN INJURY HAVE A SUPPRESSED IMMUNE RESPONSE AND WORSE FUNCTIONAL DEFICITS THAN YOUNG ADULT RATS

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Traumatic brain injury (TBI) commonly occurs in the aged population and is associated with increased mortality and poorer functional outcomes. However, the pathophysiological mechanisms responsible for these outcomes remain unclear. Initial studies suggest that immunosenescence (i.e., deterioration and dysregulation of the immune system due to age) may play a significant role in influencing TBI outcome.

Therefore, this study aimed to determine the effect of TBI on immune response and functional outcomes in young-adult (i.e.,10 week-old) versus aged (i.e., 1 year-old) male Wistar rats.

Young and aged rats were administered either a moderate fluid percussion injury (i.e., a common rat model of TBI) or sham-injury. Rats were euthanized at either 24h or 1 week post-injury to analyze immune cell populations in the brain. The 1 week recovery rats also underwent behavioral testing prior to being euthanized.

Fluorescence activated cell sorting (FACS) analysis revealed that at 24h post-injury there were fewer microglia and infiltrating monocytes in aged rats given a TBI when compared to their younger TBI counterparts. Furthermore, analysis of sensorimotor function on a beam task revealed that aged rats given a TBI had an increased number of slips and falls when compared to the young adult rats given a TBI. These findings suggest that aged rats had a suppressed neuroimmune response and worse sensorimotor deficits after TBI compared to young adult rats.

Further investigations into the influence of immunosenescence on TBI outcomes, and age-specific treatment options, are warranted.

104. DISEASE MODIFYING EFFECTS OF SODIUM SELENATE IN A RAT MODEL OF CHRONIC, DRUG RESISTANT, TEMPORAL LOBE EPILEPSY.

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Rationale: Temporal lobe epilepsy (TLE) is the most common form of chronic drug resistant epilepsy in adults and is commonly associated with significant psychiatric and neurocognitive comorbidities. There is currently no disease modifying treatment that can prevent the development of TLE, or mitigate its severity once established. We have shown in animal models that treatment with sodium selenate, which up regulates the PP2A enzyme and decreases hyperphosphorlyated tau in the epileptic brain, after an epileptogenic brain insult mitigates the severity of the epilepsy and behavioural comorbidities. However, most patients that present at the clinic already have established epilepsy. Therefore, in this study we set out to evaluate if sodium selenate would be able to modify the severity of epilepsy, including the frequency and severity of the seizures, behavioural comorbidities and neuroimaging changes in chronically epileptic rats.

Methods: 10-week old Wistar rats underwent kainic acid induced-SE for four hours. Nine weeks after SE, animals were implanted with EEG recording electrodes and video-EEG was recorded for one week. After this initial EEG recording period, rats were randomly assigned to one of four treatment groups: post-SE + sodium selenate (1mg/kg/day, n=12); post-SE + levetiracetam (200mg/kg/day, n=12); post-SE + vehicle (n=12); sham + vehicle (n=12). Treatments were delivered by continuous subcutaneous infusion via an osmotic minipump for four weeks. Four and eight weeks after completion of treatment, the animals underwent one week of continuous video-EEG monitoring to evaluate the disease modifying effects of the different treatments. After the final EEG recording, behavioural tests were performed to evaluate anxiety, depression, social interaction, motor, learning and memory. Brains were then collected for post-mortem MRI analysis.

Results: Following drug washout, post-SE animals treated with sodium selenate had a lower number of seizures ($p < 0.01$) per day when compared to vehicle treated animals. Further, animals treated with sodium selenate has better learning and memory when compared to vehicle ($p < 0.05$). Analyses of the other MRI data is ongoing.

Conclusion: These results suggest that treatment with sodium selenate has a disease modifying effect in chronically epileptic rats in the post-KA SE model of TLE, with reduced comorbid learning and memory deficits associated with this disorder. Sodium selenate has been found to have a favourable safety profile in human clinical trials for other brain diseases, so translation to a clinical trial of disease modification for chronic TLE is highly feasible.

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105. COMMUNITY ONSET VS HOSPITAL ONSET FIRST SEIZURES

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New onset seizures are frequently encountered in the community and hospital settings. It is likely that first seizures presenting in these distinct settings have different etiologies with different prognoses, requiring different investigation and treatment approaches. Studies directly comparing the presentation and management of patients with first seizures occurring in the community and hospital settings are lacking.

AIM: 1. Identify patient and clinical factors associated with community-onset versus hospital-onset seizures. 2. Describe management of first seizures in a large, private Melbourne hospital (Cabrini Malvern).

METHODS: We reviewed the medical records of patients aged 18 years or over with discharge ICD-10 codes of G40-Epilepsy, G41- Status epilepticus, or R56.9-Unspecified convulsions, who attended a general hospital in Melbourne, Australia from 1 January 2008 through 30 November 2016. Patients with new-onset and newly-recognized unprovoked or provoked seizures were included for analysis.

RESULTS: A total of 367 patients were discharged with one of the relevant ICD codes. Among them, 151 patients (median age 74 years) met inclusion criteria as having had new-onset or newly-recognized seizures: 97 presented to emergency department with community onset seizure (COS-group) and 54 experienced seizures during hospitalization for other indications (HOS-group). Provoked seizures were more common in HOS-group ($p<0.001$), with exposure to pro-convulsant drugs, tranexamic acid in particular, a major risk factor. Appropriate decision-making regarding AED-prescription for patients surviving to discharge was n=57/93 (61.3%) COS- and n=16/50 (32.0%) in HOS-cohorts; phenytoin was the most commonly prescribed AED.

CONCLUSION: Elderly hospitalized patients are at increased risk of provoked seizures, and caution should be exercised when prescribing medications and procedures. Decision making around AED-prescription is important, with many patients not fulfilling ILAE epilepsy diagnosis nonetheless receiving AED

106. DEFINING THE COGNITIVE PHENOTYPE OF BEHAVIOURAL VARIANT FRONTOTEMPORAL DEMENTIA USING A TABLET BASED ASSESSMENT TOOL

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Behavioural variant frontotemporal dementia (bvFTD) is a subtype of frontotemporal dementia caused by atrophy of the frontal and anterior temporal lobes and characterized by progressive changes in behaviour and personality, with early impairment of executive function. Clinical diagnosis remains difficult, and the development of more sensitive cognitive assessment tools is a priority. The National Institute of Health's Toolbox for the Assessment of Neurological Behaviour and Function Cognition Battery (NIHTB-CB) is a tablet-based assessment tool that presents a novel method of identifying cognitive deficits in bvFTD.

AIM: To determine whether the NIHTB-CB is sensitive to patients with bvFTD, and determine the cognitive phenotype. Secondary aims are to determine whether the NIHTB-CB can differentiate between bvFTD and Alzheimer's disease, and whether the NIHTB- CB correlates with other measures of cognition, behaviour and caregiver burden.

METHODS: 15 adults (male and female) diagnosed with bvFTD, and 20 patients with Alzheimer's disease, will be recruited to undergo cognitive assessment. Healthy controls for the NIHTB-CB will be provided by the normative sample. Patient cognition will be assessed using the NIHTB-CB, the Neuropsychiatry Unit Cognitive Assessment Tool and the California Verbal Learning Test II. Patient behaviour and caregiver burden will be assessed using the Cambridge Behavioural Inventory Revised, the Revised Self- Monitoring Scale and the Caregiver Burden Scale. Standard correlation and significance tests will be conducted.

RESULTS: 4 bvFTD patients have completed the cognitive assessments to date. These patients have a median NIHTB-CB total composite score of 87, and a median executive function score of 83. The mean(SD) for healthy controls for all scores of the NIHTB- CB is 100(15).

CONCLUSION: Preliminary results indicate that the NIHTB-CB is sensitive to cognitive deficits in patients with bvFTD, particularly on measures of executive function, providing early evidence for the NIHTB-CB being a useful tool for clinical diagnosis and monitoring of cognitive decline.

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107. CHRONIC FLUOXETINE TREATMENT ACCELERATES KINDLING EPILEPTOGENESIS INDEPENDENTLY OF 5-HT2A RECEPTORS

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Patients with epilepsy often suffer from mood disorders, and these are commonly treated with antidepressant drugs. While these drugs are often successful in mitigating depressive symptoms, how they affect the epileptogenic processes has been little studied. Recent evidence has demonstrated that treatment with selective serotonin reuptake inhibitor (SSRI) antidepressant drugs adversely promotes epileptogenesis, which may be of great concern considering the number of patients exposed to these drugs. This study investigated 5-HT_{2A} receptor signalling as a potential mechanism driving the pro-epileptogenic effects of the prototypical SSRI fluoxetine.

METHODS: Male homozygous 5-HT_{2A} receptor knockout mice or wildtype littermates (n = 9-14/group) were treated with continuous fluoxetine (10mg/kg/day s.c.) or vehicle and subjected to electrical kindling of the amygdala.

RESULTS: Compared to vehicle, fluoxetine treatment accelerated kindling epileptogenesis ($p < 0.001$), but there was no effect of genotype ($p = 0.75$), or any treatment x genotype interaction observed ($p = 0.90$).

Interestingly, fluoxetine treatment increased afterdischarge thresholds in both genotypes ($p = 0.007$). CONSLUSIONS: We conclude that treatment with fluoxetine promotes epileptogenesis in mice, but this effect is not mediated by 5-HT_{2A} receptors. This suggests that antidepressants may accelerate the onset of acquired epilepsy in patients who have experienced epileptogenic cerebral insults.

108. FACTORS THAT AFFECT COMPUTERISED COGNITIVE SCREENING IN PEOPLE WITH MULTIPLE SCLEROSIS (MS): DIURNAL VARIATION, LOCATION & PRACTICE EFFECTS.

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Cognitive Impairment is common in MS and can impact quality of life, employment and social functioning. Cognitive testing in routine clinic practice that is practical, does not require trained staff and is sensitive to changes over time remains a current unmet need. Computerized cognitive batteries (CCB) can fill this gap. To be effective in monitoring for cognitive change, CCB's must be consistent in repeat testing, and systematic factors that impact testing identified.

AIM: To implement clinic and home based cognitive monitoring using a purpose built computerized battery, and determine the acceptability, compliance and factors that affect computerized cognitive screening in people with MS.

METHODS: We enrolled 400 patients (390 RRMS) over 14 months, who agreed to 6 monthly testing at the clinic, in addition to the choice to complete tasks at home (1-3 monthly). The web-based MSReactor platform efficiently screens psychomotor speed, attention and working memory.

RESULTS: Over 80% chose to complete home testing. Acceptability of tasks was high, with over 70% happy to repeat tasks and only 5% anxious about the tasks. Using mixed models to examine testing conditions, there was a 2.5-6% difference in task performance between initial clinic test and subsequent clinic test. Reaction times for initial home-based tasks were 3% faster than those recorded at the initial clinic session. In repeat home testing, performance in the psychomotor and attention tasks were stable across the first 5 home tests, whereas working memory reaction times decreased by 0.8% for each subsequent test. Factors that affect testing were identified.

Reaction times for tasks done in the morning were 6-7% slower than those in the afternoon or night. EDSS affected performance with a 1-unit increase resulting in a 1.5-2.0% slowing in reaction time on all tasks. Location of testing also affected performance, with tasks performed at home faster than those done in the clinic ($p<0.05$). CONCLUSION: Computerized cognitive monitoring is stable across repeat testing, following an initial familiarization period, making it suitable for unsupervised cognitive monitoring. The diurnal variation and location of testing effects on task performance in particular should be considered in future study designs utilizing CCB platforms.

109. THE ROLE OF *DE NOVO* MUTATIONS IN ANTIEPILEPTIC DRUG-ASSOCIATED BIRTH DEFECTS

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AIM*:* Birth defects are major concerns of antiepileptic drug (AED) therapy in pregnancy. Mechanisms underlying their occurrence are poorly understood. Here, we investigated whether AED-induced *de novo* mutations are a potential mechanism.

METHODS*:* Whole exome sequencing (WES) was performed on child-parent trios recruited within a large international collaboration. *De novo* mutations were identified using an established bioinformatics pipeline. Fisher's Exact test was used to compare the proportion of AED-exposed children with *de novo* mutations between children with and without birth defects. The Wilcoxon rank sum test was used to test for differences in the burden of *de novo* mutations per child between children exposed to valproate *in utero* and children either exposed to other AEDs or not exposed to any AEDs *in utero*, irrespective of birth outcome.

RESULTS*:* A total of 61 child-parent trios (from 33 families) were included in the study, comprising 50 trios with AED-exposed children and 11 trios in which the child was not exposed to any AEDs *in utero*. 9/50 AED-exposed children had birth defects. Initial WES analysis identified 78 putative *de novo* mutations; after further screening, 45/78 (58%) were considered to be high-confidence *de novo* mutations, of which eight have suggestive evidence of having arisen post-zygotically. The proportion of children harbouring *de novo* mutations did not differ significantly between AED-exposed children with birth defects (n=9) and AED-exposed children without birth defects (n=41) [mean/median (range): 0.55/0 (0-2) vs 0.63/0 (0-2); p=1.0]. The number of *de novo* mutations per child did not differ significantly between VPA-exposed children (n=13) and VPA-unexposed children (n=48) (mean/median: 0.77/1 vs 0.73/1, p=0.42).

CONCLUSION: This novel WES analysis suggests that exposure to AEDs *in utero* does not increase the *de novo* mutation burden, and that this mechanism is not a major contributor to the occurrence of AED-associated birth defects.

110. "TREATMENT GAP" IN PEOPLE WITH NEWLY DIAGNOSED EPILEPSY: AN AUSTRALIAN EXPERIENCE

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Aim: To evaluate the extent of "epilepsy treatment gap" in Australia in a resource-rich specialist setting.
Background: Epilepsy is one of the most common serious chronic neurological disorders that is estimated to affect approximately 68 million people worldwide. Antiepileptic drugs are the mainstay of treatment and can render two-thirds of the treated patients seizure- free.
However, many patients with epilepsy are not receiving antiepileptic drug therapy for a variety of reasons. This "epilepsy treatment gap" is a major public health issue in resource-poor countries, where gaps are as high as 95%. To what extent it is present in high-income countries has not been well studied. The causes of the epilepsy treatment gap in the resource-rich countries are unknown.
Methods: 1,317 people who were seen at First Seizure Clinics in Western Australia between 1 May 1999 and 31 May 2016 after unprovoked epileptic seizure(s) were prospectively followed for a median of 5.4 years (interquartile range: 2.4-8.5). Epilepsy was defined by using the International League Against Epilepsy 2014 definition of epilepsy. Results 856 people (62% male) fulfilled the diagnosis of epilepsy. Among them, 78% had commenced antiepileptic drug treatment and 22% remained untreated by the end of follow-up. Compared to the treated, untreated patients were younger (median 40 vs 34 years, p1 unprovoked seizure (OR=1.61; p=0.028). Among patients with documented treatment commencement dates (n=584), 67% were treated immediately upon the diagnosis of epilepsy and 33% waited till further seizure(s).
Conclusion: Despite the resource-rich specialist setting, more than one fifth of people newly diagnosed with epilepsy did not commence treatment and when recommended was not actually started until a further seizure in one third. Untreated people were younger, more in workforce and lived in more advantaged socioeconomic areas. MRI seemed to play a greater role than EEG or symptomatic aetiology in deciding treatment initiation.

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111. THE USE OF ANTIDEPRESSANT DRUGS IN PREGNANT WOMEN WITH EPILEPSY: A STUDY FROM THE AUSTRALIAN PREGNANCY REGISTER

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AIM: To study interactions between first-trimester exposure to antidepressant drugs (ADD) and antiepileptic drugs (AED), and a history of clinical depression and/or anxiety, on pregnancy outcomes and seizure control in pregnant women with epilepsy (WWE).

METHODS: We examined data from the Australian Pregnancy Register of Antiepileptic Drugs in Pregnancy, collected from 1999 to 2016. The register is an observational, prospective database, of which this study retrospectively analysed a cohort. Prevalence data was analysed using Fisher's exact test.

RESULTS: A total 2124 pregnancy outcomes were included. 1954 outcomes were exposed to AEDs in utero, whilst 170 were unexposed. Amongst the AED exposed outcomes, further comparisons were made among three exposure groups: (1) pregnancy outcomes with first-trimester exposure to ADDs (n=88); (2) those with mothers diagnosed with depression and/or anxiety but were not medicating with an ADD (n=65); and (3) those with mothers who were not diagnosed with depression and/or anxiety and were not medicating with ADD (n=1801). There was no significant difference in the prevalence of malformations in infants between subjects exposed to both AEDs and ADDs (10.2%, 95% CI 3.9-16.6), compared to individuals in the non-ADD medicated depression and/or anxiety group (7.7%, 95% CI 1.2-14.2), or those without depression or anxiety (6.9%, 95% CI 5.7-8.1; p=0.45). The malformation rates in pregnancy outcomes unexposed to AEDs were also similar in the above groups (p=0.27). In WWE medicated with AEDs and ADDs, the frequency of convulsive seizures (p=0.78), or non-convulsive seizures (p=0.45) throughout pregnancy, did not differ across comparative groups.

CONCLUSION: Co-medicating with ADDs in WWE taking AEDs does not appear to confer a significant added teratogenic risk, nor does it affect seizure control.

112. IDENTIFYING THE CELL TYPE MEDIATING NMDA RECEPTOR HYPOFUNCTION EFFECTS ON BEHAVIOURS RELEVANT TO SCHIZOPHRENIA

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Antagonists of the NMDA receptor can produce behavioural disturbances in rodents that are reminiscent of the symptoms experienced in schizophrenia. The purpose of this study was to determine whether parvalbumin-positive (PV+) interneurons and/or forebrain pyramidal cells mediate the effects of these drugs on behaviours relevant to schizophrenia.

Transgenic mice lacking the NMDAR from PV+ interneurons (PV-Cre;NR1f/f) or forebrain pyramidal cells (CaMKIIα-Cre;NR1f/f), along with their wild-type littermates (wt), were administered MK-801 or saline at time of testing. Outcomes were: 1) accuracy and perseveration in the Trial Unique Non- matching to Location task of working memory, 2) locomotor activity and, 3) prepulse inhibition (PPI). Deletion of the NMDAR from PV+ interneurons: 1) attenuated the MK-801-induced increase in locomotion, 2) did not alter the MK-801-induced decrease in PPI and 3) enhanced the drug-induced reduction in working memory accuracy and increase in perseveration. Contrastingly, deletion of the NMDAR from pyramidal cells did not alter the ability of MK-801 to exert its effects.

These findings suggest that hyperlocomotion induced by NMDAR antagonists is mediated by PV+ interneurons, but not forebrain pyramidal cells. However, deficits in sensorimotor gating, working memory and cognitive flexibility induced by NMDAR antagonism does not appear to be exclusively mediated by either cell type. Hyperlocomotion in rodents is thought to be an analogue of psychosis. NMDAR hypofunction on PV+ interneurons may, therefore, contribute to positive symptoms in schizophrenia. On the other hand, reduced NMDAR signalling on inhibitory interneuron subtypes other than those that express PV may contribute to cognitive symptoms in the disorder.

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113. A CONCOMITANT MUSCLE INJURY DOES NOT WORSEN TRAUMATIC BRAIN INJURY OUTCOMES IN A MOUSE MODEL OF MULTITRAUMA

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Traumatic brain injury (TBI) often involves multitrauma in which concurrent extracranial injury occurs. We previously demonstrated that a long bone fracture exacerbates neuroinflammation and functional outcomes in mice given a TBI. Whether other forms of concomitant peripheral trauma that are common in the TBI setting, such as skeletal muscle injury, have similar effects is unknown.

AIM: Here we developed a novel mouse multitrauma model by combining a closed-skull TBI with a cardiotoxin (CTX)-induced muscle injury to investigate whether muscle injury affects TBI outcomes.

METHODS: Adult male mice were assigned to four groups: sham-TBI + sham-muscle injury (SHAM); sham-TBI + CTX-muscle injury (CTX); TBI + sham-muscle injury (TBI); TBI + CTX-muscle injury (MULTI). Some mice were euthanized at 24h post-injury to assess neuroinflammation and cerebral edema. The remaining mice underwent behavioral testing after a 30-day recovery period and were euthanized at 35 days post-injury for post-mortem analysis.

RESULTS: At 24h post-injury, both TBI and MULTI mice had elevated edema, increased expression of GFAP (i.e., a marker for reactive astrocytes), and increased mRNA levels of inflammatory chemokines. There was also an effect of injury on cytokine levels at 35 days post-injury. However, the TBI and MULTI mice did not significantly differ on any of the measures assessed.

CONCLUSION: These initial findings suggest that a concomitant muscle injury does not significantly affect preclinical TBI outcomes. Future studies should investigate the combination of different injury models, additional outcomes, and other post-injury time points.

114. ASSESSING THE RISK OF CERVICAL DYSPLASIA IN WOMEN WITH MS COMPARED TO WOMEN WITHOUT DISEASE USING A DATA LINKAGE APPROACH.

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The risk of persistent Human Papillomavirus (HPV) infection, cervical dysplasia and HPV-related cancers is unknown in women with multiple sclerosis (MS), who have long-term exposure to immunomodulatory treatments.

AIM: To determine the prevalence of cervical dysplasia in the MS population compared to other women. Understanding this risk may help guide vaccination guidelines for the highly effective HPV vaccine in this population.

METHODS: We identified all women aged 18 to 70 with a primary diagnosis coded at hospital separation as MS through the Victorian Admitted Episode Database. The cervical screening history of this cohort was identified using probabilistic data linkage to women who had at least one cervical screening episode between 2009 – 2013 recorded on the Victorian Cervical Cytology Registry. Cervical dysplasia outcomes identified were: cytological low- and high-grade abnormalities (LGA, HGA) and histologically confirmed abnormalities (HisA). Results were stratified by age and intergroup comparisons were performed.

RESULTS: A cohort of 2382 patients with MS was compared with 929,670 women in the general population. Overall, the results show a similar proportion of cytological and histological abnormalities between the MS-cohort and the general population. In the MS-cohort, 7.18% had LGA, 2.35% had HGA, and 1.68% had HiSA; these rates were 6.84%, 2.46% and 2.31%, respectively, in the general population. In the younger age groups (25-34 years), the MS-cohort had higher rates of all abnormalities, but these rates dropped below that of the general population in the later age groups (60-69 years).

CONCLUSION: The data demonstrates similar rates of cervical dysplasia for women with MS and the general Victorian population. While the results are reassuring, we would recommend vaccination and three yearly screening for women who may be immunodeficient. Further study is needed to determine if risk changes over time and across immunomodulatory therapies.

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115. DIFFUSION MRI ABNORMALITIES FOLLOWING REPEAT MILD TRAUMATIC BRAIN INJURY USING THE AWAKE CLOSED HEAD INJURY (ACHI) RAT MODEL.

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Mild traumatic brain injury (mTBI) is a serious health concern in the adolescent population. Repeated mTBI may cause more pronounced deficits and long-term neurological consequences, and has been associated with neurodegeneration.

AIM: The study and development of objective biomarkers to identify injury and to help guide medical management. Magnetic resonance imaging (MRI) is a clinically relevant biomarker, although standard structural imaging often lacks sensitivity and does not detect alterations in the case of mTBI. Diffusion-weighted imaging (DWI), however, is an advanced MRI technique sensitive to white matter injury that may detect abnormalities resulting from mTBI.

METHODS: This study utilized the Awake Closed Head Injury (ACHI) model of mTBI to investigate changes in DWI following sham, single or repeated mTBI in adolescent male and female rats. Injuries were delivered on postnatal day 30 (P30) to fully-conscious rats with those in the repeat injured group receiving a total of four ACHI impacts. At 24 hours and 7 days post-injury rats were euthanized, and brains collected for MRI analyses.

RESULTS: Using advanced DWI, we identified that rats sustaining repeated mTBI displayed abnormalities indicative of white matter injury as compared to sham and single mTBI rats.

CONCLUSION: These initial findings suggest that advanced DWI measures identify white matter abnormalities in a clinically relevant model of repeated mTBI. We have ongoing investigations to examine whether these changes are permanent or transient in nature.

116. TRAUMATIC BRAIN INJURY RESULTS IN LONG-TERM CHANGES RESEMBLING MOTOR NEURON DISEASE

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Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease (MND) and is pathologically characterized by the progressive death of motor neurons, degeneration of the corticospinal tract, and the presence of transactive response DNA binding protein 43 (TDP-43) inclusions. Traumatic brain injury (TBI) has been suggested to increase the risk of ALS onset, however this link remains controversial.

AIM: Here we performed experimental TBI in rats and assessed for the presence of progressive MND-like pathological and functional abnormalities.

METHODS: MRI data was acquired using a 4.7 T Bruker scanner at 1 and 12 weeks post-injury. Behavioural testing was performed at 12 weeks post-injury and brain tissue, spinal cords and muscle tissue were also examined post-mortem.

RESULTS: MRI analyses showed that rats given a TBI had progressive atrophy of the motor cortices and progressive degeneration and diffusion tensor changes in the corticospinal tracts compared to rats given a sham injury. Immunofluorescence analysis of motor cortex revealed a reduction in neurons and an increase in the number of neurons overexpressing phosphorylated TDP-43. Further, rats given a TBI also had fewer motor neurons in the spinal cord, increased expression of muscle atrophy markers, changes in muscle fibre contractile properties, and muscle atrophy. Finally, assessment of motor function on a beam task revealed severe impairments in rats given a TBI.

CONCLUSION: Taken together, these findings resemble the pathological and functional abnormalities common in ALS, and support the notion that TBI can induce a progressive disease process bearing similarities to those in MND.

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117. THE VALIDITY OF MULTI-FREQUENCY BIOELECTRIC IMPEDANCE METHODS TO MEASURE BODY COMPOSITION IN OBESE PATIENTS: A SYSTEMATIC REVIEW

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Background: Obesity is a widespread burden affecting the community, with obesity rates growing globally. Although weight loss is advocated for overall better metabolic health, excessive loss of lean body mass may have serious metabolic consequences. Thus, accurate body composition assessment methods for obese patients are required to monitor fat loss and ensure lean muscle maintenance, enabling functional gains and quality of life improvements during aggressive weight loss programmes. Bioelectrical Impedance (BI) is a simple way of assessing body composition and has gained popularity for clinical use due to its convenience, low cost and instant results. The aim of this review was to investigate if BI is a valid tool to determine body composition in morbidly obese patients compared to reference methods.

Methods: MEDLINE, EMBASE, CINAHL and CENTRAL databases were searched until March 2017. Included studies were those published in English with obese (body mass index (BMI) ≥30kg/m^2) adults (≥18 years) measuring body composition with BI methods in comparison to pre-determined reference methods.

Results: 16 studies were eligible for inclusion. Sample sizes ranged from n= 15 to 157, with BMI 26 to 48kg/m^2. BI underestimated Fat Mass (FM) and overestimated Fat Free Mass (FFM) in 10 studies in comparison to reference methods for obese subjects. The correlation of absolute values from BI and reference methods for FM and FFM were high (r=0.53-0.97). When adjustments for BMI were made to BI machine algorithms, the accuracy of body composition measurements were improved. Significant heterogeneity was evident amongst included studies and prevented meta-analysis.

Conclusions: Multiple variables, including study numbers, methodologies, algorithms and outcome reporting contributed a lack of consistency amongst studies and therefore validity of BI to assess body composition in obese patients is difficult to determine. This review highlighted the need for more robust studies that control confounding variables to establish clear validity statements.

118. LOSS OF TRIM28 IN ADIPOSE TISSUE INCREASES ADIPOSITY BUT PRESERVES METABOLIC HEALTH

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White adipose tissue (WAT) plays a significant role in metabolic regulation and energy homeostasis, which is disrupted in the setting of obesity and type 2 diabetes (T2D). Obesity can lead to health complications including insulin resistance, T2D 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 both male and female 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. 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 altering Trim28 expression may be a potential mechanism important for promoting healthy adipose tissue expansion and improving lipid storage in the setting of obesity.

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119. ESTABLISHMENT OF A BARIATRIC SURGERY CLINICAL QUALITY REGISTRY

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The prevalence of obesity continues to rise across Australia and New Zealand. Bariatric surgery is offered as a means of providing predictable and sustainable weight loss. A clinical quality registry commenced in 2012 to track the safety, efficacy and outcomes of bariatric surgery.

AIM: To record the immediate safety and efficacy of bariatric surgery in Australia and New Zealand, and to track key health changes following bariatric surgery longitudinally.

METHODS: Surgeons submitted the following data online or by hard copy: patient demographics; patient height, weight, diabetes status and treatment; type of bariatric procedure and if it was a primary operation or a revision; devices used; surgical complications; and, mortality status. Patients who did not opt out after receiving explanatory statements were considered participants of the study. Outcomes were recorded peri-operatively for all procedures and annually for primary procedures.

RESULTS: As of 31 December 2017, the registry recorded 40,270 bariatric procedures from 37,504 patients in Australia. In the perioperative period, adverse events (unplanned hospital readmission, unplanned admission to intensive care, unplanned return to theatre) were recorded in 2.5% of primary procedures and 6.3% of revision procedures. Excess weight loss and total weight loss were 64.7% and 25.8%, respectively, after 12 months. Amongst participants with diabetes at baseline, 50% required no medication after one year and those requiring insulin dropped from 23% to 8%. However, this field was under-reported. Of the 29 deceased participants enrolled on the registry, 11 have been confirmed as not attributable to bariatric surgery, 5 were likely due to the surgery, and the remainder have not been determined.

CONCLUSION: This initial data capture is promising, confirming the efficacy & safety of bariatric surgery at a community level in Australia. Increased participation rates will reduce the risk of bias & allow for more robust conclusions as the registry matures.

120. AN INTEGRATED SYSTEMS BIOLOGY APPROACH IDENTIFIED A NOVEL REGULATOR OF ACYLGLYCEROL METABOLISM, PSMD9

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Disruptions in hepatic lipid homeostasis can promote the onset of conditions such as hepatosteatosis and insulin resistance. In order to interrogate hepatic lipid metabolism, we developed an integrated systems-biology discovery platform, consisting of 107 inbred mouse strains and performed proteome and lipidome analysis on the livers of these mice.

We assessed protein:protein and protein:lipid associations in order to identify novel proteins/pathways not previously associated with lipid metabolism. This led to the identification of a previously underappreciated inter-play between proteostasis and acylglycerol metabolism. Moreover, PSMD9, a previously characterised proteosomal protein, was associated with accumulation of saturated diacylglycerol species. Utilising the human hepatic cells lines, Hep3B and HepG2, we sought to validate PSMD9 as a novel regulator of acylglycerol metabolism.

PSMD9 overexpression resulted in a ~40% reduction in DGAT2 mRNA expression ($p<0.01$) and a ~4-fold increase CGI-58 mRNA expression ($p<0.01$), consistent with modulation of DAG metabolism. Overexpression of PSMD9 in cells also led to an increase in mRNA expression of markers of ER stress, CHOP ($p<0.05$), and inflammation, TNF-α ($p<0.05$). Conversely, knockdown of PSMD9 via siRNA led to a significant increase in DGAT2 ($p<0.05$) and decrease in CGI-58 ($p<0.01$) mRNA expression in cells. Acute over-expression of PSMD9 via an adenovirus (pAdV:PSMD9) in C57BL/6J and DBA/2J mice resulted in an accumulation of pathological DAG and ceramide species in both the plasma and livers of these mice. Moreover, proteomic analysis of the livers of these mice revealed a significant enrichment of proteins associated with ER/lipid signalling and the proteasome.

These findings validate the discovery platform as a resource for identifying novel regulators of hepatic lipid metabolism. Moreover, they provide a novel link between proteostasis and acylglycerol accumulation, and validate PSMD9 as a driver of acylglycerol metabolism, which has implications for hepatic steatosis.

121. ROCKTAPE FOR OSTEOARTHRITIS OF THE KNEE

Kim McManus, B.Physio(Hons), M.Physio(Musculoskeletal) Dr Lara Kimmel, B.Physio, PhD, Professor Anne Holland, B. Physio, PhD.

Title: Rocktape provides no additional benefit over sham taping in people with knee osteoarthritis who are completing an exercise program

Objectives: To investigate the efficacy of Rocktape in combination with exercise, compared to exercise alone, in patients with knee osteoarthritis.

Methods: A single institution, prospective, randomised study was conducted in the outpatient physiotherapy department of a tertiary hospital. Thirty-six patients with osteoarthritis of the knee were recruited. Participants were randomised to either; 1) Rocktape therapeutic taping condition plus exercise or 2) sham taping plus exercise. Outcomes were assessed at recruitment (baseline), commencement of taping and immediately following first taping (at one week after baseline), two weeks and five weeks after first tape application. The primary outcomes were pain on a visual analogue scale at rest and with movement. Secondary measures included the Knee Injury and Osteoarthritis Outcome Score (KOOS), 30sec sit to stand, 40m walk and stair climb tests. Exercise adherence and analgesia use were recorded via a diary.

Results: There was no between group differences over time in pain at rest or with movement. There were also no significant differences between the groups in any of the KOOS subscales or in the performance based tests administered over time. Pain on movement significantly improved over time in both groups, whilst pain at rest only improved at the final time point.

Conclusions - There was no additional benefit of Rocktape over sham tape in patients with knee osteoarthritis who were completing a home exercise program over five weeks.

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122. NEGATIVE BELIEFS ABOUT BACK PAIN ARE ASSOCIATED WITH PERSISTENT, HIGH LEVELS OF LOW BACK DISABILITY IN COMMUNITY-BASED WOMEN

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Objectives: While pessimistic beliefs about back pain are associated with low back pain and disability, our understanding of their role in the natural history of the condition is limited. This study examined the association between beliefs about back pain and the development and progression of low back pain and disability over a 2 year period in community-dwelling women.

Methods: 506 women were recruited to participate in a two-year cohort study. Beliefs about back pain were measured at baseline using the back beliefs questionnaire (BBQ), and low back pain and disability were assessed at baseline and 2 years using the chronic pain grade questionnaire (CPG). Participants were categorised into the following groups based on their CPG scores; no, developing, resolving and persistent high intensity pain and disability.

Results: Of the 442(87.4%) participants, 108(24.4%) and 69(15.6%) reported high levels of low back pain and disability respectively. Negative beliefs about low back pain were associated with persistent, high levels of low back disability (M(SE)= 26.1(1.4) vs. 31.3(0.31), p=0.002), but not persistent, high intensity pain (M(SE)=28.9(1.02) vs 31.2(0.33), p=0.2), after adjusting for confounders. Women with persistent high intensity pain and disability had more negative responses to belief statements about the future consequences of the condition compared to those with no, resolving or developing pain and disability (P<0.001-0.03).

Conclusion: This study found that pessimistic beliefs about back pain were associated with persistent high levels of low back disability, suggesting that strategies aimed at improving negative beliefs may reduce the chronicity associated with this condition.

123. THE FERTILITY MANAGEMENT EXPERIENCES OF WOMEN AND MEN IN AUSTRALIA WITH A COMMON MENTAL DISORDER: FINDINGS FROM THE "UNDERSTANDING FERTILITY MANAGEMENT IN CONTEMPORARY AUSTRALIA" SURVEY

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Background: Achieving pregnancy when it is desired and avoiding pregnancy when it is not desired are matters of concern throughout the reproductive life course. However, little is known about the fertility management experiences of women and men who have a common mental disorder (CMD).

Aim: To identify and compare the fertility management experiences of Australian women and men with a CMD to those without a CMD.

Methods: Secondary analysis of survey data about the fertility management experiences among women and men with and without a CMD from the '*Understanding Fertility Management in Contemporary Australia'* study. Sociodemographic characteristics, contraceptive use, childbearing desires, pregnancy experiences and fertility difficulties were assessed among women and men with and without a CMD through univariate analyses and multivariate analyses.

Results: Women and men with a CMD were significantly more likely than those without a CMD to: report not consulting a doctor about contraception, fertility or pregnancy in the last two years (46.5% vs 41.1%, p=0.025); feeling uncomfortable discussing sexual matters with their healthcare provider (38.8% vs 32.6%, p=0.015) ; feeling uncomfortable asking their sexual partner to use contraception (β=-0.421, odds ratio=0.656, p=0.030); expect to have less children (β=0.301, odds ratio=1.351, p=0.009); have had an unintended pregnancy (53.3% vs 38.6%, p<0.001) and abortion (29.3% vs 21.9%, p=0.006); and have their sexual debut (β=-0.068, p=0.002) and first pregnancy at a younger age (β=-0.132, p<0.001).

Conclusions: Women and men with a CMD had different fertility management experiences compared to those without a CMD. These finding have implications for healthcare providers and individuals with a CMD and suggest that there is a need for targeted interventions that raise awareness of the relationship between having a CMD and effective fertility management.

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124. PRACTITIONERS PERSPECTIVES ON THE NEXUS BETWEEN BRAIN INJURY AND FAMILY VIOLENCE

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Brain injury among victims and perpetrators of family violence is an increasing international health concern. Brain injury can occur as a result of family violence, or alternatively, as a pre-disposing factor which can contribute to the perpetration of family violence. International research into the nexus of brain injury and family violence is sparse.

AIM: To explore the perspectives of practitioners working in family violence and brain injury relating to their experience of prevalence and contributing factors of brain injury in the context of family violence.

METHODS: Convenience sampling identified participants from social, health and justice services who work with victims and perpetrators of family violence. Qualitative data were collected via 22 semi-structured interviews and a focus group with four people. Inductive thematic analysis was carried out to identify, analyse and report emerging patterns.

RESULTS: Practitioners estimated brain injury (suspected and diagnosed) prevalence in family violence from 10-50%. Contributing factors to brain injury within family violence included assaults (through trauma or previous exposure to family violence) and transport crashes. Barriers to assessing and providing care for brain injury in the context of family violence included lack of practitioner knowledge and awareness of brain injury, needing to respond to the immediate presentation of the family/individual (safety/survival), lack of access to assessment or follow-up care services.

CONCLUSION: The identified themes provide a context for how the cultural, societal and organisational environments within Victoria influence the interface of brain injury and family violence. Influencing factors of the nexus between brain injury and remains complex with many interrelated issues that require further investigation.

125. THE COURSE AND CONTRIBUTORS TO BACK PAIN IN MIDDLE-AGED WOMEN OVER NINE YEARS: DATA FROM THE AUSTRALIAN LONGITUDINAL STUDY ON WOMEN'S HEALTH

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BACKGROUND: Back pain is the leading cause of disability worldwide. With minimal effective therapies and rising financial burden, identifying modifiable risk factors is crucial.
AIM: To determine the course of back pain in middle-aged women over a nine-year period, and assess which modifiable risk factors are associated with more frequent back pain.
METHODS: The Australian Longitudinal Study on Women's Health is a cohort study of community-based, middle-aged women who completed questionnaires every three years between 2004 and 2013. 10,530 completed the survey in 2004 (mean age 55.5 years), 9,020 completed follow-up nine years later. Self-reported data on back pain in the last 12 months and other socio- demographic factors were collected at all four surveys. 'Frequent back pain' was defined as back pain reported at ≥ 50% surveys.
RESULTS: Back pain was common and persistent, with 48% having back pain in ≥ 50% of surveys. Baseline obesity (RR 1.18, 95% CI 1.12 - 1.25), lack of vigorous physical activity (RR 1.17, 95% CI 1.10 - 1.25), depressive symptoms (RR 1.40, 95% CI 1.33 - 1.47) and low education status (RR 1.17, 95% CI 1.12 – 1.24), were independently associated with an increased risk of frequent back pain (all $p<0.001$). Overall, 28% of the risk of frequent back pain could be attributed to these factors, equating to one extra case of frequent back pain for every five women with depressive symptoms, for every 11 obese women, for every 12 women with low education status and for every 13 women who do not do vigorous physical activity, at baseline.
CONCLUSION: Obesity, depressive symptoms, low education status and lack of vigorous physical activity are associated with higher risk of frequent back pain over the following nine years among women in their mid-50s. Targeting these risk factors may lessen the burden of back pain.

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126. ASSOCIATIONS BETWEEN RED BLOOD CELL POLYMORPHISMS AND MATERNAL AND BIRTH OUTCOMES IN A MALARIA ENDEMIC REGION OF PAPUA NEW GUINEA: A COHORT STUDY

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The enormous burden of malaria has resulted in strong evolutionary selection for genes that confer resistance to *Plasmodium* infection. The best studied examples are red blood cell (RBC) polymorphisms, which have demonstrated varying degrees of protection against malaria in children, in numerous studies. However, the effect of these RBC polymorphisms on *Plasmodium* species infection in pregnant women, who are most susceptible to malaria after young children, has not been well studied. Malaria in pregnancy is a global health problem with severe consequences for both the mother and the infant.
Here we investigate the associations between RBC polymorphisms, malaria in pregnancy, and adverse maternal and birth outcomes. This study utilized 700 samples and corresponding epidemiological data from pregnant women living in a malaria endemic region of Papua New Guinea, where the prevalence RBC polymorphisms and poor maternal and birth outcomes are high. Pregnant women were genotyped for Complement Receptor 1 (CR1) deficiency, Southeast Asian ovalocytosis (SAO) and α^+-thalassemia polymorphisms, which were present at high frequencies (>90%, 5.6% and 17% respectively). Preliminary epidemiological analysis revealed low frequencies of malaria and the adverse birth outcomes low-birthweight and pre-term delivery, and no substantial associations with RBC polymorphisms. However, maternal anaemia was highly prevalent in the cohort, and haemoglobin levels were influenced by RBC polymorphisms. In particular, women with the homozygous α^+- thalassemia genotype significantly lower haemoglobin levels at enrolment and delivery, than those seen for wildtypes. While the prevalence of severe anaemia was significantly reduced in women with low CR1 expression genotypes, compared to the high CR1 expression genotype, indicating a potential protective effect. These preliminary findings highlight the need for further investigation into the mechanistic role of these RBC polymorphisms in anaemia, a key pregnancy risk factor in malaria endemic regions.

127. INCREASING PROPORTION OF HERPES SIMPLEX VIRUS TYPE 1 IN FIRST EPISODE ANOGENITAL HERPES IN AUSTRALIAN WOMEN AND MEN: A RETROSPECTIVE OBSERVATIONAL STUDY OVER 13 YEARS

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Anogenital herpes is commonly associated with herpes simplex type 2, however international studies have demonstrated a dramatic shift towards herpes simplex type 1 over the past two decades. There have been no studies examining herpes trends in Australia since 2006.
AIM: To describe the temporal trends of first episode anogenital HSV-1 & HSV-2 between 2004 and 2017 in Melbourne, Australia.
METHODS: We conducted a retrospective review of the medical records of 4517 patients who were diagnosed with a first episode anogenital HSV infection at Melbourne Sexual Health Centre between 1 January 2004, and 31 December 2017. HSV-1 and HSV-2 were calculated as a proportion of all first episode anogenital HSV infections. The change in the proportions of HSV-1 and HSV-2 over time was tested by a Chi-square trend test. Cases were analysed by gender, sexual orientation and site of infection.
RESULTS: Over the 13 year study period, the proportion of first episode anogenital herpes due to HSV-1 increased by 20% (P_{trend}<0.001). There was a reciprocal decline in HSV-2. The proportion of HSV-1 increased by 36% in women (P_{trend}<0.001) and by 8% in heterosexual men (P_{trend}=0.01). HSV-2 reciprocally declined in both groups. In men who have sex with men (MSM), the proportions of HSV-1 and HSV-2 were stable (P_{trend}=0.2), however HSV-1 caused up to two thirds of anogenital herpes in all years. Among MSM where the anatomical site was recorded, there was a rise in anal herpes infections and a reciprocal decline in penile infections over the 13 year period (P_{trend}=0.001).
CONCLUSION: Epidemiology of anogenital herpes shifted from HSV-2 to HSV-1 in the past 13 years in Melbourne, Australia. This is likely the result of declining childhood transmission of HSV-1 which leads to susceptible populations, as well as changes in oral sex behavior which results in oro-genital transmission of HSV-1.

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128. THE IMPACT OF HEPITITS C-RELATED UNCERTAINTY ON SELF-REPORTED STRESS IN PEOPLE WHO INJECT DRUGS LIVING WITH HEPATITIS C

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BACKGROUND: People who inject drugs (PWID) are the population most at risk of hepatitis C virus (HCV) infection in Australia. The landscape of HCV care is rapidly changing. The introduction of FibroScans (rapid fibrosis assessment) and new treatment will likely alter the experience of living with HCV. This qualitative study aimed to explore positive and negative influences on wellbeing among PWID living with HCV.
METHODS: The Treatment and Prevention (TAP) study examines the feasibility of treating a community-based cohort of HCV mono-infected PWID. A purposively recruited sample from TAP was identified, stratified based on age and gender. In-depth interviews were conducted with 16 participants. Participants were aware of their HCV seropositive and fibrosis status (measured by FibroScan) prior to interview. Questions were open-ended, focussing on the impact of health-status on wellbeing, social functioning and stability. Interviews were voice recorded, transcribed verbatim and thematically analysed. Analysis was guided by Mishel's (1988) theory of Uncertainty in Illness.
RESULTS: All participants reported HCV-related uncertainty, particularly mis-information or a lack of knowledge surrounding liver health and FibroScan results. Those with high-level fibrosis experienced an extra layer of prognostic uncertainty. This was particularly stressful and affected behaviour, relationships and everyday life. For all participants HCV-related uncertainty was a key motivation to seek treatment, which was seen as a way to regain some stability in life. Those who had completed treatment not only reported treatment as alleviating HCV-related stress, but promoting feelings of empowerment and confidence in navigating other challenges in their lives.
CONCLUSION: Despite advances in diagnostic tools and treatment, the HCV experience is shrouded in uncertainty, which may result in increased personal stress. This suggests the need for simple and direct education programs, resources and information on liver health targeted towards PWID living with HCV, to reduce potential mental health harms in this group.

129. 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 10-15% of the general 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: Our aim was to estimate the cost effectiveness of these interventions 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 cost of a DCB and Drug Eluting Stent (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 $12,494 for PTA, $18,883 for BMS, $11,780 for DCBs, and $19,886 for DES.

CONCULUSION: 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.

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130. THE AUSTRALIAN TRAUMA REGISTRY – A WHOLE COUNTRY VIEW OF SERIOUS TRAUMA

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BACKGROUND: In May 2016, the Senate enquiry into *Aspects of road safety in Australia* recommended that the Commonwealth Government commit to funding the operation of the Australian Trauma Registry (ATR), supported by the Royal Australasian College of Surgeons. In addition, the Australian Commission on Safety and Quality in Health Care prioritised trauma in its second highest clinical domain for clinical quality registry development.

In December 2016, Prime Minister Malcolm Turnball announced new funding for the ATR to allow it to accurately track the progress of major injuries through the major trauma centres in Australia. Support was provided by the Department of Infrastructure, Regional Development & Cities and the Department of Health.

AusTQIP is a collaboration of 27 trauma centres across the country.

AIM: To characterize serious trauma across 27 major trauma centres in Australia.

METHODS: Data is submitted based on the Bi-national Trauma Minimum Dataset for Australia and New Zealand. Data is cleaned and analysed using Excel and STATA.

RESULTS: During the 2015/2016 financial year data was collected from 8283 seriously injured patients. Men were over- represented (72%) except for patients aged ≥85 years where there were more females than males. Road-related injuries accounted for 44 percent of cases, while falls accounted for 33 percent. Two-thirds of patients were transferred from the scene directly. The median time from scene to arrival to definitive care was 1.4 hours. The median time spent in the ED was four hours 13 minutes. The median length of stay in hospital was 7 days and the median ICU length of stay was 4 days. Overall mortality was 10 percent, with 1.7 percent of deaths occurring in ED.

CONCLUSION: With Commonwealth funding, the ATR continues provides a whole country view of serious injury.

131. PATIENT REPORTED OUTCOME MEASURES FOR WOMEN WITH BREAST IMPLANTS – A PILOT STUDY FROM THE AUSTRALIAN BREAST DEVICE REGISTRY

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PURPOSE: The Australian Breast Device Registry (ABDR) assesses long-term outcomes of breast implant surgery beyond routine postoperative care, and requires high rates of follow up for unbiased assessment. The Breast-Q Implant Surveillance (BREAST-Q IS), a 5 question Patient-Reported Outcome Measure (PROM) was developed to be administered at 1, 2, 5 and 10 years after operation. We sought to pilot our engagement strategy.
METHODS: We randomly selected 200 patients enrolled in the ABDR with primary 'device insert' procedure within the previous 10-15 months (breast augmentation (BA) n=120 and breast reconstruction (BR) n=80), with mobile number recorded. They were invited to complete the 5 question PROM via text message (SMS) initially, followed by three phone call attempts if no response, an email then a letter by post as the final engagement strategy.
RESULTS: A total of 197 eligible patients were analysed (118 BA and 79 BR). Overall response rate was 77% and survey completion rate was 70%. Mean age was 41 years (BA) and 44 years (BR). For BA (n=76), 64% completed the PROM, with 51% by SMS, 25% phone call, 3% email and 21% postal. For BR (n=62), 78% completed the PROM, with 55% by SMS, 26% phone call, 3% email and 16% postal.
CONCLUSIONS: This pilot demonstrated that our engagement strategy was effective, with 77% overall response rate. Over 50% of respondents used SMS to reply to a 5-question PROM assessing long-term surgical outcomes. A variety of other strategies are being tested to further improve the response rate.

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132. EFFECTIVENESS OF REPELLENT DELIVERED THROUGH VILLAGE HEALTH VOLUNTEERS ON MALARIA INCIDENCE IN VILLAGES IN SOUTH-EAST MYANMAR: A STEPPED-WEDGE CLUSTER-RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Evidence for the effectiveness of repellents distributed to villages through Village Health Volunteers (VHV) in protecting against episodes of malaria is required to inform the implementation of repellents as a component of malaria control and elimination programs in the Greater Mekong Subregion including Myanmar.
METHOD: A 15-month stepped-wedge cluster randomised study using routinely collected data was implemented to test the effectiveness of distribution of topical mosquito repellent (N,N-Diethyl benzamide, 12% w/w cream) on *Plasmodium* spp. infection. Crossed-random effects mixed modelling was undertaken to estimate the effect of repellent distribution on *Plasmodium* spp. Infection.
RESULT: Generalized Linear Mixed Models (GLMM) showed that, conditional on the effects of time and seasonality, *Plasmodium* spp. infection was less likely once villages transitioned into repellent distribution (adjusted odds ratio [AOR]=0.25) although this difference was not statistically significant (Wald $\chi^2(1) = 0.436$, p=0.512). There was a significant decline (AOR=0.87, Wald $\chi^2(1) = 6.1$, p=0.013) in *Plasmodium* spp. infection across the length of the trial. There was significant heterogeneity observed in the nature of the effect of repellent distribution between villages and we observed a greater level of heterogeneity in *Plasmodium* spp. infection between villages than across cross-sectional testing occasions.
CONCLUSION: We observed a significant decline in of *Plasmodium* spp. infection across the study period, independent of the intervention and seasonal variations in incidence which is most likely due to the increased access to malaria services provided by the VHV. We did observe a reduction in the incidence of *Plasmodium* spp. infection once repellent was distributed to villages; however this difference was not statistically significant because *Plasmodium* spp infection incidence was also lower than expected.

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

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

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 April 2018, the ABDR had engaged 406 surgeons representing 258 sites (83% of all eligible sites). Contributing surgeons were predominantly plastic surgeons (69%), with the greatest representation from NSW, Victoria and Queensland (73%). A total of 26888 patients have data recorded in the ABDR encompassing 29715 procedures (86% bilateral, 14% unilateral). Recorded at the individual breast level, 75% of the procedures were cosmetic, 19% reconstruction and 2% due to congenital deformity (4% not stated).

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

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134. LARGER PARASPINAL MUSCLE CROSS-SECTIONAL AREA IS RELATED TO DISABILITY FROM LOW BACK PAIN, BUT NOT LOW BACK PAIN INTENSITY

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Background: The paraspinal muscles play an important role in spinal function, however their relationship with low back pain (LBP) is unclear, with a number of studies finding little evidence for an association. Disability from LBP is a functional measure so it may be more closely associated with muscle characteristics. This study aimed to investigate the relationship between paraspinal muscle characteristics and both LBP intensity and disability.

Methods: 894 participants with LBP were selected from the Danish SpineData cohort, with 588 (65.8%) followed-up at 12-months. Age, gender and body mass index (BMI, kg/m^2) were recorded, and paraspinal muscle cross-sectional area (CSA, cm$_2$) measured from MRIs at lower lumbar levels (L3-L5). Typical, current and worst pain were assessed by numeric rating scales (0-10) and averaged, and disability measured using the Roland-Morris Disability Questionnaire at baseline and follow-up. Statistical analyses involved multivariable linear regression at baseline and linear mixed-models at follow-up, with adjustment for age, gender and BMI.

Results: Multivariable analysis showed greater paraspinal muscle CSA was associated with lesser disability from LBP bilaterally and at all levels except L5 (right mean CSA: baseline beta -0.14, 95%CI -0.23, -0.05, p<0.005; follow-up beta -0.10, 95%CI -0.18, -0.01, p<0.05). There were no associations between muscle CSA and pain intensity.

Conclusions: Greater paraspinal muscle CSA was associated with lesser disability from LBP, but not pain intensity, in individuals with LBP. These results may indicate that reduction in muscle CSA is related to disuse atrophy rather than pain inhibition. Investigation into potential treatments directed at muscle CSA is needed.

135. EVALUATING THE IMPACT OF CLINICAL PRACTICE GUIDELINES FOR NUTRITION IN CHILDREN WITH CYSTIC FIBROSIS IN AUSTRALIA

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AIM: To determine the association between the implementation of the 2006 Australasian Clinical Practice Guidelines for Nutrition in Cystic Fibrosis (CF) and the nutritional status of children participating in the Australian Cystic Fibrosis Data Registry (ACFDR).

METHODS: This research consisted of a historical cohort study using ACFDR data and a survey of clinicians treating children with CF. Two cohorts of children (2-5 years and 6-11 years) were selected from ACFDR during 1998-2014 (N = 2,329). Generalised estimating equation model (GEE) was used to assess weight, height and body mass index (BMI) z-scores for each patient before and after the implementation of the nutrition guidelines. he GEE model was adjusted for sex, age, use of dornase alfa, the number of ever positive Pseudomonas aeruginosa respiratory samples and having the G551D mutation. A nationwide online survey was sent to 48 clinicians to explore the enablers and barriers to implementation of the guidelines.

RESULTS: Data analysis showed significant increase ($p<0.05$) in mean weight, height and BMI z-scores ranging from 0.06 to 0.18 after implementation of the guidelines in both cohorts of children. Nineteen (39%) clinicians participated in the survey. The majority of the respondents adopted the recommendations into their practice and used the guidelines as part of their professional development. Structural barriers included a lack of adequate staff resources and clinic space for consultations, inappropriate staff classification, high staff turnover and lack of mentoring support.

CONCLUSION: In children participating in the ACFDR, nutritional status improved after the implementation of the 2006 guidelines. Survey results revealed enablers and barriers to guideline implementation and will inform implementation strategies for the revised Australasian nutrition guidelines for CF, released in 2017.

136. UNDERSTANDING HEPATITIS C RISK BEHAVIOURS AND ATTITUDES AMONG HIV-DIAGNOSED GAY AND BISEXUAL MEN: A GROUNDED THEORY STUDY

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BACKGROUND: Due to sexual and/or parenteral exposure, gay and bisexual men (GBM) are atincreased risk of hepatitis C (HCV)/HIV co-infection. In Australia, the advent of subsidised direct-acting antivirals (DAA) for HCV treatment has rendered made eliminating HCV among co-infected GBM possible; however high HCV reinfection rates could threaten this elimination goal. To gain an understanding of the factors influencing HCV reinfection risk and identify post-treatment support needs, this study explored HCV risk perception and attitudes among HIV-diagnosed GBM recently cured from HCV.

METHODS: Fifteen in-depth interviews were conducted with HIV-diagnosed GBM in Melbourne soon after DAA-treatment success. Interviews focused on participants' experiences related to HCV risks and attitudes towards reinfection avoidance. Data collection, analysis and interpretation were guided by constructivist grounded theory.

RESULTS: Three categories conceptualise participants' experiences:

Rejecting the junkie label

Contrary to feelings of inevitability associated with HIV seroconversion, a lack of HCV risk awareness coupled with perceived knowledge about safe drug use meant that HCV-diagnosis came as a shock to most participants. Despite high prevalence of injecting drug use, participants did not identify with populations typically at risk for HCV.

Risk environments and fear of social isolation

Interviewees implicated the micro-social environments in which they were socially and sexually engaged as risk environments, where sexualised drug use was perceived as ubiquitous. Removal from high-risk environments and sexual activity to avoid HCV reinfection resulted in disengagement from their communities, leaving many feeling socially isolated.

Beyond cure

HCV was experienced as highly stigmatising and many jumped at the opportunity to achieve cure. Treatment was identified as a catalyst for substantial lifestyle changes among those who had become critical of their use of methamphetamines. A key narrative was the commitment to avoiding HCV-reinfection; conceptualising reinfection as representing a personal failure and manifest of an inability to maintain their current, healthier lifestyles.

CONCLUSION: Tailored HCV prevention campaigns need to take account of the intersectionality between multiple stigmatized social identities. An understanding of HCV-infection as both behavioural and social should form the basis of treatment support. Establishing peer support networks could mitigate social capital loss following a commitment to behaviour change and contribute to avoidance of HCV reinfection.

137. DEVELOPING A CORE SET OF MINIMUM DATA FOR BREAST DEVICE REGISTRIES TO COLLECT

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Breast device registries provide the opportunity to assess outcomes of breast implant surgery in a real-world setting. The Australian Breast Device Registry (ABDR) in collaboration with the International Collaboration of Breast Registry Activities (ICOBRA) sought to identify an internationally agreed global minimum data set (MDS) for breast device registries. A set of uniform data points and data definitions is key to combining data from international registries.
OBJECTIVE: To identify an internationally agreed minimum core set of data points, along with data definitions, to be used by all breast device registries globally.
METHODS: Data points collected by all currently operating breast implant registries were reviewed and a list of items to be used in the consensus process was defined. Participants were an international multidisciplinary panel of surgeons, consumer representatives, specialist nurses, registry experts and regulators. A modified Delphi approach was used, with surveys requiring the panellists to rate the importance of each datapoint to be included in the global minimum data set on a six point Likert scale.Consensus for a datapoint to be included in the Tier-1 global dataset was obtained if a predefined statistical criteria were satisfied.
RESULTS: Datapoints from six breast implant registries were compared. A total of 52 (61 including subpoints) datapoints which were collected by over 33% of currently running registries were identified for the consensus (Delphi) process. After four rounds, a total of 32 (59 including subpoints) datapoints formed the Tier-1 global dataset and 16 datapoints were classified as Tier-2 optional dataset for registries to collect globally. Data definitions were then agreed upon.
CONCLUSION: An internationally agreed minimum dataset to be used in breast device registries was defined. This collaborative approach to share data will allow datasets to be combined, and provide a more effective global early warning system of implant- related problems.

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138. ASSOCIATION BETWEEN METFORMIN USE AND DISEASE PROGRESSION IN OBESE PEOPLE WITH KNEE OSTEOARTHRITIS – DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Obesity acts by mechanisms of increased joint loading, systemic inflammatory and metabolic factors in knee osteoarthritis(OA). Metformin is a widely used therapy for type 2 diabetes. There are evidence that metformin may affect OA progression. This study aimed to examine the association of metformin use with cartilage volume loss over 4 years and risk of total knee replacement(TKR) over 6 years in obese individuals with knee OA.
Methods: 888 Osteoarthritis Initiative participants with radiographic knee OA(Kellgren-Lawrence grade ≥2) who were obese(body mass index(BMI) ≥30kg/m^2) and provided medication data at baseline. Knee pain was assessed at baseline using Knee Injury and Osteoarthritis Outcome Score(KOOS). Knee cartilage volume(femoral condyle and tibial plateau) was assessed using magnetic resonance imaging at baseline and 4 years and annual percentage change in cartilage volume was calculated. TKR over 6 years was assessed.
Results: There were 62(7.0%) metformin users. In participants aged <70 years, the rate of medial cartilage volume loss was 0.93%/annum in metformin users and 1.52%/annum in non-users, i.e. a reduction of 0.59%/annum(95%CI -0.01% to 1.20%, p=0.054) in metformin users, after adjustment for age, gender, BMI and KOOS pain score. The difference was significant in women that the rate of medial cartilage volume loss was 0.67%/annum in female metformin users and 1.38%/annum in female non-users(a reduction of 0.72%/annum, 95%CI 0.05% to 1.38%, p=0.03). There was a trend for metformin use to be associated with reduced risk of TKR in 6 years(odds ratio 0.34, 95%CI 0.10-1.17, p=0.09), after adjustment for age, gender, BMI, Kellgren-Lawrence grade and KOOS pain score.
Conclusions: Although not reaching statistical significance, these data suggest a beneficial effect of metformin on the knee joint, being associated with reduced rate of cartilage volume loss and reduced risk of TKR. Larger cohort studies and clinical trials are needed to confirm these findings.

139. PRE-MIGRATION SCREENING RATES OF HIV, TUBERCULOSIS AND VIRAL HEPATITIS AMONG OFFSHORE PERMANENT VISA APPLICANTS (INCLUDING OFFSHORE HUMANITARIAN ENTRANTS), AUSTRALIA, 2014- 2017

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BACKGROUND: Pre-migration health examination provides an opportunity to improve migrant health through the detection of treatable diseases. Adults applying for a permanent visa to enter Australia must complete an Immigration Medical Examination (IME) including testing for human immunodeficiency virus (HIV), tuberculosis, and in some applicants; hepatitis B virus (HBV) and hepatitis C virus (HCV). We examined screening rates across countries where the IME was conducted to shed light on process variation to inform improvements to screening effectiveness.

METHODS: The study population comprised all permanent visa applicants (including offshore humanitarian entrants) aged 15 years and over, who completed an IME offshore and met the health requirement to enter Australia between 1 July 2014 and 30 June 2017. Preliminary descriptive analysis is presented here.

RESULTS: The 278,919 participants were predominantly female (55%), aged 25-34 years (42%) and applied for skilled (47%), family (39%) or humanitarian (13%) visas. The four most common countries where IMEs were conducted were India (17%), China (17%), United Kingdom (5%), and Lebanon (5%). Over 95% of applicants in these countries were screened for pulmonary tuberculosis and HIV. Fewer than 1% were screened for latent tuberculosis in all four countries. Screening rates for HBV and HCV varied dramatically across countries (64% in Lebanon vs. 3% in China; 8% in UK and 2% in China and Lebanon, respectively).

CONCLUSIONS: Screening rates for communicable diseases as part of the Australian IME process varied across countries of exam, and do not consistently correlate with variation in disease burden. Further analysis of population-level and process-level data may provide important information for informing health examination processes, both in Australia and globally.

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140. FRACTIONATED STEREOTACTIC RADIOTHERAPY FOR CAVERNOUS VENOUS MALFORMATIONS OF THE ORBITAL APEX

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Background: Cavernous venous malformation (CVM) of the orbit, previous called a cavernous hemangioma, is a vascular lesion most commonly involving the orbital apex. Primary surgical resection is the mainstay of management but in some cases can be difficult without damaging adjacent neurovascular structures. In this situation fractionated stereotactic radiotherapy (FSRT) may be an alternative management option.

Aim: The objective of this study is to investigate the efficacy and safety of FSRT in the treatment of cavernous venous malformation (CVM) of the orbital apex.

Methods: We did a retrospective study of patients at a single centre with CVM of the orbital apex that had treatment with FSRT. We compared the symptoms, visual function and the size of the tumour pre- and post-treatment as well as reviewing the treatment details and the incidence of complications.

Results: 6 patients received treated with FSRT involving the orbital apex or the conus. The median age was 48 (range 32-63) and 50% were female. Patients received a dose of 45-50.4 Gy in 1.8-2 Gy fractions. The average tumour volume reduction at post-treatment imaging after 12 months was 63%. All patients who had proptosis or a visual field defect had an improvement in the symptoms post-treatment. There were no complications of the treatment.

141. SERELAXIN REDUCES RENAL INFLAMMATION AND FIBROSIS IN EXPERIMENTAL DILATED CARDIOMYOPATHY

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The mechanisms driving renal dysfunction in cardiorenal syndrome (CRS) type 2 are poorly understood. Emerging data suggest that fibrosis and inflammation play major pathological roles.

HYPOTHESIS: Based on the anti-inflammatory and anti-fibrotic effects of relaxin in several tissues, we hypothesized that manipulation of this pathway may be reno-protective in CRS type 2.

METHODS: 18-week-old wild-type (WT; n=20) and transgenic mice with dilated cardiomyopathy (DCM; n=16) were administered either vehicle (0.25μl/h) or serelaxin (500μg/kg/day) via subcutaneous minipumps for 8 weeks. Cardiac and renal function were measured at baseline and study end, together with analysis of renal fibrosis and inflammation.

RESULTS: Treatment with serelaxin was without effect on cardiac function (P≥0.08). Consistent with the CRS type 2 phenotype, tubulointerstitial and glomerular fibrosis were 63% and 64% greater, respectively, in vehicle treated DCM mice compared to vehicle treated WT mice (P≤0.05). Renal mRNA expression of *Tnfα* and *Il1α* were 74% and 63% greater, respectively, in vehicle treated DCM mice compared to vehicle treated WT mice (P≤0.05). Tubulointerstitial and glomerular fibrosis were 46% and 45% less respectively, in serelaxin treated DCM mice compared to those treated with vehicle (P≤0.01). Renal cortical mRNA expression of *Tnfα* and *Il1α* were 56% and 58% less respectively, in the former group compared to the latter (P≤0.05). Renal function declined in vehicle treated DCM mice compared to WT mice (P=0.05). Treatment with serelaxin had no effect on renal function in DCM mice (P=0.57).

CONCLUSION: The present data demonstrate that serelaxin exerts favourable actions on renal fibrosis and inflammation in experimental CRS type 2.

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142. CHRONIC HYPERSENSITIVITY PNEUMONITIS: A PROSPECTIVE COHORT ANALYSIS OF AN UNDER-RECOGNISED CLINICAL ENTITY

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Chronic hypersensitivity pneumonitis (CHP) is an immune mediated interstitial lung disease, caused by an antecedent exposure to an offending agent. It can be difficult to accurately distinguish from other fibrotic ILDs, and may improve with immunomodulatory treatment. Little is currently known about patient characteristics and prognosis.

AIM: to determine what features influenced diagnostic confidence of CHP at multidisciplinary meetings (MDM), and what factors might influence trajectory and mortality.
METHODS: We collected data from all patients with a consensus MDM diagnosis of CHP from the prospective Alfred ILD Registry, commenced in 2011.
RESULTS: Fifty-five patients with a consensus diagnosis of CHP were identified (mean age 55±10yrs; 43% male). MDM diagnostic confidence was only definite in 10%, probable in 61% and possible in 30%. Mean follow up was 3.6 years (0.5-7yrs). Rate of lung function decline per year was 2.6% in FEV1% (SE 0.66), 2.3% in FVC (SE 1.03), and 2.1% in TLCO% (SE 1.29). The rate of decline was affected by the use of immunosuppression, but not antigen exposure, or level of diagnostic confidence. There was 90% survival at 5 years. Risk of death was not affected by identification of clinical exposure (RR 1.7; p=0.3), or high diagnostic confidence (RR 1.2; p=0.9).
DISCUSSION: This is the first Australian cohort study in the natural history of CHP. It is the second most common diagnosis made in MDMs, and in this cohort, long term outcomes are better than other ILDs. Limitations of this study include small patient numbers, and diagnosis made in the absence of guidelines, mostly based on clinical history and HRCT findings. Guidelines for confident diagnosis of CHP are required, and additional investigations including BAL should be explored, and large, prospective multicentre registry research is required to validate such guidelines to make a more confident diagnosis and predict treatmentresponse.

143. HOME-BASED PULMONARY REHABILITATION IN THE 'REAL' WORLD

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INTRODUCTION: Pulmonary rehabilitation (PR) is an effective intervention for people with chronic lung disease; however, centre- based program access and uptake are poor. A home-based model has demonstrated equivalent outcomes in a clinical trial

AIM: To evaluate the clinical implementation of home-based PR

METHODS: Since December 2016, Hospital Admissions Risk Program clients with chronic lung disease referred for PR have been offered the option of a home-based program (one home visit in week 1, 7 once-weekly phone calls); or a traditional centre-based program (8 weeks, twice-weekly sessions). Baseline and end-rehabilitation assessments include exercise capacity (6-minute walk test [6MWT]) and health-related quality of life (Chronic Respiratory Disease Questionnaire). Home-based program completion was defined as participating in 70% of phone calls.

RESULTS: Of the 156 clients referred, 55 (28%) chose to undertake a home-based program, and 39 people commenced (24 female, mean age 71 [SD 13] years, FEV_1 58[23] % predicted, baseline 6MWT distance 357 [168] metres). Diagnoses included chronic obstructive pulmonary disease (n=26), bronchiectasis (n=5), asthma (n=4), interstitial lung disease (n= 3) and pulmonary hypertension (n=1). Reasons for choosing the home-based program included transport issues (n=19), social anxiety (n=9) and work commitments (n=11). Thirty-seven (95%) of participants stated that they would not have attended a centre-based program. There was a significant improvement in 6MWT distance (mean 25 [CI 12-38] metres); patient reported symptom score of dyspnoea (mean 4 [CI 2-5]), fatigue (mean 2 [CI 1-3]), and mastery (mean 2 [CI 1-3]) following home-based PR.

CONCLUSION: Home-based PR provides access to an effective intervention alternative for people with chronic lung disease who are not able to participate in a centre-based model.

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144. INTERVENTIONS FOR PROMOTING PHYSICAL ACTIVITY IN PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): A COCHRANE SYSTEMATIC REVIEW

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Increasing awareness of the deleterious health impacts of physical inactivity in people with chronic obstructive pulmonary disease (COPD), coupled with technological developments permitting more accurate measurements, has led to a dramatic increase in studies that aim to improve physical activity participation.

AIM: to evaluate the effectiveness of interventions to promote physical activity in people with COPD.

METHODS: Randomised controlled trials of interventions designed to increase physical activity for people with COPD using objective measures for physical activity were identified from the Cochrane Airways Group's Specialised Register (to March 2018). Two review authors independently assessed studies for inclusion and risk of bias, then undertook data extraction. Results are for the primary outcome of steps/day at program completion, using published data.

RESULTS: 1977 citations were screened, 196 papers assessed and 29 of 48 included studies reported steps/day. Four studies assessing the impact of pulmonary rehabilitation were able to be meta-analysed and demonstrated no significant effect (compared to usual care, mean difference 176 [95% CI -144 to 496] steps/day). The greatest improvements were seen following pulmonary rehabilitation with physical activity counselling (compared to pulmonary rehabilitation alone, 1 study, 3266 [589 to 5944] steps/day), pedometer with physical activity counselling (compared to counselling alone, 1 study, 2942 [1881 to 4002] steps/day) and high- intensity interval training (compared to usual care, 1 study, 1683 [721 to 2646] steps/day). A deterioration in step count was seen following singing classes (compared to film workshops, 1 study, -1774 [-2848 to -700] steps/day).

Risk of selection and detection bias was generally low, with high or unclear ratings for performance and reporting bias.

CONCLUSION: A range of interventions, particularly those involving physical activity counselling, can improve physical activity as measured by daily steps. These results suggest that targeted interventions may be useful to improve physical activity in people with COPD.

145. INTRODUCTION OF THE METANEB FOR AIRWAY CLEARANCE THERAPY (ACT) IN CYSTIC FIBROSIS (CF); A CLINICAL AUDIT OF FEASIBILITY, SAFETY AND PATIENT REPORTED OUTCOMES

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Intrapulmonary percussive ventilation has been available in internationally for decades and recently introduced to Australia as the Metaneb with little evidence in CF.

AIM: To evaluate feasibility, safety and patient reported outcomes after using the Metaneb for ACT in adults with CF.

METHODS: Patients with persistent mucus plugging not improving with usual ACT were selectively treated with the Metaneb providing nebulised mucolytic therapy combined with constant positive airway pressure (CPEP) and constant high frequency oscillations (CHFO). Patients were treated with individualized dosage of repeated 2-3 minute cycles of each modality with pauses for expectoration. Patients recorded their experiences on visual analogue scales (VAS) with anchors from -5 (most negative) to 0 (no difference) to +5 (most positive) outcome after treatment with the Metaneb compared with usual ACT.

RESULTS: Thirty-two patients (12 male) were treated with the Metaneb. Data presented: mean (SD), range. Age: 35.9(11.2)20-76 years; FEV1: 46.2(16.8)25-87% predicted; FVC: 65.9(15.0)47-105%; BMI 22.0(4.0)17.7-40.2; VAS scales: Effectiveness of ACT: 3.4 (1.2) 1 to 5; Sputum volume cleared: 2.8 (1.5) 0 to 5; How clear/free breathing after treatment: 3 (1.6) 0 to 5; ACT time taken: 0.3, (2.1) -3 to 3; How tiring Metaneb treatment: 1.1 (2.9) -3 to 5; How easy breathing with Metaneb: 1.6 (1.9) -1 to 5; Preference for Metaneb with exacerbations: 4.6 (1.1) 1 to 5; Mucolytics used: Isotonic saline 2/3, Hypertonic Saline 1/3 of patients; CPEP and CHFO pressures: 10-20cmH2O; CHFO frequency: 230 RPM. Treatment time was similar to usual ACT (PEP/Oscillating PEP/Autogenic drainage/Forced Expirations). Clinical reasons for selecting the Metaneb refractory mucus plugging (n=32). Two declined use of the Metaneb after one session for unrelated haemoptysis and inability to co-ordinate breathing. There were no adverse events.

CONCLUSIONS: Treating selected adults with CF with the Metaneb was feasible, safe and more effective in clearing refractory mucus plugging than usual ACT.

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146. EXPLORING REAL LIFE EXPERIENCES OF LUMACAFTOR/IVACAFTOR IN CYSTIC FIBROSIS PATIENTS WITH SEVERE LUNG FUNCTION AT ALFRED HEALTH

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Cystic Fibrosis Transmembrane Regulator (CFTR) modulators including lumacaftor/ivacaftor (LUM/IVA) are novel treatments for certain cystic fibrosis (CF) mutation types, however evidence from non-trial environments is lacking.

AIM: To analyse longitudinal effects of LUM/IVA on lung function and body mass index (BMI) in patients receiving LUM/IVA in clinical practice, and to investigate the influence of baseline lung function or previous fungal microbiology.

METHODS: All patients prescribed LUM/IVA for >1month since its availability in January 2016 and not taking part in another clinical trial were included. Pulmonary function ($ppFEV_1$) and BMI 12-months prior to and at LUM/IVA initiation, then one month, 3-4 months, 5-8 months, 9-12 months, and over 12-months post-initiation, were analysed. Clinical variables including positive fungal cultures and hospital admissions were recorded. Difference in lung function and BMI were analysed using Intention to Treat analysis and Linear Mixed Model.

RESULTS: Thirty patients were included (47% male, mean age 32years, mean $ppFEV_1$ 33.4% (SD 7.2%) at LUM/IVA initiation, median duration of treatment 401 days [IQR 327-520]). No statistically significant absolute change from baseline in $ppFEV_1$ was observed. Increasing duration of LUM/IVA treatment was significantly associated with increasing BMI at all time points ($p<0.05$). Previous fungal cultures had no association with $ppFEV_1$ or BMI changes. Compared to the 12-months prior to LUM/IVA, patients experienced a statistically significant reduction in the decline of ppFEV1 after commencing LUM/IVA, from a median annual decline of 3% prior to LUM/IVA to a median increase of 2% at 12-months following treatment initiation ($p<0.01$), and an overall 54% decrease in hospital admissions ($p<0.01$).

CONCLUSION: While an absolute increase in lung function was not observed, differences in overall lung function change over twelve months suggests LUM/IVA has a clinically significant, positive effect on CF disease stability. Patients also experienced positive, indirect outcomes including increased BMI and reduced hospital admissions.

147. EXAMINING ACCESS AND TIMELINESS OF LINEAR ENDOBRONCHIAL ULTRASOUND (EBUS) UTILISATION IN LUNG CANCER. A RETROSPECTIVE OBSERVATIONAL STUDY

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The use of linear endobronchial ultrasound (EBUS) with bronchoscopy has high diagnostic yield in the assessment of mediastinal lymphadenopathy, and in the staging and diagnosis of lung cancer.

AIM: To explore access and timeliness of linear EBUS in evaluating lung cancer and mediastinal lymphadenopathy.

METHODS: A retrospective review of a pre-existing record of EBUS cases undertaken at the Alfred Hospital between August 2013 and August 2016 was conducted. Recorded dates of referral and EBUS procedure were used to assess the time interval between the two. Furthermore, for patients diagnosed with lung cancer that underwent linear EBUS, electronic records of diagnosis and treatment dates were collected to assess time interval from EBUS date.

RESULTS: 108 linear EBUS procedures were completed at the Alfred Hospital between August 2013 and August 2016 on 97 patients aged 23-88 years old. Of these patients, 47(45%) were diagnosed with lung cancer, while 58(55%) were diagnosed with conditions other than lung cancer, including 11(10%) who were diagnosed with metastatic cancer from another origin. Median interval between referral for EBUS and EBUS procedure was 5 days (IQR 3-9) across the entire study population. Overall, 61% of linear EBUS occurred within one week of referral, while 91% occurred within two weeks of referral. The median time from referral to diagnosis of lung cancer was 11 days (IQR 6-21), with 34 patients diagnosed with lung cancer based on EBUS. The median time from referral to treatment initiation was 43 days (IQR 25-62.5).

CONCLUSION: Nearly one tenth of subjects (9%) waited >2 weeks for EBUS within our institution and the impact of this delay on staging and diagnosis warrants further evaluation. Timeliness in diagnosis and staging in lung cancer management is likely to reduce patient distress, improve patient experience and facilitate earlier treatment. Barriers to timely investigation will require further investigation.

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148. A DONOR ARTERIAL PAO_2/FIO_2 LESS THAN 300 DOES NOT DETERMINE GRAFT FUNCTION OR SURVIVAL AFTER LUNG TRANSPLANTATION

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A donor arterial PO_2/FiO_2 (P/F ratio) <300 cut-off is so entrenched in lung transplantation (LTx) practice that such a measurement would invariably result in rejection of the donor lungs or placement on ex-vivo lung perfusion (EVLP).

AIM: To investigate the veracity of the 300 threshold for donor lung acceptability.

METHODS: In consecutive brain dead (BD) donors arterial blood gases were drawn in the ICU and from each of the 4 donor pulmonary veins in the operating room (OR) at procurement (performed by The Alfred team). No donor lungs were excluded based on the last ICU or OR P/F ratios and EVLP was not used. Recipients were followed up 6 and 12 months post LTx. The primary outcome was death <12 months from LTx and secondary outcomes were, primary graft dysfunction (PGD) score and ventilation duration.

RESULTS: 99 donors, mean age 42±16 years, 56% male, 52% smoking history and median ventilation duration of 64 hours (IQR 38-90) were analysed. If a P/F ratio threshold was used donor lungs may be rejected by some programs at 2 points with 12% rejected in ICU and 24% rejected in the OR at procurement. There were no differences between recipients receiving donor lungs where the ICU P/F ratio was <300 compared to ≥300 in time to extubation [median, 35 (IQR 21-45) vs 24 (IQR 18-46) hours, p=0.20] or PGD. Six recipients died <12 months following transplantation, one from the <300 and five from the ≥300 P/F ratio subgroups.

CONCLUSION: From this study, if the traditionally accepted donor P/F threshold of 300 was adhered to for donor lung acceptability, 36% would have been rejected. The donor P/F ratio threshold of 300 used for acceptability of donor lungs is excessively conservative and results in wastage of donor lungs and the application of unnecessary EVLP

149. HIGH INCIDENCE OF CARDIOVASCULAR EVENTS IN PATIENTS WITH A LRTI: A NEED FOR CLOSER FOLLOW- UP?

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Introduction/Aim: Lower respiratory tract infection(LRTI) is a common reason for hospital admission. Cardiovascular events occur in 14-19%[1] following admissions with community acquired pneumonia (CAP). However, there is no similar data for LRTI without radiological consolidation. The DISPNOEA study evaluated the outcomes of patients admitted with LRTI without chronic lung disease and normal chest-xray (CXR).

Methods: Retrospective audit of patients admitted to Alfred Hospital in 2016 with discharge diagnoses of LRTI, chest infection, bronchitis, pneumonia or influenza. Patients chronic lung disease, immunosuppression and hospital acquired pneumonia were excluded. Patient demographics, cardiac history, SMART-COP and CORB scores, in-hospital cardiac events and 30-day re-admission data was obtained from medical records.

Results: For 231 patients (103=Male), median age was 82 years with average LOS of 3 days. The mean Charlson co-morbidity index was 5 with past history of Ischaemic heart disease (IHD) and heart failure documented in 25% and 12% respectively. 34.6% were on anti- platelets on admission. 85.3% were classified as low severity of infection by the SMART-COP score. Inpatient stay was complicated by a cardiac event in 17.7%(n=41). Acute decompensated heart failure(ADHF) occurred in 13.9%(n=32) which was a new diagnosis in 24 patients. Other events include new atrial fibrillation in 4.8%(n=11) and myocardial infarction in 3.9%(n=9). There were no ICU admissions however inpatient mortality rate was 3.5%(n=8). The 30-day re-admission rate to the same hospital was 13.9% (n=32), 40.6% of them secondary to cardiovascular complications (n=13) of which ADHF was most common(n=10).

Conclusion: Our study revealed that nearly 20% of patients admitted with LRTI with normal CXR suffered subsequent cardiac events, often resulting in high readmission rates. These results are comparable with prior studies of patients with CAP. This highlights the need for close follow-up of these patients post hospital discharge and adequate optimisation of their cardiac risk factors.

Grant Support: Nil References: 1. Musher D, Rueda A, Kaka A, Mapara S, Clinical Infectious Diseases, 2007, 45, 158-165

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150. DORNASE ALFA DURING LOWER RESPIRATORY TRACT INFECTION POST LUNG TRANSPLANTATION

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Lung transplant (LTx) recipients are at a high risk of lower respiratory tract infection (LRTI) secondary to immunosuppression, while altered respiratory physiology can make it difficult to clear secretions. Inhaled mucoactive agents alter mucus properties and/or facilitate mucocilliary clearance in suppurative lung disease. However there are no randomised controlled trials (RCTs) studying these effects post LTx

AIM: To evaluate the safety and efficacy of nebulised dornase alfa compared to isotonic saline during LRTI > 2 months post LTx. METHODS: Inpatient adults with LRTI and sputum production following bilateral sequential LTx were eligible for this assessor blinded RCT. Randomisation was stratified by LTx indication (±cystic fibrosis (CF)). Participants received either 5ml isotonic saline, or 2.5ml dornase alfa, nebulised once daily for 1 month followed by 2 months symptom diary only. The primary outcome was change in lung clearance index (LCI2%) measured by multiple breath washout. Secondary outcomes included adverse events; spirometry; quality of life; readmission; length of stay and self-reported exacerbations at baseline, 1 month and 3 months.

RESULTS: 32 participated, 16 each group (18M,14F), mean(SD) age 50±14, FEV1% 58±22, median(IQR) length of stay 7±5, days since LTx 1275±2482. LTx indications included CF (n=11) and chronic obstructive pulmonary disease (n=11). There were no significant between-group differences in LCI2% at any time point (one month mean difference -0.34, 95% confidence interval (CI) -1.57 to 0.89; three months mean difference -0.76, 95% CI -2.29 to 0.78, both favouring dornase alfa). Secondary outcomes were not different between groups. There was no increased risk of adverse event with dornase alfa use. Self-reported exacerbations increased within both groups between 1 and 3 months after cessastion of treatment (isotonic saline 2.67±2.19; dornase alfa 1.71±2.05).

CONCLUSION: These results do not support the routine use of dornase alfa during LRTI in LTx recipients.

151. INVESTIGATING THE LINK BETWEEN BRONCHOPULMONARY DYPLASIA (BPD) AND RETINOPATHY OF PREMATURITY (ROP) IN PRETERM INFANTS

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Bronchopulmonary dysplasia (BPD) and Retinopathy of Prematurity (ROP) are two debilitating disorders afflicting preterm infants. The two disorders arise as a consequence of supplemental oxygen exposure used to treat respiratory distress in premature neonates and can progress into lifelong disabilities, including chronic obstructive pulmonary disorder (COPD) in the lung and vision loss. The overall incidence rate of BPD and ROP is about 50% and 98%, respectively, among infants born with birth weights less than 1000g.

AIM: To establish if the supplemental oxygen model that is commonly used to assess ROP will simultaneously lead to BPD to further assess the link underlying the lung and eye disorders.
METHODS: Neonatal C57Bl/6 mice were exposed to 75% oxygen (supplemental oxygen) for 5 days from postnatal day (PN) 7 until PN12, following the gold standard model of ROP. Mice were then returned back to room air (21% oxygen) until PN18, PN40 and PN80. Early and late-stage eye and lung damage were assessed at each of these time-points in the same mice. Assessment of eye histopathology was conducted via wholemounts of the retina stained with FITC conjugated isolectin to show dysregulation of blood vessel development at PN12 and PN18 along with eye paraffin sections stained with Haematoxylin and Eosin (H&E) to show structural choroidal damage at PN40 and PN80. Damage to alveolar structure was assessed via lung paraffin sections stained with H&E. Bronchoalveolar lavage fluid was used to evaluate concentration of inflammatory cells in the airspaces and their activation state via cytology.
RESULTS: Qualitatively, at the early time-points mild histopathology was evident in the lungs with the expected vascular degeneration in the inner retina. In the late time-points, the lesion progressed to severe airspace enlargement and simplification in the lungs, with concurrent thinning in the outer layer of the retina. Inflammation was observed in the lungs in the early and late stages of the supplemental oxygen model compared to age-matched room air controls.
CONCLUSION:Short term supplemental oxygen therapy has a severe and long-lasting impact on the lungs and the retina. This model of coincident BPD and ROP provides an opportunity to evaluate the links between the two disorders which may involve inflammatory and oxidative stress pathways. Translationally, this model could provide the opportunity to develop a treatment strategy targeting these pathways would simultaneously ameliorate the two debilitating disorders via a single therapy.

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152. CAN PARAMEDICS TRIAGE PATIENTS AND PREDICT CLINICAL COURSE OR DISPOSITION UPON ARRIVAL IN ED? A SYSTEMATIC REVIEW

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Pre-hospital providers (PHPs) spend a considerable amount of time with patients prior to arrival at ED. The ability of PHPs to predict clinical course or assign triage scores to patients has not been adequately explored.

AIM: To assess the ability of PHPs to predict clinical course or assign triage scores to patients they have transported.
METHODS: A systematic review of the literature was conducted. Manuscripts were screened and eligible for inclusion if they met the following criteria: Population – all patients transported by non-physician PHPs to the ED; Exposure – PHP prediction of triage score, clinical course, treatment requirements, or disposition from ED; Comparator – actual triage score, clinical course, treatment requirements, or disposition from ED; Outcome – Concordance. All study designs were included.
RESULTS: The literature search returned 5,922 unique articles. After screening and full text review, nine studies were included for analysis. Of these, five assessed prediction of disposition (admission versus discharge) from ED, two compared triage score application, one assessed prediction of clinical requirements, and one assessed prediction of mortality. PHPs were able to predict admission to hospital with specificities ranging from 0.65 – 0.89 and rule out admission with sensitivities between 0.61 and 0.77. Triage score application had weighted kappa variables of 0.409 and 0.452 indicating moderate agreement between PHPs and triage nurses.
CONCLUSION: PHPs appear to be able to adequately assign triage scores, predict clinical course, and predict disposition from the ED for the patients that they transport. This represents an area of potential expansion for paramedic practice with improvements in patient flow through EDs.

153. RAPID AND SAFE DISCHARGE FROM THE EMERGENCY DEPARTMENT: A SINGLE TROPONIN TO EXCLUDE ACUTE MYOCARDIAL INFARCTION

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Background: Rapid and safe exclusion of a diagnosis of acute myocardial infarction (AMI) among patients at risk is of paramount importance to ensure efficient patient care as well as to minimise ED overcrowding and limit healthcare costs.
Objectives: To determine variables that could facilitate safe discharge from the Emergency Department (ED) following a single High Sensitivity Troponin I (HsTnI) result to exclude acute myocardial infarction (AMI).
Methods: A retrospective cohort study was performed at a tertiary hospital of all patients that had serial HsTnI performed within the first 12 hours of arrival to the ED over a 3 year period. The primary exposure variable of interest was a very low troponin initial result (HsTnI<5ng/L). Medical record review was undertaken for all patients with the exposure variable of interest and an abnormal second troponin measurement (HsTnI ≥16ng/L in women and HsTnI ≥26ng/L in men). A risk stratification score calculation was performed for all patients that were diagnosed with an AMI.
Results: There were 11,970 patients who presented between 01/07/2013 and 30/06/2016 that had serial HsTnI measurements performed. Of these, 4,172 (34.9%) patients had an initial HsTnI measurement <5ng/L. Of the patients with an initial HsTnI<5ng/L that met inclusion criteria, 56 (1.3%) had a second troponin result above the 99th percentile and 32 (0.8%) cases of Non ST elevation AMI were diagnosed as well as 15 (0.4%) cases of ST elevation AMI. There were 44 (93.6%) of all AMI cases that met criteria for high risk presentations under the National Heart Foundation of Australia guidelines. The negative predictive value of an initial HsTnI<5ng/L to exclude AMI was 98.9% (95% CI 98.5-99.1).
Conclusions: An initial HsTnI measurement <5ng/L in conjunction with robust risk assessment can be safely used a rapid rule out strategy to exclude AMI among patients presenting to the ED.

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154. THE PREVENT STUDY: PROACTIVE REVIEW BY THE ED BEFORE INTER-HOSPITAL TRANSFER

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Inter-hospital patient transfers may ensure proper and timely care, but are associated with adverse events, move patients away from their communities, and generate additional costs.
AIM(S): To determine the population of patients where transfer may be prevented by assessment of an ED advanced trainee at the referring hospital, and to undertake cost-effectiveness analyses for implementation of an ED outreach program.
METHODS: Patient data were extracted on all patients transferred from Caulfield Hospital (CGMC) to The Alfred from 01 July to 31 December 2016. Medical records were reviewed independently by two clinicians to determine preventability of the transfer, and whether attendance at CGMC by a senior ED registrar could have prevented the transfer. Disagreement between the two reviewers were referred to a panel of three clinicians for resolution.
RESULTS: There were 220 patients included with a mean age of 73.7(15.2) years. The median time spent in the E&TC was 4 (2-8) hours with a max of 21 hours, and 196(89.1%) were admitted to The Alfred. There were 107 (48.6%) transfers deemed preventable or potentially preventable, with 104 (97.2%) preventable by attendance of a senior ED registrar. There were 55(25.0%) patients transferred after sustaining a physical injury with 36 (65.5%) deemed preventable or potentially preventable, with odds of being preventable or potentially preventable if transferred for the primary indication of trauma being 3.9 (95%CI:2.1-7.1;p<0.001). Assuming emergency road transport fees of $1,000, the minimum cost of preventable transfers was estimated at $150,000 over 6- months, not accounting for costs of duplication of care.
CONCLUSION: This proof-of-concept study suggests that strategies to strengthen primary care and reduce patient transfer should be further explored. An outreach program for acute assessment of patients at the referring hospital by ED clinicians prior to transfer, particularly after acute trauma, may be a cost-effective option that warrants further exploration.

155. IN-HOSPITAL TRAUMA TRIAGE IN INDIA – IMPLEMENTATION AND EVALUATION FO THE THREE-LEVEL TRAUMA FLAG SYSTEM

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BACKGROUND: The Australia-India Trauma Systems Collaboration (AITSC), funded by the Australian and Indian Governments, is a program aimed at improving care of the injured in Australia and India.
AIM: To implement and evaluate a traffic light trauma triage reception system in India.
METHODS: Four trauma hospitals in India were collaborators of the AITSC. One site had a clearly defined traffic light trauma triage system - Red (serious but salvageable life-threatening injury/illness), Yellow (moderate to serious injury/illness - not immediately life-threatening) and Green (walking wounded). This system was introduced into three other sites. Arrival trauma flag and mortality data for yellow and red trauma triage patients was collected in- line with the AITSC In-hospital trauma registry. Data was collected for 12 months from 1st May 2016 – 30th April 2017.
RESULTS: The traffic light trauma triage system was implemented in different ways by different hospitals according to the hospital infrastructure, funding and in-hospital processes. During the first year of collection trauma triage data was collected from 5144 patients. Of these 43 % (range 30% to 79%) were Yellow and 57% (range 21% to 70%) were Red patients. The overall patient mortality rate for red patients was 86% (range 60% - 100%) whilst for yellow patients was at 14.4% (0 – 41%).
CONCLUSION: The traffic light trauma triage reception system was successfully implemented in three Indian hospitals for the first time. AITSC registry data provided data that identified a trauma quality improvement opportunity to improve trauma triaging in at least one hospital.

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156. THE DEVELOPMENT OF WIRELESS TRAUMA RECEPTION AND RESUSCITATION © (TRR©) HEADS-UP DISPLAY (HUD) FOR ENHANCED TRAUMA RESUSCITATION DECISION SUPPORT: AN EARLY FEASIBILITY AND USEABILITY STUDY

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The TRR© system has been developed at The Alfred Hospital in Melbourne, the largest adult Level 1 Trauma Center in Australasia. It provides real-time computer-aided decision support to hospital trauma teams during the first 60 minutes of resuscitation where a critical decision is required every 72 seconds. The system has been shown to significantly reduce errors of omission and associated morbidity – particularly during the initial resuscitation and management of shocked patients.
Wearable HUDs are starting to revolutionise patient monitoring methods and may improve the efficiency of clinical interventions.
In this feasibility and usability study, we present a novel approach to display vital signs parameters and provide decision support, including capabilities to transmit images and consult with experts remotely. The proof of concept device is a successful integration of the existing TRR© software and Google Glass hardware. It resulted in an operable prototype that can be used for demonstration purposes and in emulation settings.
An initial bench top testing shows stable WIFI connectivity, speech recognition and battery life. The software interface also went through several iterations to optimise the patient data delivery whilst reducing the cognitive load. As an exploratory assessment, it was hypothesised that the projection of patient vital signs and 'action prompts' standardised triggers, increased situational awareness and improved decision making processes linked to the likelihood of survival. Potential impact for this application extends beyond trauma management in a hospital setting. The TRR© HUD prototype shows great promise for improving patient outcomes in prehospital environment and combat casualty trauma.

157. THE REHABILITATION PRESCRIPTION ALLOWING IMPROVED INJURY RECOVERY (REPAIR) APP - AN APPLICATION FOR POST TRAUMA REHABILITATION

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Studies of medium- to long-term recovery have shown that patients who survive to hospital discharge are substantially influenced by post-hospital treatments, care and support. In developing countries and rural communities, the resources are often unavailable, or are piecemeal, poorly organised, and difficult to access.

AIM: The aim of this study was to develop a smartphone application for a home-based physiotherapy rehabilitation program for trauma patients.

METHODS: A variety of post-trauma injuries were considered. Exercises were selected and a software company employed to develop the first-generation application. Development of an android app was commenced due to the predominance of android phones in India.

RESULTS: The RePAIR app was developed for trauma patients with lower limb fractures. A series of 30 exercises were selected for the app for non-weight bearing, partial-weight bearing, full-weight bearing groups, and high impact – and these exercises transformed into simple 3-dimensional animations. Doctors and/or physiotherapists manage the patient exercises (e.g. selection, number of reps and frequency) from a web-based application. Patients download the app onto their smartphone where the list of exercises assigned to them is populated on the screen. Patients select the exercises from their list, which opens the exercise animation and instructions. The app sends reminder notifications to the patient 3 x daily to complete exercises. Completion data is sent to the web-based platform back-end and can be downloaded by the assigned Doctor/ Physiotherapist who can make changes to the assigned exercises which is then automatically updated on the patient app.

CONCLUSION: The RePAIR app will be tested for useability in Australian patients with lower limb injuries. Subject to favourable useability a larger range of trauma rehabilitation exercises will be incorporated into RePAIR and an RCT undertaken to determine the effectiveness.

158. EVALUATING THE INTRODUCTION OF RESUSCITATIVE BALLOON OCCLUSION OF THE AORTA (REBOA) FOR CONTROL OF EXSANGUINATING TRAUMA RELATED HEMORRHAGE IN AN ADULT LEVEL 1 AUSTRALIAN TRAUMA CENTER (THE ACE STUDY)

Fitzgerald M[1,2], Lendrum R[3,4,5], Bernard S[6,9,10], Moloney J[3,7], Smit D[2,8,10], Mathew J[1,2,8], Nickson C[9,11], Lin RM[9,12], Yeung M[1,2], Martin K[1,2], Bystrzycki A[2,8], Niggemeyer L[1,2], Mitra B[2,8,10]

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BACKGROUND: Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) has recently been promoted for temporary haemorrhage control as life-saving intervention in patients with severe, non-compressible haemorrhage prior to definitive haemorrhage control.

AIM: This study sought to determine if the introduction of REBOA for Aortic Control of Exsanguinating Trauma Related Haemorrhage at an adult Australian Adult Major Trauma Centre would improve survival for major trauma patients (aged 18-60 years, transported directly from scene with exsanguinating, sub-diaphragmatic haemorrhage and hypovolemic shock or hypovolemic cardiac arrest) until hospital discharge.

RESULTS: During the 14-month study period 3,032 patients were admitted direct from scene through the Alfred Emergency & Trauma Centre with an overall mortality of 97 (3.71%). Of these patients 3,019 had trauma centre vital signs recorded in the dataset (99.57%) and 1,523 were between the ages of 18-60 including 143 patients with a Shock Index of >1.0 (4.74%) – marker indicative of haemorrhagic shock - and 13 (0.43%) with a Systolic Blood Pressure <70 mmHg and/or cardiorespiratory arrest on arrival. The mortality in this group was 6/13 (46.15%). Of these 13 patients, there were 2 (0.07% of the total cohort) where REBOA was attempted.There were no eligible patients for whom REBOA was achieved. Although commenced, the REBOA procedure was abandoned during the resuscitation of the 2 patients. Both patients survived due to immediate abdominal operative intervention and direct haemorrhage control. One 80-year-old patient with multisystem trauma, including neurotrauma, underwent successful REBOA deployment despite temporarily losing cardiac output during insertion. The patient died in Intensive Care on day 2 secondary to severe neurotrauma. None of the other 6 patients who died would have benefited from REBOA.

CONCLUSION: Despite considerable training and resource allocation to ensure 24-hour availability, the introduction of REBOA failed to demonstrate any impact on patient outcome for this patient cohort.

159. THE AUSTRALIA-INDIA TRAUMA SYSTEMS COLLABORATION (AITSC) – REDUCING THE BURDEN OF INJURY IN INDIA AND AUSTRALIA THROUGH IMPROVED SYSTEMS OF CARE

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Commencing in 2013, the Australian and Indian Governments invested research funding to find the best ways of delivering needed care to injured people. The AITSC brings together governments, industry, clinicians and researchers to improve information and resources, and to pilot new systems of care.

AIM: To reduce the burden of injury in India and Australia through improved systems of care by the:

- Introducing and evaluating pre-hospital notification in India
- Adaption and evaluation of a computerised decision support system to improve patient care
- Development and evaluation of a structured trauma quality improvement meeting (TQIM)
- Develop a post-trauma rehabilitation prescription system

METHODS:

Intervention were largely undertaken in India before being adapted to the Australian context. Interventions were underpinned by the development of the AITSC trauma registry. Technology based solutions were considered and explored for each intervention – due in part to the huge uptake of mobile technology in both countries.

RESULTS AND CONCLUSION:

- The AITSC registry collected data for two years - laying the foundations for a national trauma registry in India. A registry report of the first year was presented to the governments in March 2018.
- A pre-hospital notification app, Suchana, was developed and trialled in two hospitals in India with great success.
- The Alfred Trauma Reception and Resuscitation decision support software was adapted to the Indian setting and trialled at one site.
- Structured TQIMs were introduced into four sites and a checklist app, TraumaMeet, developed.
- A rehabilitation RCT was conducted and a post trauma rehabilitation app (RePAIR) developed.

160. AIIMS TRAUMA RECEPTION AND RESUSCITATION© (TRR©) SYSTEM: A PRELIMINARY TRIAL OF THE INTRODUCTION OF TRAUMA RESUSCITATION DECISION SUPPORT TO INDIA

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Background & Aims. The TRR© system provides the Trauma Team with computerised decision support for the management of major trauma, improves protocol compliance and reduces errors of omission. The primary outcome of this study was to determine whether the TRR© significantly improves real-time vital signs data capture and documentation. The secondary outcome measure evaluated the frequency of Life Saving Interventions (LSIs) and the time taken to perform them.
Methods. The TRR© system was installed into 2 of the 6 resuscitation area bays within AIIIMS JPN Apex Trauma Center. In the TRR group, 82 patients were enrolled with 41 non-TRR controls. Data was extracted automatically from the TRR© system. Matching control data was entered on-line via a purpose-built REDCap™ secure web application.
Results. Resuscitation procedures were more accurately recorded, in real time by staff when TRR© system was in use. There was a statistically significant difference in the time taken to insert intercostal catheters between the TRR treatment group and the controls ($p < 0.05$). Moreover, the treatment group exhibited shorter time from arrival to endotracheal tube (M = 13, SD =0.09), as opposed to 23 minutes (SD =21.08) for controls ($p < 0.005$). Importantly, there was a greater variability in the time taken to perform LSIs in the control group in comparison to the clinicians assisted with computerised decision prompts.
Conclusions. The TRR© system was successfully introduced and applied at Level I trauma center in India. With continued use and further data analyses, it shows great potential to be implemented as standard of care for trauma management.

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161. DOES ANTERIOR INTERBODY GRAFT CHOICE AFFECT PATIENT OUTCOMES IN CERVICAL SPINE TRAUMA

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AIM: There has been a paucity of spine trauma literature comparing the outcomes of anterior cervical interbody graft with polyetheretherketone (PEEK) cage and iliac crest bone graft (ICBG). Synthetic graft usage prevents morbidity associated with the harvesting of ICBG (up to 19%), and reduces the operative and anaesthetic time. This study aims to evaluate patient reported outcomes of anterior cervical stabilization surgery using synthetic cage in comparison to ICBG following cervical spine injury.
METHODS: An ambispective review was conducted on consecutive patients, aged 18-80 who required standalone anterior cervical stabilisation following spine injury (2011-2016) treated at a state service Level 1 trauma centre. The Alfred has an established clinical-quality trauma registry. Primary outcome measures were the Neck Disability Index (NDI) and patient satisfaction. Secondary outcomes were radiographic evidence of fusion and revision surgery. All patients had follow-up for at least 1 year.
RESULTS: Out of 104 disc levels (95 patients), ICBG were used in 32% and PEEK cage in 68%. Both groups had indifferent demographics. Multivariate analysis showed no difference in the primary outcome measures between the graft types: (1) Patient satisfaction, p=0.61; (2) NDI, p=0.51. There was no significant difference in rates of radiological fusion (p=0.238). One patient from each cohort required revision cervical spine surgery.
CONCLUSION: There was no significant difference in spine trauma patient reported outcomes between the usage of PEEK cage and ICBG in anterior cervical surgery. This study is the impetus for further studies required to clarify this position as it has significant fiscal implications on the in-hospital and community costs.

162. PEOPLE WHO ARE HOMELESS FRQUENTLY PRESENT TO HOSPITAL EMERGENCY DEPARTMENTS BUT HOMELESS STATUS IS OFTEN NOT IDENTIFIED AND DOCUMENTED

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Homelessness is common in people attending hospital emergency departments (ED) and increases re-presentation risk. Less is known about why people who are homeless attend EDs or the accuracy with which homeless status is identified and documented by health services.
AIM: Prospectively assess housing status in consecutive patients presenting to The Alfred ED and explore in people identified as homeless why the presented. A secondary aim was to compare the prevalence of patients identified as homeless via prospective housing screen or housing status coded in the Victorian Emergency Minimum Dataset (VEMD).
METHODS: All patients presenting to the ED between 16-23 January 2017 were invited to complete a housing screen. If identified as experiencing primary, secondary or tertiary homelessness, they completed a survey assessing use of primary and community services and ED use that day. A retrospective audit of all presenting episodes occurred to supplement prospective data collection.
RESULTS: Of 1,208 unique patients, 504 were prospectively screened, and 40 (7.9%) were identified as homeless. This compared with 0.8% of all ED patients during the study period coded in the VEMD as homeless. Patients had a significantly higher odds of being homeless if they: were male, arrived with police/emergency ambulance; had a psychosocial or drug primary diagnosis; or had at least 3 ED presentations in the previous 12 months. Twenty-nine homeless patients were surveyed. Illness, injury, psychiatric/drug issues and housing stressors were reasons for attending. Almost one-third of participants stated that they viewed ED staff as a regular source of support, and that lack of suitable housing, available general practitioners, or money for medication had contributed to ED attendance.
CONCLUSION: Improved identification of homelessness and strengthened pathways to integrated and accessible community- based health, housing and psychosocial support is required to address the needs for homeless patients presenting to ED and reduce ED visits.

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163. THE ALFRED HOSPITAL EXPERIENCE OF TARGETED MUSCLE REINNERVATION FOR IMPROVING UPPER LIMB PROSTHESIS CONTROL

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Purpose: Upper limb amputation is a devastating injury. Prosthetic options available to amputees include passive, traditional body-powered or myoelectric prostheses, which are driven by myogenic electromyographic (EMG) signals. Targeted muscle reinnervation (TMR) aims to surgically create strong and reliable signals to permit the intuitive use of a myoelectric prosthesis with the greatest number of movements possible. We review the Alfred Hospital experience of using TMR to improve upper limb prosthesis control.

Method: A retrospective review of all cases of TMR performed at the Alfred Hospital was undertaken. Patient demographics, injury, surgical complications and outcomes were examined. Comparison was made to pre-operative prosthesis use.

Results: 7 patients have undergone TMR to improve upper limb prosthesis control at the Alfred Hospital between 2015 and 2018. Within the patient group, pre-TMR EMG signal numbers ranged from 1-2, and post-TMR signal numbers range from 3-5. 6 patients were able to achieve 6 degrees of freedom post-operatively, and one patient achieved 4 degrees. No patients required the use of co-contraction to switch function post operatively. There were no significant surgical complications.

Conclusion: The use of TMR to improve and increase the number of EMG signals has been successful in generating more degrees of freedom for upper limb amputees with myoelectric prostheses.

164. NEW BEGINNINGS - PRE-HOSPITAL NOTIFICATION OF INJURED PATIENTS PRESENTING TO TRAUMA CENTRES IN INDIA

Matthew J[1 2], Mitra B[1 3 4], Howard T[1], O'Reilly G[1 3 4], Stephenson M[6], Meadley B[6], Cudini D[6], Kumar V [7], Jarwani B[8], Fahey M[1], Pandit A[9], Yadev A[9], Abraham A[9], Patel P[8], Thakor A[8], Dharap S[7], Gruen R[11], Walker T[6], Misra M[5] , Gupta A[5], Fitzgerald M [1 2], on behalf of the on behalf of the AITSC Investigator Group

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Prehospital notification is the communication by emergency service personnel to a receiving hospital of the impending arrival of a patient requiring emergency care. It is an integral component of an advanced prehospital care system associated with reduced mortality in trauma centres. There is currently no system or obligation for pre-hospital notification in India.
AIM: To develop and introduce a system for prehospital notification and trauma team activation in India.
METHODS: Suchana is an Android app to facilitate the notification of major trauma cases from the ambulance to emergency department. Simple data is entered by an emergency medical technician (EMT), generating a trauma triage flag in a corresponding app on duty mobile phone held by a designated person within the ED. Only "red" major trauma patients are notified, triggering a Trauma Team Activation to notify trauma team members for early preparation and readiness to receive the patient.
RESULTS AND CONCLUSION: Pre-hospital notification using the Suchana commenced in Mumbai and Ahmedabad in May/June 2017 – Jan/Feb 2018. Suchana was used a total of 470 injured patients. The use of Suchana reduced patient handover time and sped up initiation of treatment for critical patients. Unexpected benefits included: improvement in care to notified patients; proactive surveillance of patient care and immediate resolution of issues; increase in trauma patients directed to one trauma hospital; trauma team and trauma bay ready; and increased communication with the trauma centre.Ultimately both the Mumbai and Ahmedabad public ambulance companies are looking to invest in pre-hospital notification as a concept.

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165. HAEMODYNAMICS AS A DETERMINANT OF NEED FOR PRE-HOSPITAL APPLICATION OF A PELVIC CIRCUMFERENTIAL COMPRESSION DEVICE IN ADULT TRAUMA PATIENTS

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Pelvic circumferential compression devices (PCCDs) improve position and stability of open-book pelvic fractures, and can improve haemodynamics in hypovolaemic shock. However, PCCDs may cause adverse outcomes including worsening of fracture patterns and routine use is associated with high costs. Controversy regarding indication for PCCD exists with some centres recommending PCCD for hypovolaemic shock compared to placement for any suspected pelvic injury.
AIM: To assess the need for PCCD application based on pre-hospital vital signs and mechanism of injury.
METHODS: A retrospective cohort study was conducted in a single adult major trauma centre examining a 2-year period. 376 patients with PCCD in-situ on hospital arrival were included. Patients were sub-grouped based on initial pre-hospital and emergency department observations as haemodynamically normal (heart rate <100 bpm, systolic blood pressure ≥100 mmHg and Glasgow Coma Scale ≥13) or abnormal. Diagnostic accuracy of pre-hospital haemodynamics as a predictor of pelvic fracture requiring intervention within 24 hours was assessed.
RESULTS: 137 patients (36.4%) had pelvic fracture. Of these, 39 (28.5%) were haemodynamically normal and 98 (71.5%) were haemodynamically abnormal. Of those with fractures, 40 patients (29.2%) required pelvic intervention within 24 hours; 8 (20%) were haemodynamically normal and 32 (80%) were haemodynamically abnormal. As a test for pelvic fracture requiring intervention within 24 hours, abnormal pre-hospital haemodynamics had a sensitivity of 0.80 (95% CI 0.64-0.91), specificity of 0.32 (95% CI 0.27-0.38) and NPV of 0.93 (95% CI 0.88-0.96). In combination with minor mechanism of injury, normal haemodynamics had a sensitivity 1.00, specificity 0.51 (95% CI 0.36 - 0.66) and NPV of 1.0 for pelvic intervention within 24 hours.
CONCLUSION: Normal haemodynamic status, in combination with low velocity mechanism can be used to rule out requirement for urgent pelvic intervention. In other patients with suspected pelvic injury, the practice of liberal application of PCCDs should continue.

166. EFFICACY OF P.A.R.T.Y. PROGRAM DELIVERY MODEL FOR REGIONAL PARTICIPANTS – OUTREACH VERSUS IN-HOSPITAL

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Introduction: The Prevent Alcohol and Risk related Trauma in Youth (P.A.R.T.Y) Program uses vivid clinical reality to build resilience and prevent injury among young people by following a trauma patient's journey through hospital. The Alfred in Melbourne delivers two models of this program- the in-hospital program, which runs within the hospital setting and the outreach program, which converts regional performing arts centres to replicate the hospital setting. The aim of this study was to compare the two programs for perceptions of safety of driving after alcohol, driving after drinking alcohol, seatbelt use and perceptions of likelihood of injury after risk taking activities.

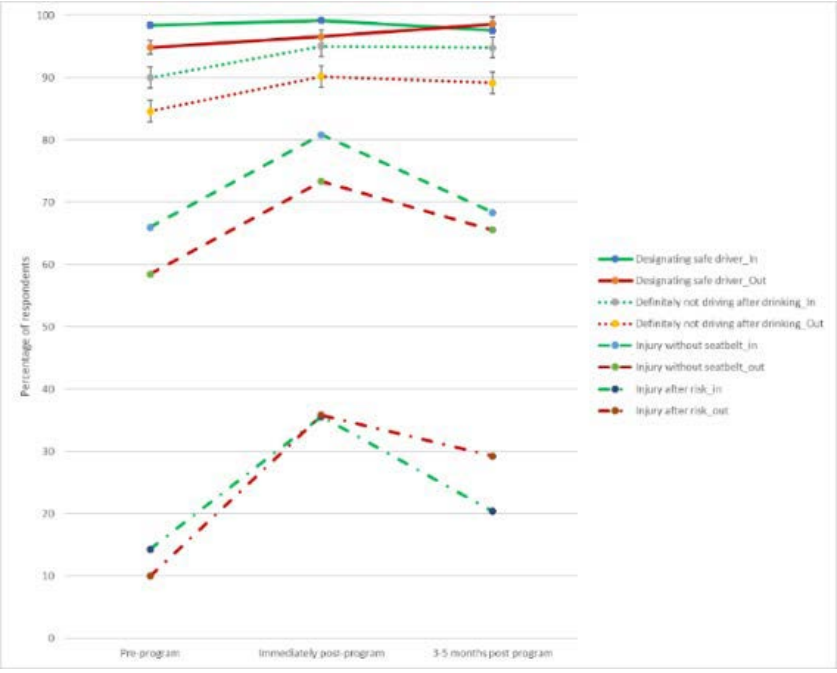
Methodology: Pre-program, immediately post program and 3-5 months post program surveys with objective questions focused on the program aims were distributed to all consented participants from regional areas that attended either the in hospital or outreach model. The results from each participant group were then compared and analysed for any outcome difference.

Results: There were 1318 participants during the study period and 547 (42%) responses surveys were received, with 296 (54%) in the outreach program and the remaining 241 (46%) in-hospital. The mean age was 16.4 (SD 0.7) years, 313 (58.1%) were female and 423 (78%) possessed a learner's permit for driving with no significant differences among participants across the two models of delivery.

Pre-program, a significantly lower proportion of participants in the outreach model (85% vs 91%) reported 'definitely not' to driving after drinking, 'definitely' designating a safe driver after drinking (95% vs 98%), perceived the risk of injury after not wearing a seatbelt and car crash (58% vs 66%) and associated risk taking behaviors with injury (10% vs 14%).

Immediately post program, a higher proportion of participants in the outreach program reported 'definitely not' to drinking and driving (n=267, 90%, p=0.042), but dropped to 264 (89%; p=0.10) at 3-5 month follow-up. In the outreach program, the perception of designating safe drivers after drinking alcohol demonstrated sustained improvement (p=0.010), while improvements with some decay were observed for other outcomes (See Figure 1 next page). In the outreach program, proportion of participants reporting improvements appeared to be better sustained.

Conclusions: While demographically similar, the P.A.R.T.Y. Program outreach model engaged youths with significantly different perceptions to alcohol, risk taking and injury. There were significant differences in the effect of the program, in particular, demonstrating less decay in positive perceptions in the follow-up survey. The findings suggest greater effectiveness of the P.A.R.T.Y. program when delivered as an outreach model.



167. DEFIBRILLATION ENERGY DOSE DURING PEDIATRIC CARDIAC ARREST: SYSTEMATIC REVIEW OF HUMAN AND ANIMAL MODEL STUDIES

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AIM: To determine the optimal initial defibrillation energy dose to achieve sustained return of spontaneous circulation (ROSC) during paediatric cardiac arrest with ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT).

METHODS: A systematic review was performed using the following databases were searched: Medline, Embase, Cochrane library and clinicaltrials.org. Human studies and animal model studies of pediatric cardiac arrest having assessed defibrillation energy dosing were considered for inclusion. Primary outcome was sustained ROSC. Survival and defibrillation-induced complications were also retrieved.

RESULTS: The search strategy retrieved 12 775 citations of which 225 manuscripts were reviewed. A total of 10 human and 10 animal model studies fulfilled the inclusion criteria. Human studies were prospective (n=6, 60%) or retrospective (n=4, 40%) cohort studies and included between 11 and 266 patients (median = 46 patients). Sustained ROSC ranged from 0 to 61% (n=7, median = 45%). No studies reported a statistically significant association between the initial defibrillation energy dose and the rate of sustained ROSC (n=7) or survival (n=6). Doses < 2 joules/kg frequently showed a trend towards less frequent ROSC (n=3) when compared to higher doses. No meta-analysis was considered appropriate due to clinical heterogeneity. The overall risk of bias was moderate for human studies. All animal studies were randomized controlled trials having studied between 8 and 52 (median = 27) piglets. ROSC was frequently achieved (85%) with energy dose ranging from 2 to 7 joules/kg (n=7). The defibrillation threshold varied according to the body weight. Attenuated energy electrodes were associated with less left ventricular dysfunction (n=3).

CONCLUSION: Defibrillation doses, repeat doses and thresholds varied according to the body weight and trended higher for infants. No definitive association between initial defibrillation doses and the outcomes of sustained ROSC, ROSC or survival could be demonstrated. Multicentre randomised controlled trials are required to compare lower vs higher energy shocks after paediatric cardiac arrest.

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168. SECURITY INTERVENTIONS FOR WORKPLACE VIOLENCE IN THE EMERGENCY DEPARTMENT

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Despite a policy of zero-tolerance towards workplace violence (WPV) in Australian public hospital EDs, the incidence of WPV continues to increase.

AIM: The aim of this study was to characterise security responses to WPV within an adult level 4 ED.

METHODS: A retrospective single-centre review of episodes of WPV perpetrated by adults occurring within the ED was conducted between January 1st 2013 and December 31st 2015. Cases were identified using a prospectively recorded security register that records all events of security personnel attendance. The presence of police officers on initial presentation was the primary exposure variable.

RESULTS: There were 1853 violent episodes committed by 1224 patients requiring security intervention during the study period, with half the episodes (n=916; 49%) involving perpetrators who had committed at least two or more violent acts during the study period. Most cases (n=1057, 57%; 95% CI: 55-59) occurred in the absence of police presence. Only 144 (7.8%) cases were managed by the presence of security personnel without physical security interventions.

CONCLUSION: EDs should not rely on police response to prevent or handle violence. The finding of a high proportion of events being perpetrated by repeat offenders indicate that data sharing between EDs for identification of perpetrators of WPV can be useful for prevention of future episodes. ACEM policy for WPV in EDs should encompass further details on security credentialing and preventive strategies towards minimisation of WPV in Australian EDs.

169. THE VALUE OF AN IN-HOSPITAL TRAUMA DATA REGISTRY IN INDIA – AN AUSTRALIA-INDIA TRAUMA SYSTEM COLLABORATION PROJECT

O'Reilly G[1,2,3], Howard T[1,5], Mathew J[1,2,5], Gupta A[7], Cheung Z[1], Roy N[6], Mitra B[1,3,8], Cameron P[1,3], Fahey M[1], Kumar V[10], Kaushik G[7], Jhakel A[7], Sharma A[7], Mahindrakar S[7], Shrivastava N[11], Wamik S[11], Sheth S[12], Mhaske P[12], Arokel A[10], Dungdung A[10], Jarwani B[12], Thakor A[12], Soni K[7], Sharma N[11], Patel P[12], l Gruen R[9], Misra M[7], Fitzgerald M[1,2,5] on behalf of the AITSC Investigator Group

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BACKGROUND: A key component of trauma systems are in-hospital trauma registries that document acute care delivered to patients hospitalised with injuries. Through the Australia-India Trauma Systems Collaboration (AITSC), funded by the Australian and Indian Governments, an 81-item trauma registry was developed and implemented in four trauma hospitals across India.
AIM: To characterize major trauma presenting to four hospitals across India
METHODS: Four trauma hospitals in India collected the data in-line with the AITSC In-hospital trauma registry. Data collection occurred for 12 months from 1st May 2016 – 30th April 2017. The data was analysed using STATA and then reported to the AITSC investigators/sites and the Indian Government (March 2018). Site specific reports were supplied to each hospital.
RESULTS: During the first year of collection the registry collected data from 5,319 major trauma patients across four sites. Data completeness was 99.8%. The overall patient mortality rate was 12% (range 7% - 25%). Most patients were male (83%), were injured on roads or highways (61%) and arrived direct from scene using non-ambulance modes of arrival (75%). Falls accounted for 29% of all trauma. One site had a disproportionately high number of patients injured in railway incidents (17%) compared to the average across all sites (4%). Times to immediate care varied significantly across the four sites.
CONCLUSION: A multi-centre trauma registry has been successfully implemented to describe the demographics, injury case, processes of care and outcomes. This will be useful for strengthening services for injured patients, allow benchmarking of trauma systems, and inform trauma quality improvement programs.

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170. EVALUATION OF A MULTIFACETED, COLLABORATIVE MANAGEMENT PROGRAM FOR PATIENTS WITH CELLULITIS IN THE EMERGENCY DEPARTMENT

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While cellulitis is frequently treated in Emergency Short Stay Units (ESSU), there is limited literature to guide admission criteria. Local research demonstrated a high ESSU management failure rate (34.8%), with a large proportion of patients requiring inpatient admission or overstaying the specified ESSU time period.
AIM: To determine if the introduction of a multifaceted, collaborative cellulitis management program in the Emergency Department (ED) would reduce ESSU management failure rates to less than 15%, defined as a stay in ED / ESSU greater than 28 hours or transfer of care to an inpatient unit. The study also aimed to determine if such a program would improve antimicrobial use for patients with cellulitis in the ESSU.
METHODS: A retrospective cohort study with historical controls was conducted to compare the management of patients diagnosed with cellulitis and admitted to the ESSU at the Alfred Hospital, before and after implementation of the ED cellulitis management program (control period: January 1, 2013-December 31, 2014, and post-intervention period: February 17, 2017-August 31, 2017). The program involved development and dissemination of a new local guideline, education and early involvement of the ED pharmacist with the treating ED clinician.
RESULTS: A total of 131 patients were admitted to the ESSU in the post-intervention cohort. 46 patients (35.1%) received the full intervention with early ED pharmacist involvement. Interim analysis shows the intervention led to a non-significant decrease in the ESSU management failure rate (21.7% vs. 34.8%; p=0.07). There was no significant difference between groups in the proportion of patients readmitted to hospital within seven-days (4.3% vs. 3.8%; p=0.65).
CONCLUSION: A collaborative cellulitis management program may improve the proportion of patients with cellulitis successfully managed in the ESSU. While the 15% failure rate target was not achieved, the preliminary results are of clinical significance and warrant further investigation.

171. VIDEO-TUBE THORACOSTOMY IN TRAUMA RESUSCITATION

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Background: Complications related to incorrect positioning of tube thoracostomy (TT) have been reported to be as high as 30%. The aim of this study was to assess the feasibility of flexible videoscope guided placement of a pre-loaded chest tube, permitting direct intrapleural visualization and placement (Video-Tube Thoracostomy [V-TT]).

Methods: A prospective, single centre, phase 1 pilot study with a parallel control group was undertaken. The population studied were adult thoracic trauma patients requiring emergency TT who were haemodynamically stable. The intervention performed was V-TT. Patients in the control group underwent conventional TT. The primary outcome was tube position as defined by a consultant radiologist's interpretation of chest x-ray (CXR) or CT. The trial was registered with ANZCTR.org.au (ACTRN: 12615000870550).

Results: There were 37 patients enrolled in the study - 12 patients allocated to the V-TT intervention group and 25 patients allocated to conventional TT. Mean age of participants was 48 years (SD 15) in intervention group and 46 years (SD 15) years in the control group.

In the V-TT group all patients were male; the indications were pneumothorax (83%), haemothorax (8%) and haemopneumothorax (8%). The median injury severity score was 23 (16-28). There were 1 positional and 1 insertional complications. In the control group 72% of patients were male, the indications were pneumothorax (56%), haemothorax (4%) and haemopneumothorax (40%). The median injury severity score was 24 (14-36). There were 8 (32%) positional complications and no insertional complications.

Conclusion: V-TT was demonstrated to be a feasible alternative to conventional thoracostomy and merits further investigation.

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172. FACEM EXPOSURE TO TRAUMA MANAGEMENT IN THE VICTORIAN STATE TRAUMA SYSTEM: AN EDUCATIONAL NEEDS ANALYSIS FOR SENIOR MEDICAL STAFF

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One third of trauma patients in Victoria are initially treated outside a Major Trauma Service (MTS). Transfer protocols ensures over 80% of major trauma patients receive definitive care at a MTS. This concentration maximises expertise in the MTSs, however clinicians working outside these centres may lose confidence and ability in trauma management as a result. There is no mandated required time in a MTS, nor requirements to complete any trauma specific competency training, within the Australasian College for Emergency Medicine (ACEM) training or fellowship CPD. These factors combined may make the Victorian State Trauma System vulnerable.

AIM: To identify the fraction of work FACEMs in Victoria do in MTSs, their trauma specific training pre- and post-fellowship, their estimated exposure to major trauma procedures (including trauma team leading) & their self-reported confidence in the same.

METHODS: We distributed a cross-sectional survey to all FACEMs working in Victoria.

RESULTS: 145 FACEMs working across Victoria responded. 35% of non-MTS FACEMS had never worked in an MTS as a registrar or consultant. EMST uptake was moderate with 27% of non-MTS FACEMs and 23% of MTS FACEMs reporting having never done EMST. 21% of Non-MTS FACEMS reported not leading a trauma team response in the last 12 months and 17% reported only a single case. Non-MTS FACEMs were significantly less confident in trauma management than MTS FACEMS.

CONCLUSION: Since one third of major trauma patients are received at a non-MTS there are potential trauma training gaps in the non-MTS emergency medicine workforce that should be addressed to improve state-wide trauma care.

173. EMERGENCY DEPARTMENT MANAGEMENT OF PATIENTS PRESENTING WITH SUPRATHERAPEUTIC INRS ON WARFARIN: A PRE AND POST EDUCATION STUDY

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In clinical practice warfarin is a challenging medication to manage due to its narrow therapeutic index and potential for many significant medication interactions. Numerous international healthcare systems have developed appropriate guidelines to improve the safe use of warfarin. However, despite these guidelines adverse events to warfarin are common.

AIM: To evaluate the efficacy of an educational program focused at improving emergency clinician compliance with the Thrombosis and Haemostasis Society of Australia and New Zealand (THANZ) evidence-based guidelines for management of patients that presented to the Emergency Department (ED) with supratherapeutic INR levels. Supratherapeutic INRs, especially those exceeding 4.5, are associated with increased risk of haemorrhage.
METHODS: A pre and post intervention cohort study was conducted. The intervention involved the development and delivery of an educational program in accordance with the current THANZ guidelines. Retrospective data from 1 July 2014 to 30 June 2015 and prospective data 1 Jan 2016 to 31 Dec 2016 were collected on ED patients currently anticoagulated with warfarin. This study was conducted in a large tertiary care hospital in Melbourne, Australia where subjects included all consecutive patients in the study periods that presented to the ED with an initial INR result of >4.5 on warfarin only. Subjects managed by an admitted team or anticoagulated with direct oral anticoagulants were excluded. Data collection included baseline demographics, medical history, INR results, bleeding risk assessment, the presence of active bleeding, and administration of fresh frozen plasma, prothrombinex and vitamin K.
RESULTS: Data on 158 patients with an INR >4.5 were collected. Of these, data on 46 patients were excluded. Overall management in 31 (27.7%) patients did not follow recommended guidelines. There was no difference detected between pre and post groups with 17 (28.3%) compliant with guidelines pre-intervention and 14(26.9%) post intervention; p=0.87.
CONCLUSION: Emergency department management of patients on warfarin with supratherapeutic INR's requires continual quality improvement. Frequency of emergency clinician compliance with the current evidence-based guidelines was moderate and did not improve significantly with targeted education. This highlights the complexities of warfarin management and the need for multi-disciplinary engagement of patients presenting with supratherapeutic INRs.

174. VARIABLES ASSOCIATED WITH PULMONARY THROMBOEMBOLISM IN INJURED PATIENTS: A SYSTEMATIC REVIEW

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BACKGROUND: Pulmonary thromboembolism (PTE) is a dangerous complication of traumatic injury, with varied risk profiles and treatment options. This systematic review aimed to describe reported incidence and variables associated with PTE among severely injured patients.
METHODS: Searches were conducted using PubMed, Cochrane and MEDLINE. Relevant studies were identified by two independent reviewers based on predetermined inclusion criteria. Incidence of PTE was the primary outcome measure. Variables associated with PTE were secondary outcome measures. The Newcastle-Ottawa Scale was used to assess quality of included studies.
RESULTS: There were eight studies that satisfied inclusion criteria. The diagnosed incidence of PTE in these populations ranged from 0.35 to 24%. The most common variables associated with PTE were pelvic or lower limb injury, chest injury, higher total Injury Severity Score, male sex and age. Variables that were less commonly associated with PTE were previous warfarin use, head injury, high serum lactate, soft tissue injury, more than one operation, more than three days on a ventilator, presence of a subclavian central venous catheter, need for a blood transfusion, systolic blood pressure <90 mmHg, abdominal injury, presence of a deep venous thrombosis, inferior vena cava filter placement and isolated liver spleen or spinal injuries.
CONCULSIONS: The reported incidence of PTE after major trauma is variable and dependent on inclusion criteria, diagnostic criteria and study design. Identified variables differed to those reported for venous thromboembolism in other populations. Current prediction tools for risk of VTE may not be applicable to the trauma population. Further studies linked to patient-specific variables will assist in more precise risk-stratification and interventions.

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175. DISASTER EDUCATION AND PREPAREDNESS IN THE ACUTE CARE SETTING: A CROSS SECTIONAL SURVEY OF OPERATING THEATRE NURSES DISASTER KNOWLEDGE AND EDUCATION

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Background: Operating theatre services can be heavily relied upon during mass casualty disaster events, which require nurses to have adequate training and education of hospital disaster management plans to respond appropriately. The evidence-base of disaster preparedness in the acute setting is limited, particularly with regard to operating theatre nurses.
Objectives: Explore operating theatre nurse's disaster knowledge of their role in a mass casualty event, and identify the preferred mode of disaster education and training to improve disaster preparedness.
Design: A cross-sectional research design was employed with data collected using a survey tool.
Settings: The research was undertaken on operating theatre nurses in a tertiary hospital in Victoria, Australia.
Participants: The participants in this research included 53 operating theatre nurses, 51 Registered Nurses and 2 Enrolled Nurses.
Methods: The survey was based on a disaster questionnaire for emergency department nurses from South Australia and was altered to be specific and relevant to the operating theatre environment and broadened to focus on the training needs of perioperative nurses.
Results: The survey of 53 operating theatre nurses identified that few had previous disaster experience (19.9%). The majority of respondents were aware of their disaster management policy (Code Brown policy) (94.1%), of reporting lines, and appropriate triage (80.4%). Finally, disaster nursing general knowledge amongst staff was poor; a mean of 1.79 (SD=1.20) correct answers out of a possible 7.
Conclusions: This study highlights that disaster education and training methods for disasters be specific to the role required by nurses and all staff during a disaster activation, and training should occur regularly in view of staff turnover; training drills are preferred although face-to-face education is practical.

176.CRUCIFORM POSITION FOR TRAUMA RESUSCITATION

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BACKGROUND: Multiply injured patients represent a particularly demanding subgroup of trauma patients as they require urgent simultaneous clinical assessments using physical examination, ultrasound and invasive monitoring together with critical management, including tracheal intubation, thoracostomies and central venous access. Concurrent access to multiple body regions is essential to facilitate the concept of 'horizontal' resuscitation. We reviewed cases of severe trauma and argue for a cruciform position in trauma resuscitation.

METHODS: A retrospective review of 6 years between 1 July 2008 and 30 June 2014 of severe trauma (Injury Severity Score (ISS) >15) using the Abbreviated Injury Severity scale 1998) at The Alfred Hospital. We determined the incidence of life-saving procedures.

RESULTS: There were 6296 presentations of major trauma. Of these patients, 2668 (42.4%) were intubated and 1360 (21.6%) had 1938 Intercostal Catheters (ICCs) inserted. One in 14 (456 or 7.2%) patients required two or more ICCs. A massive transfusion protocol was initiated and blood was given for 713 (11.3%) patients within the first 4 h after hospital arrival

CONCULSIONS: Severely injured trauma patients have multiple lifesaving interventions simultaneously. The current positioning of trauma patient, with arms adducted, restricts this approach. Instead, the therapeutic cruciform positioning, with arms abducted at 90 may allow for better planning and performing of multiple lifesaving interventions. This positioning also provides a practical surgical field with improved sterility and procedural access

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