INTRODUCTION

Welcome to the 26th annual Austin LifeSciences Research Week. Once again we take time out to recognise and celebrate the quality and the breadth of the research being performed on this site through Austin health and its departments, its affiliated universities and research institutes, and also Mercy Hospital for Women. It is a time when people can share experiences and set up new collaborations, and to think towards the future in terms of cooperative grant applications, attracting future students and scientists, and cementing our place as one of the leading research centres in Australia. The research culture at Austin is vibrant and part of what we do every day. Already this is leading to changes in health care policy and practice and ultimately to better health outcomes for all of us.

This is the third year of the event being named ResearchFest as the number of activities spills across two weeks. The ResearchFest Committee has considered your feedback very carefully and made changes to the format. We recognise that not every solution is perfect for everyone and we will gratefully consider suggestions for future years.

In 2018 we have:
• instituted a Chairman’s Selection of posters of leading abstracts
• continued the format of two separate poster sessions;
• livestreamed the Plenary session;
• continued the ResearchFest debate that promises to be both entertaining and thought-provoking.

Several excellent abstracts have been chosen for oral presentation and will be competing for a substantial prize at the Austin LifeSciences Symposium.

Our plenary session this year is highlighted by Dr C. Glenn Begley MBBS., PhD., FRACP, FRCPA, FRCPath., FAHMS, CEO of BioCurate.. His presentation is entitled “10% of the time, it works every time”

As always, the ResearchFest awards will also be presented at the plenary session. Make sure you lock all these exciting events into your diaries.

We thank all of our new and returning sponsors, and the contribution of the dynamic and energetic ResearchFest Committee without whom ResearchFest would not be possible.

I hope you find Austin LifeSciences ResearchFest 2018 to be most interesting and enjoyable.

Prof Paul Johnson
Chair
Austin LifeSciences ResearchFest Committee
ResearchFest 2018 would like to thank our sponsors. Your support is vital to the success of ResearchFest

Austin Medical Research Foundation
Austin Health

Mercy Hospital for Women

East Ivanhoe and Heidelberg Community Bank
Illumina
Fresenius-Kabi
Gilead Sciences
Novartis Pharmaceuticals Australia
Sir Edward Dunlop Medical Research Foundation
Sanofi
Elsevier
Ovid Technologies
| Tues1 | Joseph O'Brien | Acute pericarditis - a rare complication of Plasmodium falciparum malaria. |
| Tues2 | Joseph O'Brien | Gender specific findings among patients admitted to the Emergency Department (ED) with Atrial Fibrillation (AF). |
| Tues3 | Joseph O'Brien | Multiple stroke prophylaxis 'treatment gaps' identified in the management of atrial fibrillation. |
| Tues4 | Joseph O'Brien | Heart rate and blood pressure as predictors of hospital length of stay in patients presenting to the Emergency Department with atrial fibrillation. |
| Tues5 | Joseph O'Brien | The role of appropriate advanced care directives in patients with pulmonary hypertension |
| Tues6 | Hnin Oo | Prevalence of elevated lipoprotein(a) in coronary artery disease patients |
| Tues7 | Mohammad Omair | Postoperative Atrial Fibrillation and Cardiac Complications after Liver Transplantation |
| Tues8 | Alexandra Murphy | Case Study: Unique presentation of coronary artery fistula with infective endocarditis in the setting of a previous penetrating chest injury |
| Tues9 | Alexandra Murphy | Clinical Outcomes of Patients with Established Coronary Artery Disease Presenting with Acute Coronary Syndromes |
| Tues10 | Alexandra Murphy | Clinical Characteristics of Patients with Stable Coronary Artery Disease Undergoing Angiography by Trans-femoral versus Trans-radial Approach |
| Tues11 | Hamid Salehi | Dobutamine Stress Echocardiography Compared With Coronary CT Angiography In Screening For Coronary Artery Disease in End Stage Liver Disease Patients Being Assessed for Liver Transplantation |
| Tues12 | Hamid Salehi | The Role Of Dobutamine Stress Echo In Predicting Outcomes In Subjects Being Assessed For Liver Transplantation |
| Tues13 | Jay Ramchand | This abstract is not included at the request of the author |
| Tues14 | Jay Ramchand | This abstract is not included at the request of the author |

**Clinical Haematology**

| Tues15 | Clare English | Development and implementation of an algorithm to manage mucositis pain in patients post autologous and allogeneic stem cell transplant |
| Tues16 | Joseph Rigano | Evaluation of the automated HemosIL® AcuStar HIT IgG chemiluminescent immunoassay for the diagnosis of HIT |
| Tues17 | Joseph Rigano | Validation of the Lamson pneumatic tube system for the transportation of blood components from Blood Bank to Intensive Care and Ambulatory Care |
| Tues18 | Joseph Rigano | P-selectin as a marker of cardiovascular risk in normal controls and myeloproliferative neoplasm. |

**Critical care and Emergency Medicine**

<p>| Tues19 | David Taylor | Determination of the best early warning scores to predict important outcomes among emergency department patients |
| Tues20 | David Taylor | Patient perceptions of participation in emergency medicine research projects |
| Tues21 | David Taylor | Temporal trends in the publication of emergency medicine original research |
| Tues22 | David Taylor | Utility of calcium, magnesium and phosphate testing in the emergency department |</p>
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<thead>
<tr>
<th>Tues23</th>
<th>Vishal Goel</th>
<th>This abstract is not included at the request of the author</th>
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<tr>
<td>Tues24</td>
<td>Robyn Purcell</td>
<td>Simulation Gamification: LIVE. DIE. REPEAT.</td>
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<td>Tues25</td>
<td>Carl Lee</td>
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<tr>
<td>Tues26</td>
<td>Anita Panayiotou</td>
<td>Preventing Avoidable Hospital Admissions for People with Dementia (PAHA-D) - A collaborative project to identify current dementia care practices</td>
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<tr>
<td>Tues27</td>
<td>Micah Wong, Mainak Majumdar, Jeffrey Presneill</td>
<td>Critical Care Short-term Outcomes of Cancer Patients in Australasia</td>
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<tr>
<td>Tues28</td>
<td>Laurent Bitker</td>
<td>The impact of pre-morbid glycemic control on glycemia, insulinemia and C-peptidemia in critically ill diabetic patients</td>
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<td>Tues29</td>
<td>Laurent Bitker</td>
<td>The impact of exogenous insulin on insulinemia and C-peptidemia in critically ill diabetic patients treated with permissive hyperglycemia</td>
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<td>Tues30</td>
<td>Laurent Bitker</td>
<td>The effect of sepsis on insulinemia and c-peptide levels in critically ill diabetic patients</td>
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<td>Tues31</td>
<td>Laurent Bitker</td>
<td>Performance of urinary cell cycle arrest biomarkers for the prediction of acute kidney injury in critically ill patients</td>
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<td>Tues32</td>
<td>Laurent Bitker</td>
<td>Impact of furosemide on urinary oxygenation in septic shock patients</td>
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<td>Tues33</td>
<td>Fumitaka Yanase</td>
<td>Comparison of the hemodynamic effects of a room temperature and warm 4% albumin fluid bolus after cardiac surgery.</td>
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**Endocrinology and Metabolism**

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<th>Tues34</th>
<th>Audrey Eer</th>
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<tr>
<td>Tues35</td>
<td>Thinn Thinn Khine</td>
<td>Are patients with diabetes at greater risk for contrast induced nephropathy than those without diabetes?</td>
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<tr>
<td>Tues36</td>
<td>Rufi Chen</td>
<td>A randomised controlled trial to assess the effects of initial triple versus sequential therapy on beta cell function in people with newly diagnosed type 2 diabetes</td>
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<td>Tues37</td>
<td>Glen Chiang</td>
<td>Assessing the efficacy of telemedical interventions in older people with diabetes: A systematic review and meta-analysis.</td>
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<td>Tues38</td>
<td>Trish Russell</td>
<td>This abstract is not included at the request of the author</td>
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<td>Tues39</td>
<td>Alastair Anderson</td>
<td>Exercise challenges faced by adults with type 1 diabetes: a cross-sectional study</td>
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<td>Tues40</td>
<td>Xiaofang Wang</td>
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**Infectious Diseases**

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<th>Natasha Holmes</th>
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<td>Rebekah Moran</td>
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<td>Norelle Sherry</td>
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**Medical Imaging**

| Tues52  | Xin Lyn Goh | This abstract is not included at the request of the author |
| Tues53 | Michael Hildebrand | This abstract is not included at the request of the author |
| Tues54 | Linda Dalic | Cortex leads thalamus in tonic seizures of Lennox-Gastaut Syndrome |
| Tues55 | Amy Schneider | The epilepsy phenotypic spectrum associated with a recurrent CUX2 variant |
| Tues56 | Remika Mito | Investigating microstructural heterogeneity of white matter hyperintensities in Alzheimer’s disease using advanced diffusion MRI |
| Tues57 | Karen Borschmann | Brain Repair Requires A Collective Overhaul Of Research Methods: Recommendations From 1st Stroke Recovery and Rehabilitation Roundtable |
| Tues58 | Bronwyn Grinton | This abstract is not included at the request of the author |
| Tues59 | Wasim Khan | Distinct functional properties of the posteromedial cortex reveal aberrant functional connectivity patterns in Alzheimer’s disease |

**Neurosciences**

| Tues60 | Laura Jenkins | This abstract is not included at the request of the author |
| Tues61 | Ian Luk | This abstract is not included at the request of the author |
| Tues62 | Camilla Reehorst | This abstract is not included at the request of the author |
| Tues63 | Nhi Huynh & Chelsea Dumesny | Depletion of PAK1 increases survival via upregulating immune response in mouse pancreatic cancer model. |
| Tues64 | Irvin Ng | This abstract is not included at the request of the author |
| Tues65 | Peter Wookey | This abstract is not included at the request of the author |
| Tues66 | Pathum Thilakasiri | This abstract is not included at the request of the author |
| Tues67 | Terence Low | γδ T Cells as Markers of Immune Engagement in Metastatic Melanoma |
| Tues68 | Stefan Bader | Anti-metastasis therapy via nanoparticle mediated drug delivery |
| Tues69 | Sylvia Hanna | Are contours required for MRI cervical brachytherapy planning? A dosimetric comparison. |
| Tues70 | Adam Parslow | This abstract is not included at the request of the author |
| Tues71 | Wee Loon Ong | Androgen deprivation therapy (ADT) use with post-prostatectomy radiotherapy (PPRT) in the Prostate Cancer Outcomes Registry Victoria (PCOR-Vic) |
| Tues72 | Karen Manley | Symptoms and solutions for cancer patients receiving chemotherapy |
| Tues73 | Karen Manley | Changes in weight, nutritional intake and symptoms in breast cancer patients receiving chemotherapy |

**Oncology**

| Tues74 | Matthew Perich | This abstract is not included at the request of the author |
| Tues75 | Emma Cohen | Introduction of huddles during nursing shifts to promote teamwork, staff development and patient outcomes |

**Nursing**

| Tues76 | Sandra Iuliano | This abstract is not included at the request of the author |

**Nutrition**

| Tues77 | Kayt Macdonald | Impact of the National Disability Insurance Scheme on a spinal outreach service. |
| Tues77A | Leanne Rees | Telehealth - connecting specialist health services to Victorians with spinal cord injury |
| Tues78 | Catherine Cooper | Nerve transfers in Tetraplegia - a worldwide perspective |
| Tues79 | Ruby Lipson-Smith | A framework for stroke rehabilitation facility design: A multi-disciplinary approach |
| Tues80 | Winnie Pei | Use of Polyethylene-Glycol Hydrogel in Novel Stem Cell therapies for Hirschsprung Disease |
### Rheumatology

| Tues81 | Sam Shan | Could CD14+/CD16+ monocyte population be used as a predictor of chronic pain post total knee replacement, adjusting for subclinical fibromyalgia as major confounder? |

### Palliative Care

| Tues82 | Hilary Hodgson | Reducing Falls: It's all in the timing |
| Tues83 | Hilary Hodgson | Implementing a delirium framework into a Palliative Care setting |

### Pathology

| Tues84 | Marsali Newman | Retrospective review of 27 cases reported as low grade serous ovarian carcinoma. |

### Pharmacy

| Tues85 | Amanda Cross | This abstract is not included at the request of the author |
| Tues86 | Claire Keith | Finding the needles in a haystack - automated detection of Adverse Drug Reactions through ICD-10 coding |
| Tues87 | Claire Keith | Imported medicines: a pre-emptive approach to procurement, striving to enhance point-of-care medication safety |
| Tues88 | Claire Keith | Special handling required! Implementing a guideline for hazardous medication handling at a major tertiary hospital |

### Quality

| Tues89 | Melanie Stephenson | To tell or not to tell? How we do open disclosure. |
| Tues90 | Melanie Stephenson | Never wait to escalate! |
| Tues91 | Karen Detering | This abstract is not included at the request of the author |

### Renal

| Tues92 | Marcus Sellars | A case-control study of end-of-life treatment preferences and costs following advance care planning for adults with end stage kidney disease. |

### Respiratory and Sleep Medicine

| Tues93 | Marnie Graco | Burden versus benefit of Continuous Positive Airway Pressure therapy for the treatment of obstructive sleep apnoea in chronic tetraplegia: a mixed methods study. |
| Tues94 | Marnie Graco | Understanding the clinical management of obstructive sleep apnoea (OSA) in tetraplegia: a qualitative study using the theoretical domains framework (TDF). |
| Tues95 | Sang Jin Han | Pulmonary function testing for the early detection of drug-induced lung disease: A systematic review of test accuracy in adults treated with non-chemotherapeutic agents associated with pulmonary toxicity |
| Tues96 | Shamsi Shekari Soleimanloo | This abstract is not included at the request of the author |
| Tues97 | Nicole Sheers | Respiratory function in people with neuromuscular disease: characteristics and association with respiratory tract infection |
| Tues98 | Monica Hatch | Baseline Inflammatory Markers and Survival in Patients with Interstitial Lung Disease |
| Tues99 | Jennifer Cori | This abstract is not included at the request of the author |
| Tues100 | Alex Dobrovic | This abstract is not included at the request of the author |

### Speech Pathology

<p>| Tues101 | Michelle Cimoli | This abstract is not included at the request of the author |
| Tues102 | Michelle Cimoli | This abstract is not included at the request of the author |</p>
<table>
<thead>
<tr>
<th>Tues103</th>
<th>Pith Soh Beh</th>
<th>Smartphone Addiction: The Rise of Whatsapp® and Incessant Work</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tues104</td>
<td>Mat Radojcic</td>
<td>Australian and New Zealand colorectal surgeons in the modern era: the rise of social media</td>
</tr>
<tr>
<td>Tues105</td>
<td>Malachy Feeney</td>
<td>A Systematic Review of Stenting for Bowel Obstruction for Extracolonic Malignancies - a data deficit?</td>
</tr>
<tr>
<td>Tues106</td>
<td>Amanda Nikolic</td>
<td>The Use of Communication Applications in the Australian Health Care System</td>
</tr>
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<td>Tues107</td>
<td>Amanda Nikolic</td>
<td>Internal seton for supravelator Sepsis: An effective technique for complex fistulae</td>
</tr>
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<td>Tues108</td>
<td>Mat Radojcic</td>
<td>Twenty years of research output by Australasian colorectal surgeons; more clinical trials are needed</td>
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<td>Tues109</td>
<td>Creski Gilong</td>
<td>Ethics Applications in Australian Health Services: a novel scoring system</td>
</tr>
<tr>
<td>Tues110</td>
<td>Jason Kong</td>
<td>Efficient Surgical Research Projects - Concept to Completion In 12 weeks</td>
</tr>
<tr>
<td>Tues111</td>
<td>Golnaz Sharafi</td>
<td>The effects of CBD and THC on pancreatic cancer cell proliferation</td>
</tr>
<tr>
<td>Tues112</td>
<td>Nien-Hung Lee</td>
<td>Functions of CXC ligand Family in Pancreatic Cancer</td>
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<td>Tues113</td>
<td>Lai Kwan Soo</td>
<td>Does hypoxia inducible factor - 1 alpha affect the survivability of prostate cancer cells?</td>
</tr>
<tr>
<td>Tues114</td>
<td>Jonathan Tiong</td>
<td>Comparison of Risk factors in Patients Undergoing Mitral Valve Surgery</td>
</tr>
<tr>
<td>Tues115</td>
<td>George Kastrappis</td>
<td>The effect of Renin Angiotensin System (RAS) inhibition on liver regeneration</td>
</tr>
<tr>
<td>Tues116</td>
<td>Georgina E Riddiough</td>
<td>Characterisation of a novel method of colorectal liver metastasis induction in mice</td>
</tr>
<tr>
<td>Tues117</td>
<td>Ernest Cheung</td>
<td>The effects of zinc on ischemia-reperfusion injury in the liver in a global ischemia rat model</td>
</tr>
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<td>Tues118</td>
<td>Dora Vallejo-Ardila</td>
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**Medical Imaging**

<table>
<thead>
<tr>
<th>Tues119</th>
<th>Shiwei Huang</th>
<th>Optimising Resources for Endovascular Clot Retrieval for Acute Ischaemic Stroke: A Discrete-Event Simulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tues120</td>
<td>Goran Mitreski</td>
<td>Audit of routine colonoscopy following an episode of acute diverticulitis diagnosed by CT: What is the value and clinical implications?</td>
</tr>
<tr>
<td>Tues121</td>
<td>Julian Maingard</td>
<td>Endovascular flow-diversion of visceral and renal artery aneurysms using dual-layer braided nitinol carotid (CASPER) stents</td>
</tr>
<tr>
<td>Tues122</td>
<td>Anthony Lamanna</td>
<td>Use of CT and MRI for occult neck of femur fractures: the Austin Health experience</td>
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<tr>
<td>Thurs1</td>
<td>Simon Yates</td>
<td>Preoperative Ordering of HbA1C in Upper Gastrointestinal and Endocrine Surgical Patients</td>
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<td>Thurs2</td>
<td>Annie Xin</td>
<td>Audit of use of sublingual ketamine at Austin Health 2012 - 2017</td>
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<td>Thurs3</td>
<td>Philip Peyton</td>
<td>Intravenous and inhalational anaesthesia and lung ventilation-perfusion matching</td>
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<td>Jefferson Tang</td>
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<td>Thurs5</td>
<td>Kwangtaek Kim</td>
<td>Attitudes of anaesthetists attending the funeral of patients they care for: a cross-sectional survey amongst Australian and New Zealand anaesthetists</td>
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<td>Thurs6</td>
<td>Victor Hui</td>
<td>Analgesia Pathway following Trans Arterial Chemo Embolisation</td>
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<td>Thurs7</td>
<td>Lois Mackley</td>
<td>Intubation in the Emergency Department: do we need to improve and how?</td>
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<td>Thurs8</td>
<td>Angus Pritchard</td>
<td>Rapid Response Team activations after major hip surgery: can we catch you before you fall?</td>
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<tr>
<td>Thurs9</td>
<td>Cheryl Lee</td>
<td>&quot;Rebound Pain&quot; after Interscalene Brachial Plexus Blockade in Shoulder Surgery - How Often, How Bad?</td>
</tr>
<tr>
<td>Thurs10</td>
<td>Kai Wen Leong</td>
<td>Peak serum potassium levels during reperfusion in adult patients undergoing primary cadaveric liver transplantation</td>
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**Cardiology**

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<tr>
<td>Thurs11</td>
<td>Anoop N Koshy</td>
<td>Computed Tomographic Coronary angiography and coronary artery calcium score in perioperative risk stratification prior to noncardiac surgery: A systematic review and meta-analysis</td>
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<td>Thurs12</td>
<td>Thalys Sampaio Rodrigues</td>
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<td>Thurs13</td>
<td>Julian Giovannucci</td>
<td>Assessing the prevalence of familial hypercholesterolaemia in coronary artery disease patients</td>
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<td>Thurs14</td>
<td>Karen Page</td>
<td>Delivery heart failure system change through quality initiatives</td>
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<td>Thurs15</td>
<td>Karen Page</td>
<td>Feasibility of undertaking standardised PROMs in those with heart failure</td>
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<td>Thurs16</td>
<td>Danielle Robinson</td>
<td>Cyclosporin dosing and toxicity and Posaconazole interactions following allogeneic transplantation</td>
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<td>Steven Walker</td>
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<td>Thurs18</td>
<td>Joel Wight</td>
<td>Diffuse large B cell lymphoma (DLBCL) presenting with synchronous CNS and systemic disease at diagnosis: Results from an international collaborative study</td>
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**Critical Care and Emergency Medicine**

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**Endocrinology and Metabolism**

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<tr>
<td>Thurs24</td>
<td>Karen Tan</td>
<td>Association of diabetes and HbA1c with outcomes for people hospitalised with influenza</td>
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**Gastroenterology**

| Thurs25 | Dinali Fernando | Advanced glycation end products (AGEs) derived from diets have more impact on the progression of fatty liver disease than endogenously derived AGEs |
| Thurs26 | Dinali Fernando, | Marination of food with vinegar offers a simple and effective approach to prevent advanced glycation end products (AGEs)-induced NAFLD progression |

**Geriatrics**

| Thurs27 | Joe Wei | Retrospective audit factors associated with falls presentations to the emergency department from residential care facilities |
| Thurs28 | Nan Jordan | Are brain changes found on MRI associated with presence of frailty in a memory clinic? |

**Hepatobiliary**

| Thurs29 | Dona Indu Rajapaksha | Liver directed angiotensin converting enzyme 2 (ACE2) gene therapy for chronic biliary fibrosis and NAFLD |
| Thurs30 | Lakmie Gunarathne | Mas related G-protein coupled receptor type-D (MrgD) is a novel therapeutic target to reduce splanchnic vasodilatation in portal hypertension |
| Thurs31 | Lakmie Gunarathne | Splanchnic vasodilatation is associated with a reduced activity of the classic axis of the renin-angiotensin system in a rat model of non-cirrhotic portal hypertension |
| Thurs32 | Lakmie Gunarathne | Targeting the receptors of the renin-angiotensin system to improve splanchnic vascular resistance in cirrhosis |
| Thurs33 | Samuel (Sam) Grigg | mTOR-inhibitors following liver transplantation for hepatocellular carcinoma: a meta-analysis |

**Infectious Diseases**

| Thurs34 | Sharmila Khumra | Counting the cost of critical antibiotic shortages |

**Medical Imaging**

| Thurs35 | Xiao Chen | Outcome and safety of targeted liver biopsies for indeterminate lesions in patients with chronic liver disease - a single centre experience |
| Thurs36 | David Abbott | Multiband fMRI and simultaneous EEG |
| Thurs37 | Michelle Foo | Australian Students' Perspective on Interventional Radiology Education (ASPIRE): A Prospective Cross-Institutional Study |
| Thurs38 | Suraindra Rajadurai | This abstract is not included at the request of the author |

**Musculoskeletal**

| Thurs39 | Michele Clarke | This abstract is not included at the request of the author |
| Thurs40 | Catherine Said | This abstract is not included at the request of the author |

**Physiotherapy**

| Thurs41 | Jannette Blennerhassett | The demography of patients admitted for stroke rehabilitation has changed |
| Thurs42 | Leona Dowman | Effectiveness of a submaximal cycle test to prescribe cycle based exercise training intensity |

**Respiratory and Sleep Medicine**

<p>| Thurs43 | Leona Dowman | Achieving the minimal important difference following exercise training in interstitial lung disease |
| Thurs44 | Yet Hong Khor | This abstract is not included at the request of the author |</p>
<table>
<thead>
<tr>
<th>Thursday</th>
<th>Name</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thurs45</td>
<td>Lauren Booker</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs46</td>
<td>Melinda Jackson, Maree Barnes, Gerard Kennedy</td>
<td>Psychological Predictors of Adherence to Continuous Positive Airway Pressure in the Treatment of Obstructive Sleep Apnoea</td>
</tr>
<tr>
<td>Thurs47</td>
<td>Elie Gottlieb</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs48</td>
<td>Sarah Curnow</td>
<td>Nurses' clinical risk management of delirium in cardiac surgical patients.</td>
</tr>
<tr>
<td>Thurs49</td>
<td>Karen Sadler</td>
<td>Trial of Arrow® VPS Rhythm® Device with TipTracker™ Technology to Insert Peripherally Inserted Central Catheter</td>
</tr>
<tr>
<td>Thurs50</td>
<td>Lorelle Martin</td>
<td>Barriers to timely STEMI management as reported by paramedics and Triage nurses: a cross-sectional study</td>
</tr>
<tr>
<td>Thurs51</td>
<td>Lorelle Martin</td>
<td>Are the new European Society of Cardiology (ESC) STEMI performance targets feasible?</td>
</tr>
<tr>
<td>Thurs52</td>
<td>Brooke Chapman</td>
<td>Continuous terlipressin infusion improves dietary intake and muscle strength in patients awaiting liver transplantation</td>
</tr>
<tr>
<td>Thurs53</td>
<td>Brooke Chapman</td>
<td>Coffee reduces steatosis in non-alcoholic fatty liver disease</td>
</tr>
<tr>
<td>Thurs54</td>
<td>Katherine Cherry</td>
<td>Are you Sure? Measuring decisional conflict around dialysis treatment choice in patients with End Stage Kidney Disease.</td>
</tr>
<tr>
<td>Thurs55</td>
<td>Jessica Kong</td>
<td>The Effect of Residual Kidney Function on Uraemic Solutes and Symptom Burden in Haemodialysis Patients</td>
</tr>
<tr>
<td>Thurs56</td>
<td>Zhong Yang Li</td>
<td>Incidence and demographics of abnormal eGFR in the Austin Health outpatient population 2012-2017</td>
</tr>
<tr>
<td>Thurs57</td>
<td>Mardiana Lee</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs58</td>
<td>Marcus Sellars</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs59</td>
<td>Rachael Ellis</td>
<td>Increased expression of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase isoforms in urinary exosomes in pre-eclampsia</td>
</tr>
<tr>
<td>Thurs60</td>
<td>Alexandra McCutchan</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs61</td>
<td>Nimita Paul Origanti</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs62</td>
<td>Rebecca Williamson</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs63</td>
<td>Hilary Grover</td>
<td>Factors Influencing Caesarean Section Rate after Induction of Labour in Nulliparous Women</td>
</tr>
<tr>
<td>Thurs64</td>
<td>Caitlyn Nguyen-Ngo</td>
<td>Polphenols as preventatives for gestational diabetes mellitus (GDM)</td>
</tr>
<tr>
<td>Thurs65</td>
<td>Matt Burgess</td>
<td>An audit of genetic testing of minors at the Austin Health Clinical Genetics Service</td>
</tr>
<tr>
<td>Thurs66</td>
<td>Alan Gemmill</td>
<td>Maternal antenatal mood and child development: an exploratory study of treatment effects on child outcomes up to 5 years.</td>
</tr>
<tr>
<td>Thurs68</td>
<td>Emma Peleg</td>
<td>Developing a Spinal Cord Research Hub for all SCI Research Stakeholders</td>
</tr>
<tr>
<td>Thurs69</td>
<td>Asmara Jammali-Blasi</td>
<td>Urine cultures: Let's have a wee think</td>
</tr>
<tr>
<td>Thurs70</td>
<td>Rose Lin</td>
<td>Gamification: A novel approach to improve hand hygiene compliance amongst healthcare workers</td>
</tr>
<tr>
<td>Thurs71</td>
<td>Gemma Skaczkowski</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs72</td>
<td>Gemma Skaczkowski</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs73</td>
<td>Juli Moran</td>
<td>Bridging the gap between hospital and home for older cancer patients</td>
</tr>
<tr>
<td>Thurs74</td>
<td>Juli Moran</td>
<td>Why are residential care residents being admitted to a hospital palliative care unit?</td>
</tr>
<tr>
<td>Thurs75</td>
<td>Juli Moran</td>
<td>Trial of weekend palliative care consult nurses in a hospital without on-call registrars</td>
</tr>
<tr>
<td>Thurs76</td>
<td>Juli Moran</td>
<td>Can a Palliative Care Consultation Service Reduce Health Care Costs?</td>
</tr>
<tr>
<td>Thurs77</td>
<td>Yi Xing</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs78</td>
<td>Zoe Loh</td>
<td>Effect of Reasons for Screen Failure (RFSF) on Standard of Care in Cancer Patients Screened for Clinical Trials</td>
</tr>
<tr>
<td>Thurs79</td>
<td>Anthony Lamanna</td>
<td>Adverse events following TACE - a single centre experience</td>
</tr>
<tr>
<td>Thurs80</td>
<td>Polly Dufton</td>
<td>An evidence-based, nurse-led model of care, to support cancer patients</td>
</tr>
<tr>
<td>Thurs81</td>
<td>Xue Wang</td>
<td>A nurse led symptom and urgent review clinic in the ambulatory cancer care setting</td>
</tr>
<tr>
<td>Thurs82</td>
<td>Angela Mellerick</td>
<td>Symptom and Urgent Review Clinic (SURC) - A nurse led model for patients experiencing toxicities associated with Cancer treatment</td>
</tr>
<tr>
<td>Thurs83</td>
<td>David Williams</td>
<td>Predictive value of mutant TP53 overexpression for response to 5-fluorouracil based chemotherapy in microsatellite stable BRAF wild type colorectal cancers</td>
</tr>
<tr>
<td>Thurs84</td>
<td>Puey Ling Chia</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs85</td>
<td>Kai Wang</td>
<td>All-trans retinoic acid inhibits pancreatic cancer growth and enhances gemcitabine sensitivity by down-regulation of PAK</td>
</tr>
<tr>
<td>Thurs86</td>
<td>Robin Anderson</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs87</td>
<td>Riley Morrow</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs88</td>
<td>Mariah Alorro</td>
<td>Systemic and Non-Tumoural Stat3 Inhibition Restricts Gastrointestinal Tumour Growth in Mice</td>
</tr>
<tr>
<td>Thurs89</td>
<td>Janson Tse</td>
<td>MicroRNA-21 mediates Stat3-dependent gastric tumourigenesis.</td>
</tr>
<tr>
<td>Thurs90</td>
<td>Jennifer Huynh</td>
<td>IL-11 as a therapeutic target to treat colorectal cancer</td>
</tr>
<tr>
<td>Thurs91</td>
<td>Aadya Nagpal</td>
<td>Evaluation of Neratinib efficacy and mechanisms of resistance in a new syngeneic model of spontaneous breast cancer brain metastasis</td>
</tr>
<tr>
<td>Thurs92</td>
<td>Farshad Foroudi</td>
<td>Assessment of urinary bladder motion and bladder cancer location using cine Magnetic Resonance Imaging (cineMRI)</td>
</tr>
<tr>
<td>Thurs93</td>
<td>Sharon Tran</td>
<td>The Role of Beclin1 in Gastrointestinal Health and Disease</td>
</tr>
<tr>
<td>Thurs94</td>
<td>Jessica Da Gama Duarte</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs95</td>
<td>Surein Arulananda</td>
<td>Targeting cell survival pathways in malignant mesothelioma</td>
</tr>
<tr>
<td>Thurs96</td>
<td>Surein Arulananda</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs97</td>
<td>Robert O'Donoghue</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs98</td>
<td>Sean Macdonald</td>
<td>This abstract is not included at the request of the author</td>
</tr>
<tr>
<td>Thurs99</td>
<td>Jean Berthelet</td>
<td>Investigating the cellular and molecular basis of metastatic heterogeneity in triple negative breast cancer.</td>
</tr>
<tr>
<td>Thurs100</td>
<td>Kelly Tran</td>
<td>This abstract is not included at the request of the author</td>
</tr>
</tbody>
</table>
### Oncology

| Thurs101 | Simone Ostrouska | This abstract is not included at the request of the author |
| Thurs102 | Dani Tutuka | PLX8394, a New Generation BRAF Inhibitor, Selectively Inhibits BRAF in Colonic Adenocarcinoma Cells and Prevents Paradoxical MAPK Pathway Activation |
| Thurs103 | Jason Wasiak | Surveying retracted studies and notices within the field of radiation oncology |
| Thurs104 | Drew Smith | This abstract is not included at the request of the author |

### Neurosciences

| Thurs105 | Magdalena Kowalczyk | This abstract is not included at the request of the author |
| Thurs106 | Magdalena Kowalczyk | This abstract is not included at the request of the author |
| Thurs107 | Chris Tailby | This abstract is not included at the request of the author |
| Thurs108 | Carolina Restrepo | This abstract is not included at the request of the author |
| Thurs109 | David Vaughan | Olfactory fMRI can reveal lateralised dysfunction of Piriform Cortex in Temporal Lobe Epilepsy |
| Thurs110 | Nicholas Crump | A Retrospective Study of Patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): Identifying Ultrasonographic Features for Diagnosis and Prognosis |
| Thurs111 | Julian Maingard | CODE STROKE ALERT - Development of a new open-source platform to streamline acute stroke care |
| Thurs112 | Mangor Pedersen | This abstract is not included at the request of the author |
| Thurs113 | Mohamed Salah Khliif | Medial temporal lobe atrophy in ischaemic stroke patients is modulated by presence of the apolipoprotein E (APOE) epsilon-4 (ε4) allele |
| Thurs114 | Rosemary Burgess | Epilepsy of Infancy with Migrating Focal Seizures: a genetically heterogeneous developmental and epileptic encephalopathy |
| Thurs115 | John Damiano | This abstract is not included at the request of the author |
| Thurs116 | Laura Bird | This abstract is not included at the request of the author |
| Thurs117 | Laura Bird | This abstract is not included at the request of the author |
| Thurs118 | Dhamidhu Eratne | Utility of Whole Exome Sequencing in Complex Neurologic and Neurodegenerative Disorders |
| Thurs119 | Venesha Rethnam | This abstract is not included at the request of the author |
| Thurs120 | Donna Parker | This abstract is not included at the request of the author |
| Thurs121 | Stephen Cain | Factors associated with stroke survivors' return to work in A Very Early Rehabilitation Trial (AVERT) |
| Thurs122 | Sarah Calvert | This abstract is not included at the request of the author |
Acute pericarditis – a rare complication of *Plasmodium falciparum* malaria.

We describe a case of pericarditis secondary to *P. falciparum* malaria, which has only been described a handful of times before in the world literature. A 67-year-old male presented with a 7-day history of fevers, headache, malaise and positional chest pain after returning from rural Ghana. Blood film revealed early trophozoites characteristic of *Plasmodium falciparum* with 3.09% parasitaemia. Initial ECG showed widespread ST elevation. Serial troponin-T results were static at 5ng/L. Chest radiography showed no evidence of effusions or cardiomegaly. Transthoracic echocardiography demonstrated normal ventricular function and trivial pericardial effusion without evidence of tamponade. Other complications of malaria included mild acute kidney injury and a laboratory diagnosis of disseminated intravascular coagulation with profound thrombocytopenia (platelet nadir 14), elevated fibrinogen and prolonged international normalised ratio, without bleeding events. Treatment was commenced with a 72-hour course of intravenous artesunate, followed by a 60-hour course of oral artemether + lumefantrine with full resolution of fevers and parasitaemia. Colchicine was commenced, but non-steroidal anti-inflammatories were withheld due to thrombocytopenia. Chest pain, thrombocytopenia, and acute kidney injury improved with treatment. Pericarditis complicating malarial infection has been described, but never in an Australian patient. This case highlights a rare and fascinating cardiac manifestation of malaria.

Authors: O’Brien JM, Sutherland N, Meher-Homji Z, Jones E, Chua KYL.
Gender specific findings among patients admitted to the Emergency Department (ED) with Atrial Fibrillation (AF).

**Background and Methods.** Gender differences have been reported in the management of common cardiac conditions. Under-treatment with oral anticoagulants has previously been reported among women with AF. We looked for gender-specific differences in clinical characteristics and management of 661 patients presenting to our ED with AF (DRG I48.9) in 2016. The cohort containe 352 women and 309 men.

**Findings.** Clinical characteristics and therapies are tabulated.

<table>
<thead>
<tr>
<th>n = 661</th>
<th>M</th>
<th>F</th>
<th>Univariate P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63 ± 15</td>
<td>74 ± 12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>171 (55%)</td>
<td>244 (69%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>128 ± 22</td>
<td>133 ± 24</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CHA2DS2VASc</td>
<td>1.8 ± 1.6</td>
<td>3.5 ± 16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ED Cardioversion</td>
<td>79 (26%)</td>
<td>44 (13%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>44 (14%)</td>
<td>24 (7%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Digoxin/Calcium Channel Blocker (CCB)</td>
<td>13 (4%) / 6 (2%)</td>
<td>40 (11%) / 11 (6%)</td>
<td>both 0.001</td>
</tr>
<tr>
<td>Mean length of stay</td>
<td>1.4 ± 2.9 days</td>
<td>1.6 ± 2.9 days</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Although women were older and more frequently hypertensive, the incidence of diabetes, previous stroke and other cardiovascular co-morbidities did not differ between groups. Beta blockers were used in 68% (no gender difference) but rhythm control with amiodarone was utilised more often in males. Logistic regression analysis identified age and HR>100 as predictors of DCR (both p<0.001) but gender was not an independent predictor of DCR or rhythm control therapies.

**Conclusion.** In this cohort, baseline clinical variables especially age, appeared to be the principal determinants of most management outcomes.
Multiple stroke prophylaxis ‘treatment gaps’ identified in the management of atrial fibrillation.

**Background:** International experience is that among patients with atrial fibrillation (AF), stroke prophylaxis with oral anticoagulant (OAC) medications is often omitted and in some, mono-antiplatelet therapy (MAPT) is utilized inappropriately.

**Methods:** Patients presenting to the Emergency Department in 2016 with a primary diagnosis of AF (I48.9) were stratified according to thromboembolic risk. Increased risk was defined as a CHA2DS2VASc score ≥1 for men ≥2 in women. Treatments for 548 patients were determined at discharge, and at 12±3 months follow-up.

**Results:** Thirty two percent of patients at low-risk received OACs at discharge. Treatment assignments among patients at high risk are tabulated.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Discharge</th>
<th>Follow-up</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOAC</td>
<td>44.0%</td>
<td>52.3%</td>
<td>0.01</td>
</tr>
<tr>
<td>VKA</td>
<td>14.5%</td>
<td>13.6%</td>
<td>NS</td>
</tr>
<tr>
<td>DOAC or VKA</td>
<td>58.5%</td>
<td>65.9%</td>
<td>0.01</td>
</tr>
<tr>
<td>New OAC</td>
<td>21.5%</td>
<td>15.2%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>MAPT only</td>
<td>29.9%</td>
<td>24.4%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>No therapy</td>
<td>11.6%</td>
<td>19.7%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** In line with current literature, we found that a small number of low risk patients receive OACs outside current guidelines. Among those at increased risk; approximately 60% of patients were discharged on OACs and 30% at increased risk received MAPT in lieu of OACs. A small but significant number of patients received no MAPT or OAC. We have identified two treatment gaps in our cohort; patients at increased risk who do not receive OACs, and patients who receive MAPT instead of guideline-mandated OACs; these gaps contribute to an ongoing risk of ischaemic stroke. Although some favourable prescribing trends were observed at follow-up, significant gaps persist. Hospital discharge appears to be a key influencing point in patient management and specifically, in optimizing stroke prophylaxis.

Authors: O’Brien JM, Martin L, Judkins S, Yeoh M, Chan T, Taylor D, Horrigan MCG.
Heart rate and blood pressure as predictors of hospital length of stay in patients presenting to the Emergency Department with atrial fibrillation.

**Background:** Despite established management guidelines for atrial fibrillation (AF), practices vary widely. In some centres, management of uncomplicated AF is predominantly outpatient while in others, hospital length of stay (LOS) remains significant. Anecdotal experience suggests that heart rate (HR) often has a disproportionate effect on medical decision-making among patients with AF.

**Methods:** In 2016 Austin Health Emergency Department (ED) assessed 662 patients with a primary diagnosis of AF (DRG I48.9). Using coding inputs, 509 consecutive ED presentations with complete data for analysis were identified. The interaction of HR and systolic blood pressure (SBP) on hospital LOS was analysed using a standard, non-parametric technique.

**Results:** Table showing interaction of HR, SBP, and LOS.

<table>
<thead>
<tr>
<th>Total LOS (days)</th>
<th>SBP &lt; 110mmHg (n = 79)</th>
<th>SBP ≥ 110mmHg (n = 430)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 509</td>
<td>LOS: 2.3 ± 3.7 days</td>
<td>LOS: 1.4 ± 2.8 days</td>
</tr>
<tr>
<td>HR &lt; 100bpm</td>
<td>(n = 13)</td>
<td>(n = 105)</td>
</tr>
<tr>
<td>LOS: 1.0 ± 2.1 days</td>
<td>LOS: 3.1 ± 4.8 days (p = 0.26)</td>
<td>LOS: 0.7 ± 1.5 days (p &lt; 0.001)</td>
</tr>
<tr>
<td>HR ≥ 100bpm</td>
<td>(n = 66)</td>
<td>(n = 325)</td>
</tr>
<tr>
<td>LOS: 1.7 ± 3.2 days</td>
<td>LOS: 2.1 ± 3.4 days (p &lt; 0.01)</td>
<td>LOS: 1.7 ± 3.1 days (p &lt; 0.001)</td>
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</table>

The majority of patients (84%) were normotensive, but their total LOS exceeded 33 hours. Normotensive patients (SBP > 110mmHg) with HR >100bpm had an average LOS of over 40 hours.

**Conclusion:** Heart rate appears more influential than haemodynamic stability in determining LOS among patients with AF. A shift in focus from HR to haemodynamics could facilitate earlier discharge, improving efficiency and access to services.
The role of appropriate advanced care directives in patients with pulmonary hypertension.

**Background:** Despite advances in the cardiovascular management of pulmonary hypertension (PHT), mortality remains high. Analysis of the REVEAL Registry\(^1\) demonstrated 68% 5-year mortality after diagnosis at right heart catheterisation. Advanced care directives (ACDs) are advised for all people living with chronic illness but are especially relevant to those with poor long-term prognosis.

**Methods:** An audit of the electronic medical records of all current patients under the care of the Pulmonary Hypertension Service at Austin Health was conducted.

**Results:** There were 105 patients in the audit. Patients from all five groups within the World Health Organisation clinical classification system for PHT were included. The median age was 71 years (IQR = 60-75) with 28 males and 77 females. Eight patients (7.7%) had an ACD – five people being treated with a pulmonary vasodilator, and three under guideline-mandated surveillance.

**Conclusion:** Despite a multidisciplinary approach with input from Cardiologists, Respiratory Physicians, Rheumatologists, and General Practitioners, we found only a small fraction of patients living with PHT had an ACD. As a specialist service, we should provide a standardised, embedded process as routine care, in keeping with the recommendations outlined in the Medical Treatment Planning and Decisions Act 2016. It is hoped that this data is a reminder to ours and similar services to improve our ability to counsel and support our patients through their illness trajectory and empower them to be active and informed participants in their own healthcare.

**References:**

Prevalence of elevated lipoprotein(a) in premature coronary artery disease patients

1. Austin Health
2. The University of Melbourne

Aim
Elevated lipoprotein(a) (Lp(a)) is an inherited lipid disorder and an independent risk factor for cardiovascular disease. Although its prevalence in the general population has been well-established, the prevalence of elevated Lp(a) in patients with premature coronary artery disease (CAD) remains to be defined. In this study, we hypothesized that there is an over-representation of elevated Lp(a) in patients with early-onset CAD compared to the general population.

Methods
We screened consecutive patients aged ≤ 70 years who presented to the Austin Hospital with any of the following criteria: (1) acute coronary syndrome (ACS); (2) percutaneous coronary intervention; or (3) coronary artery bypass grafting between February 6 and June 8, 2018. Elevated Lp(a) was defined as concentrations ≥ 0.5 g/L. Patients with excess Lp(a) were also screened for other cardiovascular risk factors including hypertension, type 2 diabetes mellitus, and familial hypercholesterolemia (FH) using the Dutch Lipid Clinic Network Criteria.

Results
158 patients were screened; 63 (39.9%) were under 60 years of age. Overall, elevated Lp(a) was identified in 53 patients (36.1%). Of these, 9 patients (17%) also had probable or definite FH.

Conclusion
Elevated Lp(a) is more prevalent in patients with premature CAD compared to the general population and may contribute to previously unappreciated residual cardiovascular risk. Patients who present with early-onset CAD should be routinely screened for elevated Lp(a) as it may have implications on the management of their cardiovascular risk.
Background
Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with significant morbidity and mortality. Postoperative AF has been increasingly identified in non-cardiac surgical patients as a poor prognostic marker. Liver transplantation (LT) outcomes have improved in last 2 decades but cardiovascular complications remain the leading cause of death.1 This is primarily due to the complexity of operation and haemodynamic shifts, which occur intraoperatively. Therefore, LT candidates undergo perioperative cardiac workup. The impact of postoperative AF in LT patients is largely unknown.

Aims
Our aim was to look at the prevalence of AF and postoperative complications.

Methods
A retrospective analysis of all the patients who underwent liver transplantation between 2011-2016. Major adverse cardiac event (MACE) was defined as postoperative acute coronary syndrome, arrhythmias or pulmonary oedema/heart failure. Non-cardiac complications including bleeding (needing blood transfusion), acute kidney impairment (dialysis dependent) or rejection were also assessed.

Results
249 patients underwent LT, of which 3.6% had pre-existing and 10% had postoperative AF. The AF population was significantly older with a higher prevalence of Diabetes (Table 1). MACE was recorded in 8/248 patients (Figure 1); 4 of these had either pre-existing (1/4) or new (3/4) AF. 56% of patients who had AF in perioperative phase also had non-cardiac postoperative complications. 28% of new AF patients were discharged on anticoagulation while 1 patient (not anticoagulated) re-presented with acute stroke within a year of transplantation.

Conclusion
AF occurs in approximately 10% of patients undergoing LT and is associated with increased cardiovascular morbidity and postoperative complications. Further evidence is necessary to guide anticoagulation in postoperative AF in LT patients.
Case Study: Unique presentation of coronary artery fistula with infective endocarditis in the setting of a previous penetrating chest injury

Presentation: A 56-year-old man was admitted with a 6-week history of fevers and constitutional symptoms. Following extensive investigation, a diagnosis of aortic valve endocarditis with associated severe aortic regurgitation was made. He was incidentally found to have a coronary fistula communicating between the left anterior descending artery and the right ventricle. This was identified on pre-operative angiography prior to aortic valve replacement. There was a history of a motorcycle accident 39 years ago at which time he sustained a penetrating injury to the anterior chest wall with cardiac trauma and tracheal perforation requiring sternotomy, thoracotomy and the construction of an artificial trachea.

Findings: Enterococcus faecalis was isolated from blood cultures and vegetations on the aortic valve were identified on echocardiogram. Evidence of a severely dilated left main coronary artery on echocardiogram raised the suspicion of a coronary artery aneurysm. An angiogram was undertaken as part of the preoperative workup prior to aortic valve replacement in order to exclude significant coronary artery disease. The left anterior descending artery was a large calibre, aneurysmal and tortuous vessel which drained into the right ventricle, creating a left to right shunt. The distal LAD was collateralised by the distal right coronary artery. The patient subsequently underwent aortic valve replacement with ligation of the fistula and coronary artery bypass grafting of the LAD.

Conclusion: This is a dramatic and rare case of an acquired coronary fistula likely from previously unrecognised traumatic coronary rupture more than 30 yrs ago.
Clinical Outcomes of Patients with Established Coronary Artery Disease Presenting with Acute Coronary Syndromes

**Background:** The risk of major adverse cardiovascular events remains high in patients with established coronary artery disease (CAD). As survival post myocardial infarction (MI) improves, the population of patients with established CAD will increase and management should be aimed at the prevention of recurrent cardiac events. The prognostic significance of established CAD in patients who present with acute coronary syndromes (ACS) has not been fully explored in contemporary literature.

**Methods:** Consecutive patients from the Melbourne Interventional Group registry who presented with ACS and underwent percutaneous coronary intervention (PCI) between 2005 and 2015 were included. Patients with a history of MI, PCI or coronary artery bypass surgery were included in the established CAD cohort. The primary endpoints were 12-month mortality and 12-month major adverse cardiac and cerebrovascular events (MACCE).

**Results:** Of the 12,878 ACS patients included in our study, 3542 (28%) patients had established CAD and 9336 (72%) patients had de novo CAD. Over the 10-year study period, the proportion of patients presenting with established CAD decreased (30.7% to 25.2%) with a corresponding increase in the proportion of patients with de novo CAD (69.3% to 74.8%) (p-for-overall-trend<0.001). NSTEMI was the most prominent presentation in the established CAD cohort (45.1%), followed by STEMI (29.6%) and UA (25.3%). STEMI was most prominent in the de novo CAD cohort (51%), followed by NSTEMI (39.9%) and UA (9.1%) (p-value for trend <0.001). The patients in the established CAD cohort were older, had more co-morbidities and were more likely to present with high risk features such as atrial fibrillation, left main disease, multi-vessel CAD and LV dysfunction (all p<0.001). Regarding revascularisation in STEMI presentations, symptom-to-door time was shorter, whereas DTBT was longer in those with established CAD (p<0.001). On multivariate analysis, established CAD was an independent risk factor for 12-month MACCE (OR 1.40, 95% CI 1.23-1.58, p<0.001), but not for 12-month mortality (OR 1.08, 95% CI 0.77-1.52, p=0.66).

**Conclusion:** Patients with a history of myocardial infarction or previous revascularisation, whether surgical or percutaneous, have a higher rate of major cardiovascular events at 12 months. Despite this, they do not appear to suffer from higher mortality. Further studies are needed to identify modifiable factors which contribute to recurrent cardiovascular events.
Clinical Characteristics of Patients with Stable Coronary Artery Disease Undergoing Angiography by Trans-femoral versus Trans-radial Approach

Background: The benefits associated with trans-radial coronary angiography (TR-CA) and percutaneous coronary intervention in patients with acute coronary syndromes has not been replicated in those with stable CAD. Furthermore, TR-CA may cause structural injury to the radial artery making it an unattractive conduit for bypass graft surgery.

Aims: We aim to describe clinical characteristics of patients with stable CAD undergoing trans-radial vs trans-femoral angiography and to identify variables likely to result in coronary artery bypass surgery (CABG).

Methods: Patients undergoing elective angiography for stable CAD between August and November 2017 at a major tertiary centre were included. Clinical characteristics, stress test findings and angiogram results were collected and stratified by access for angiography (radial vs femoral).

Results: Of the 199 patients included, 133 (67%) underwent TR-CA. 51 (26%) patients underwent PCI, 25 (13%) underwent bypass surgery and 123 (62%) were treated medically. There was no difference in baseline clinical characteristics (including diabetes; 40% vs. 35%, p=0.5) or rates of a positive stress test (16.6% vs 19.7%, p=0.63) between patients undergoing radial or femoral access angiography. In patients undergoing TR-CA, there was a trend towards lower rates of patients ultimately treated with coronary artery bypass surgery (9.8% vs 18.2%, p=0.09). There was a significantly higher proportion of diabetics who ultimately underwent bypass surgery (60% vs. 35%, p=0.02).

Conclusion: In patients with stable CAD, only a minority of patients are treated with bypass surgery. The only clinical characteristic associated with higher rates of bypass surgery is diabetes mellitus. Thus in this patient population, transfemoral access may be considered to preserve the radial artery as a possible bypass conduit.
Dobutamine Stress Echocardiography Compared With Coronary CT Angiography in Screening For Coronary Artery Disease in End Stage Liver Disease Patients Being Assessed for Liver Transplantation

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5. Liver Transplant Unit, Austin Health, Melbourne

BACKGROUND:
Patients with end stage liver disease (ESLD) and concomitant coronary artery disease (CAD) are at increased perioperative risk during liver transplantation. Both non-invasive functional imaging with dobutamine stress echocardiography (DSE) and non-invasive anatomical imaging with computed tomography coronary angiography (CTCA) are used to screen for CAD in potential liver transplant candidates, but their effect on perioperative management and outcomes in this population is unclear.

PURPOSE:
To compare DSE with CTCA for detection of severe CAD in patients with ESLD, and to determine their effect on perioperative management and outcomes.

METHODS:
161 consecutive ESLD patients who underwent both DSE and CTCA during evaluation for liver transplantation were analysed retrospectively. Positive DSE was defined as new regional wall motion abnormality on stress. Severe CAD on CTCA, and on subsequent invasive coronary angiography (ICA) if performed, was defined as ≥70% stenosis. Moderate CAD was defined as 50-69% stenosis.

RESULTS:
Patient characteristics included: mean age 61 years; male 81%; hypertension 63%; type 2 diabetes 54%; hypercholesterolemia 27%; smoking 11%; family history of premature CAD 4%. DSE was positive in 4 patients (2.5%). Of these, subsequent CTCA or ICA showed minimal CAD in 2, moderate CAD in 1 (managed medically) and severe CAD in 1. CTCA showed severe CAD in 13 patients (8.1%). Of these, subsequent ICA showed moderate CAD in 10 (managed medically) and severe CAD in 3. All 3 patients with severe CAD (1.8%) underwent coronary revascularisation (2 percutaneous, 1 surgical) before liver transplantation. Revascularisation was predicted by CTCA in all 3 patients, but by DSE in only 1.

CONCLUSION:
Severe CAD requiring revascularisation is infrequently detected in selected liver transplant candidates despite a high prevalence of coronary risk factors. Preoperative anatomical imaging with CTCA may be the preferred method of screening for CAD in this population.
The Role Of Dobutamine Stress Echo In Predicting Outcomes In Subjects Being Assessed For Liver Transplantation

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BACKGROUND:
Patients with end stage liver disease (ESLD) and coronary artery disease (CAD) are at increased perioperative risk during liver transplantation. Dobutamine stress echocardiography (DSE) is commonly used to predict major adverse cardiac events (MACE) in potential liver transplant candidates, but its effect on perioperative management and outcomes is unclear.

PURPOSE:
To determine the effect of DSE on perioperative management of patients with ESLD, and prediction of perioperative MACE in transplant recipients.

METHODS:
560 consecutive ESLD patients who underwent DSE during evaluation for liver transplantation (2010-2017) were analysed retrospectively of which 319 became transplant recipients. Positive DSE was defined as new regional wall motion abnormality on stress. Severe CAD on subsequent invasive coronary angiography (ICA) was defined as ≥70% stenosis. Usefulness of DSE was evaluated in predicting perioperative (within 30 days) MACE (myocardial infarction, cardiac death, cardiac arrest)

RESULTS:
Of 560 ESLD patients, mean age was 56 years; 75% were male. DSE was positive in 21 patients (4%). Of these, severe CAD was confirmed in 6; of whom 1 received same-day liver transplantation and surgical revascularisation. 9 patients with positive DSE and 296 with negative DSE underwent transplantation without MACE. MACE occurred in 14 transplant recipients (4%), all with negative DSE.

CONCLUSION:
Positive DSE leads to changes in perioperative management in a small proportion of potential liver transplant candidates. Negative DSE predicts absence of MACE in 96% of transplant recipients. DSE remains useful for risk stratification in this population.
Development and implementation of an algorithm to manage mucositis pain in patients post autologous and allogeneic stem cell transplant

Aim
The aim of this poster is to describe the development and implementation of an algorithm purposefully designed for the management of mucositis pain post autologous and allogeneic stem cell transplant on pain assessment, prescribing practices and patient pain outcomes.

Evidence from clinical practice highlighted that the management of mucositis pain in patients undergoing stem cell transplantation for a haematological disease is frequently suboptimal. There is a paucity of evidence specific to the management of mucositis pain in the extant literature despite acknowledgement that in addition to causing significant pain, mucositis frequently impacts patient's nutrition and length of stay.

Methods
An assessment and treatment algorithm for mucositis was developed using the literature and expert consensus from the anaesthetic and haematology units at Austin Health. The algorithm provides guidance for the assessment, prescription, and administration analgesics from the onset of mouth pain to the resolution of pain.

A longitudinal, multi-method design including patient survey and medical record audit will used to evaluate the efficacy of the algorithm.

Results
The algorithm has been implemented into practice. The preliminary findings indicate improved:

1) consistency in prescribing practices
2) understanding of mucositis management by nursing staff in both the haematology and acute pain services teams
3) processes for responding to patients’ pain.

Conclusion
This study has highlighted the significant benefit of multidisciplinary, multi-unit collaboration in both the development and implementation of a consensus based algorithm on the pain outcomes for patients post stem cell transplant experiencing mucositis.
Rigano J¹, Pett M¹, Hogan CJ¹

Evaluation of the automated HemosIL® AcuStar HIT IgG chemiluminescent immunoassay for the diagnosis of heparin-induced thrombocytopenia

1. Haematology Department, Austin Health, Heidelberg, Victoria, Australia

Aim
Heparin-induced thrombocytopenia (HIT) is a severe complication of heparin therapy, due to IgG antibodies binding to platelet factor 4 (PF4) and heparin complexes. These complexes cause platelet activation and subsequent aggregation, contributing to venous and arterial thromboses. Diagnosis includes the 4T score, based on clinical presentation and laboratory findings. This study compared the AcuStar HIT IgG chemiluminescent immunoassay with the established HPIA IgG ELISA and STic Expert® HIT methods.

Method
The HemosIL® AcuStar HIT IgG chemiluminescent immunoassay detects IgG antibodies directed against PF4 when complexed with heparin. Magnetic particles, coated with PF4 and complexed to polyvinyl sulfonate, capture PF4-Heparin (PF4-H) antibodies. Added isoluminal-labelled anti-human IgG antibody tracer subsequently binds to the PF4-H antibodies, and a luminescent reaction is initiated by the addition of a trigger reagent. Emitted light is measured optically as relative light units and is directly proportional to the PF4-H IgG antibody concentration. AcuStar HIT IgG was performed on thawed citrated platelet poor plasma stored at -80°C, from patients who had previously been tested for IgG PF4-H antibodies using HPIA IgG ELISA and STic Expert® HIT assays. Results obtained from the confirmatory serotonin release functional assay (SRA) were also evaluated.

Results
34 patients were tested (21 positive and 13 negative by ELISA) using the AcuStar HIT IgG assay with a sensitivity and specificity of 90% and 100% respectively. Sensitivity is further improved by optimising the diagnostic cut-off provided by the manufacturer. The automated AcuStar produced a result in approximately 40 minutes, compared to 4 hours using the manual ELISA technique.

Conclusion
The AcuStar HIT IgG assay is diagnostically comparable to the HPIA IgG ELISA method. However, the AcuStar assay has the added benefit of a decreased cost per test with a reduction in workload and result turnaround time.
Dowell E¹, Kolar D¹, Rigano J¹, Hogan C¹

Validation of the Lamson pneumatic tube system for the transportation of blood components from Blood Bank to Intensive Care and Ambulatory Care

1. Blood Bank Department, Austin Health, Heidelberg, Victoria, Australia

Aim
The Lamson pneumatic tube system (PTS) utilises pressure and vacuum suction to transport carriers through a network of pipes from one location to another. The air-flow within the system is generated by blowers which control the speed of the carriers through the pipes. This validation focused on the suitability for the safe and timely transportation of blood components by the PTS from Blood Bank to the Intensive Care Unit (ICU) and Ambulatory Care Centre (ACC). Validation of a PTS is a National Pathology Accreditation Advisory Council (NPACC) requirement.

Method
Blood components routinely prepared and issued by the Blood Bank were tested. These included packed red blood cells (PRBC), fresh frozen plasma (FFP), extended life plasma (ELP), cryoprecipitate and platelets. The effect of the inherent nature of the PTS on blood components was evaluated as well as appropriate transit time and intended destination. Blood components were subjected to physical and laboratory testing pre and post PTS transportation.

Results
Post transportation, the PTS had no effect on blood components when visually inspected. Transit times and temperatures of the carriers and all blood components were within acceptable ranges. All carriers arrived at their intended destination. There was no significant change in the platelet count or the platelet function of the platelets and the degree of haemolysis in PRBC was below the TGA requirement.

Conclusion
This validation has determined that the Lamson PTS is suitable for the safe and timely transportation of blood components from Blood Bank to ICU and ACC.
Rigano J\textsuperscript{1}, Ng C\textsuperscript{2}, Nandurkar H\textsuperscript{3}, Lim H\textsuperscript{2,3}, Ho P\textsuperscript{2}

P-selectin as a marker of cardiovascular risk in normal controls and myeloproliferative neoplasm

1. Haematology Laboratory, Austin Health, Heidelberg, Victoria, Australia;
2. Clinical Haematology, Northern Health, Epping, Victoria, Australia;
3. Australian Centre for Blood Diseases, Monash University, Melbourne, Australia

Aim
P-selectin is an adhesion molecule secreted both by the endothelium and platelets and has been shown to be higher in patients with cardiovascular risk factors. Given its role in inflammation and thrombogenesis, we evaluated its role in normal controls and those with myeloproliferative neoplasm (MPN).

Methods
Normal controls, without history of cardiovascular disease or thrombotic disease, and patients with MPN were recruited. Thromboelastography (TEG) was performed on whole blood while the remaining global coagulation assays (calibrated automated thrombogram (CAT), overall haemostatic potential (OHP) and P-selectin) were performed on thawed double-centrifuged, platelet poor plasma previously stored at -80°C.

Results
Eighty-nine normal controls (59 females, 30 males) and 37 MPN patients (20 females, 17 males) were recruited. MPN patients had markedly higher median P-selectin levels (109 vs 49 ng/mL, p<0.01) with higher platelet counts (p<0.01). Higher P-selectin levels were associated with decreased vWF activity (74% vs 101%, p=0.04) and factor VIII levels (91% vs 123%, p=0.02). No differences were seen in global coagulation assays. In normal controls, higher P-selectin is associated raised LDL and triglycerides and older age. CAT parameters were lower with reduced velocity index and thrombin peak.

Conclusion
P-selectin is markedly higher in MPN patients and is likely related to increased platelet secretion, however, this did not impact global coagulation assays and is associated with decreased vWF activity and factor VIII levels. In normal controls, higher P-selectin is associated with poor lipid profile, older age and male sex, and could serve as a marker of cardiovascular risk.
Determination of the best early warning scores to predict important outcomes among emergency department patients

1. University of Melbourne
2. Austin Hospital

Aim

Early warning scores (EWS), based largely on emergency department (ED) patient physiological data, aim to identify patients at risk of adverse outcomes. However, the best EWS are unknown. We aimed to directly compare 13 EWS to determine which best predicts admission to hospital and ICU, significant clinical deterioration (MET call/Code Blue) and mortality at 2 days.

Method

We undertook a prospective cohort study in a tertiary referral ED. Consecutive adult patients in the ED cubicles were enrolled and their EWS scores calculated. Outcome data were extracted from the medical record after 28 days. Area under the Receiver Operator Characteristic curve (AUROC) evaluated the predictive ability of each EWS for the outcomes of interest.

Results

Of 1730 patients enrolled, 690 were admitted. All EWS poorly predicted admission and significant deterioration at 2 days (Table). Only the Worthing Score was fairly predictive of ICU admission at 2 days. Most EWS were good/excellent predictors of mortality at 2 days.

Conclusion

The usefulness of EWS for most outcomes is limited. However, many EWS are highly predictive of mortality at 2 days. VitalPAC scores could be automatically calculated from electronic data to flag patients at risk of death. This will inform their optimal care and may change patient management.

Table. AUROC values for admission and outcomes at 2 days

<table>
<thead>
<tr>
<th>early warning score</th>
<th>admission</th>
<th>ICU</th>
<th>deterioration</th>
<th>mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>VitalPAC</td>
<td>0.68</td>
<td>0.69</td>
<td>0.65</td>
<td>0.96</td>
</tr>
<tr>
<td>National</td>
<td>0.68</td>
<td>0.69</td>
<td>0.65</td>
<td>0.95</td>
</tr>
<tr>
<td>Abbreviated</td>
<td>0.68</td>
<td>0.69</td>
<td>0.64</td>
<td>0.95</td>
</tr>
<tr>
<td>VitalPac Worthing</td>
<td>0.68</td>
<td>0.72</td>
<td>0.66</td>
<td>0.90</td>
</tr>
<tr>
<td>all others (range)</td>
<td>0.51-0.68</td>
<td>0.51-0.70</td>
<td>0.54-0.70</td>
<td>0.62-0.91</td>
</tr>
</tbody>
</table>

References:

Patient perceptions of participation in emergency medicine research projects

1. University of Melbourne
2. Austin Hospital

Aim
Emergency Department (ED) research is difficult with many unwell patients. It should be informed by patient perceptions and expectations. We aimed to determine patient perceptions of ED research and their expectations for consent, privacy, and barriers/enablers

Method
We conducted a cross-sectional survey in a tertiary hospital ED. A convenience sample of adults was enrolled (February-June, 2018). Patients with communication/reading difficulties or severe illness were excluded. The questionnaire was project-designed, based upon medical literature, and trialled on patients before use.

Results
315 (87%) of 363 invited patients participated (males 52%, aged 41-65 years 47%). Overall, patients perceived ED research favorably and that consent was important (Table). Both written and verbal information were reported as necessary before observational and experimental studies (38.6% and 37.8%, respectively). Written consent was reported as necessary before observational and experimental studies (39.8% and 68.5%, respectively). Data privacy was considered important.

Conclusion
Overall, patients are supportive of ED research. Perceptions are mixed about information provision and consent processes. The need, by many, for consent before medial record audit is of concern.

Table. Patient perceptions

<table>
<thead>
<tr>
<th>questionnaire item</th>
<th>agreed/strongly agreed n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED research is important</td>
<td>309 (98.1)</td>
</tr>
<tr>
<td>I welcome participation</td>
<td>212 (68.5)</td>
</tr>
<tr>
<td>I feel pressured to participate</td>
<td>26 (8.4)</td>
</tr>
<tr>
<td>Accessing medical records without consent is acceptable</td>
<td>161 (51.6)</td>
</tr>
<tr>
<td>Consent should be obtained in observational studies</td>
<td>231 (75.5)</td>
</tr>
<tr>
<td>Consent should be obtained in experimental studies</td>
<td>279 (91.5)</td>
</tr>
<tr>
<td>Consent can be obtained after enrolment in an emergency</td>
<td>148 (48.4)</td>
</tr>
<tr>
<td>Patients should receive a summary of results</td>
<td>208 (68.0)</td>
</tr>
</tbody>
</table>
Temporal trends in the publication of emergency medicine original research

1. University of Melbourne
2. Austin Hospital

Aim
Little is known about publication trends in emergency medicine research, with most reports being outdated.¹ We aimed to determine temporal trends of 31 article characteristics, over a 20 year period

Method
We undertook a retrospective review of journals with the highest impact factors. Original research articles were included if they were published in AnnEmergMed, AcadEmergMed, EurJEmergMed or EMJ in 1997, 2002, 2007, 2012 or 2017. Full-text search functions allowed abstraction of bibliometric data. Kruskal-Wallis and Chi square tests were employed.

Results
1,413 articles were examined. Between 1997 and 2017, author numbers increased and male authors decreased (Table). There were also increases (p<0.01) in acronyms (6.8% to 16.1%), funding reports (20.2% to 71.2%) and conflicts of interest reports (0% to 96.1%). Study design, statistical analysis and reporting became more sophisticated (Table). However, the proportion of randomised trials decreased and cohort studies increased. There were increases (p<0.01) in median sample sizes (365 to 1368.5), data collection periods (172 to 674.5 days) and reference numbers (18.7 to 28.2).

Conclusion
Original research has increased its methodological rigor and reporting standards. However, there remains considerable scope for improvement.

Table. Article characteristics over time

<table>
<thead>
<tr>
<th>Article characteristic</th>
<th>1997</th>
<th>2017</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author number (mean)</td>
<td>3.6</td>
<td>6.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male authors (%)</td>
<td>73.0</td>
<td>61.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Author contribution (%)</td>
<td>0.4</td>
<td>96.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Multi-centre studies (%)</td>
<td>22.2</td>
<td>47.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Parallel randomised clinical trials (%)</td>
<td>18.5</td>
<td>9.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cohort studies (%)</td>
<td>6.9</td>
<td>21.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Consecutive sampling (%)</td>
<td>36.3</td>
<td>48.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Inferential statistics (%)</td>
<td>32.8</td>
<td>59.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Confidence interval use (%)</td>
<td>41.9</td>
<td>75.1</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

References
Utility of calcium, magnesium and phosphate testing in the emergency department

Aim
Calcium, magnesium and phosphate levels are commonly measured in the emergency department (ED). However, their usefulness in this setting is questionable. We aimed to determine how frequently each electrolyte level is measured, the yield of abnormal levels, and how frequently the results change patient management.

Methods
We undertook a retrospective study of all adult patients who presented to a tertiary referral ED between January-June, 2017. Patients who had serum calcium, magnesium or phosphate levels ordered were included. Data were extracted from the electronic medical record: laboratory values, symptoms, co-morbidities, medications and management changes initiated in the ED. Chi square tests compared proportions within patient subgroups (e.g. low/high level versus normal). Logistic regression identified patients at risk of low/high electrolyte levels.

Results
1,716 (5.2%) of 33,120 patients had at least one calcium, magnesium or phosphate test. 776 (16.2%) of 4,776 individual electrolyte tests were abnormal. 57 tests (7.3% of abnormal tests, 1.2% of all tests) were associated with a change in ED management to correct the abnormality. 50 (2.9%) patients had management changes despite normal electrolyte levels. Specific patient characteristics were significantly associated (p<0.05) with abnormal calcium (e.g. paraesthesia, confusion, cancer), magnesium (e.g. alcohol abuse, proton pump inhibitor medication) and phosphate (e.g. nausea, glucocorticoid medication) levels.

Conclusion
Although these electrolyte levels are frequently measured, they rarely change patient management. Some patients have management changes despite normal levels. The regression results will inform guidelines to better target patients at risk of abnormal levels, consistent with the Choosing Wisely initiative.

References
Simulation Gamification: LIVE. DIE. REPEAT.

Aim
Inspired by the concept of simulation gamification, a multi-level simulation was designed for Emergency Department medical registrar training, with an aim to explore different methods of simulation for ongoing education.

Method
Recursive Objective Based Game-play (ROBG) is a methodology in which trainees must navigate through a number of progressively more difficult levels of simulation scenarios. Each level has one critical action to be achieved and a time limit. If the critical action is not achieved within the time limit, then the patient deteriorates and arrests, the game is stopped, and the level repeated. The trainees are allowed infinite lives to achieve the critical action for progression. Debriefing occurs in between the game levels, regardless of outcome, to review the learning goals, reflect on practice and improve performance.

Results
Simulation Gamification has been conducted once in 2017 and twice in 2018, with a total of 41 Emergency Department registrars participating in a 2.5 hour program where six levels of a scenario, including debriefing and level repetition were completed.

A locally designed feedback survey was used to assess the participant’s learning experience in terms of: orientation to the scenario; session format in meeting their learning needs; and the effect of debriefing on reflection of individual practice. Participants rated the value of these components on a 5 point scale (range: 1 = Not at all to 5 = Completely) with an opportunity to add further comments.

Program feedback was positive with the majority of participants rating all components highly. The opportunity to engage in immediate repetition led to an improvement of clinical performance and participants also reported experiencing reduced levels of anxiety due to the game-like environment.

Conclusion
Simulation Gamification provides an opportunity for trainees to learn with deliberate practice through the simulation of multiple time critical situations and interventions in a safe learning environment.

References
TITLE: Preventing Avoidable Hospital Admissions for People with Dementia (PAHA-D) - A collaborative project to identify current dementia care practices

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2Austin Health, Heidelberg, Vic
3Royal Melbourne Hospital & Melbourne EpiCentre, University of Melbourne, Parkville, Vic
4Northern Health, Epping Vic
5Academic Unit for the Psychiatry of Old Age, Department of Psychiatry, University of Melbourne & NorthWestern Mental Health, Melbourne Health, Parkville, Vic
6Department of Health and Human Services, Melbourne Vic
7Dementia Australia VIC, Parkville Vic
8North Western Melbourne Primary Health Network, Parkville Vic
9On behalf of the Melbourne Ageing Research Collaboration.

Background: Nine percent of all hospitalisations in Australia are potentially avoidable if conditions were managed earlier. These are known as ambulatory care sensitive (ACS) conditions. Older people make up 27% of all potentially avoidable hospitalisations. Compared to age-matched peers, people living with dementia (PLWD) are at greater risk of ACS conditions, have twice the rate of hospitalisation, have more long-term health conditions, and are 2-3 times more likely to have poor outcomes from hospitalisation. Seventy-five percent of dementia-related hospitalisations are from those living in the community.

Aim: To understand why PLWD from community settings attend Emergency Departments (ED).

Method: Audit of 150 ED records of PLWD across three hospitals; survey of hospital staff and family carers regarding experiences, practices and attitudes.

Results: Of the 150 records, 25% of PLWD live alone, 37% have dementia of unknown type, PLWD have an average of 5.5 comorbidities, 25% have documented visual or hearing impairments, and 58% arrived afterhours. The most common reasons for presentation were pain, falls, functional decline, infection, and digestive/gastrointestinal. Most presentations were not considered immediately avoidable and resulted in admission.

Staff perceived falls, delirium/confusion, infection, carer stress, and worsening behaviour as the most common reasons for presentation.

Conclusion: ED records did not contain clear information about dementia. Although most presentations were not considered immediately avoidable and resulted in admission, preventative practices in the weeks/months leading to presentation may have been indicated and efforts should still be made to avoid harms that may result from hospitalisation. Staff perceptions differ from actual reasons for presentation and there is an opportunity for education. Education for staff and family carers is needed and should focus on assessment and management of pain in PLWD; improving understanding of the health system; and improving the ED care environment for PLWD.
ABSTRACT:

Introduction: Cancer treatment has leaped forwards in the last 20 years, with a 20% decrease in overall ICU mortality whilst making around 15% of ICU admissions. The outcomes of ICU patients with a cancer diagnosis has not been extensively studied in Australasia.

Objectives: We aim to compare the short-term outcomes of cancer patients in Australasian ICUs with a general cohort similarly admitted, comparing survival between cancer types and admission factors associated with mortality. Our hypothesis is that there is no longer a gap in survival outcomes between non-cancer and cancer patients.

Method: This project is designed as a retrospective cohort database enquiry- using of Australia New Zealand Intensive Care Society (ANZICS) adult patient database, identifying cancer patients by their APACHE-III-J sub-diagnoses. Study population was a general cohort of all patients admitted to Australasian ICUs between 2011-2015. These were separated into Surgical Oncology, Medical Oncology and Haematological Oncology streams for comparison. Statistical analysis was done using STATA software. Kaplan-Meier survival curves were compared using Cox regression.

Results: Between Jan 2011 to Dec 2015, there were 684,855 admissions to ICU, with 6.61% (45,278) being cancer patients. This cancer cohort comprised of 96.38% surgical oncology patients, 2.35% medical oncology and 1.27% haematological oncology patients. ICU and hospital mortality between general and cancer cohorts was 5.79% vs 1.32% and 9.11% vs 3.48% respectively. Kaplan-Meier survival curves indicated that overall our hypothesis was supported in that overall that cancer cohort had similar survival. However, on subgroup analysis medical and haematological oncology groups had decreased survival whilst surgical oncology had survival better than the general cohort.

Conclusion: At first glance, ICU and hospital mortality are better for cancer patients. However this appears to be due to the predominance of surgical oncology patients. Further study will be required looking at non-elective admissions and comparing longer-term survival.

Keywords:
Critical care, intensive care, survival, short-term outcomes, cancer, tumour, malignancy, Australasia
The impact of pre-morbid glycemic control on glycemia, insulinemia and C-peptidemia in critically ill diabetic patients

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**Aim:** Glycaemic control in diabetic critically ill patients remains controversial and pre-ICU glycaemic control may impact the patient’s endocrine response during critical illness. We aimed to explore how pre-ICU glycaemic control modifies endogenous insulin secretion and glycaemic control during ICU stay.

**Methods:** In our single-centre prospective observational study, we included 49 type 2 diabetic critically ill adults treated with permissive moderate hyperglycaemia (targeted blood glucose range 10 – 14 mmol/L). Pre-ICU glycaemic control was assessed by ICU admission HbA1c level. Glycaemia, insulinemia, C-peptide levels, and concurrent anti-diabetic therapy were recorded at ICU admission and on the following 2 days. Values are reported as number (percentage) or median [interquartile range].

**Results:** Median age was 66 [59, 77] years and 28 (57%) were male. ICU admission HbA1c was ≤7% in 27 patients and > 7% in 22 patients (6.3 [5.8, 6.7] vs 8.1 [7.6, 9.4], p<0.01, respectively). Between these groups and at inclusion, no difference in glycaemia, C-peptide levels, insulinemia, or in anti-diabetic therapy 24 hours before inclusion was observed. Over the observation period, C-peptide levels progressively and significantly increased in patients with HbA1c ≤7% compared to those with HbA1c >7% (day 1: 1.6 [1.2; 2.4] vs 1.2 [0.6; 2]; day 2: 1.7 [1.1; 4.1] vs 1.4 [0.6; 1.7]; day 3: 3.2 [1.4; 4.3] vs 1.2 [0.7; 2.2], p=0.01, respectively). Glycaemic control using oral hypoglycaemic therapy during ICU stay was also less frequent if HbA1c at admission was ≤7%. No difference existed in glycaemia, insulinemia, and exogenous insulin administration between those 2 groups.

**Conclusions:** Pre-admission glycaemic control modifies the acute endogenous response to hyperglycaemia in ICU. Our findings support the value of measuring HbA1c in diabetic patients admitted to ICU.
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The impact of exogenous insulin on insulinemia and C peptidemia in critically ill diabetic patients treated with permissive hyperglycemia

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**Aim:** Moderate permissive hyperglycaemia (10-14 mmol/L) is feasible and safe in critically ill diabetic patients, yet no study has assessed how β-cells respond to more liberal glycaemic control strategies. We aimed to explore the pancreas endocrine response to moderate permissive hyperglycaemia and exogenous insulin therapy.

**Methods:** In this single-centre prospective observational study, we included 50 type 2 diabetic critically ill adults, treated with moderate permissive hyperglycaemia. Glycaemia, insulinemia, C-peptide levels, and concurrent anti-diabetic therapy were recorded at inclusion, and on the following 2 days. Univariate comparisons were performed between patients requiring insulin administration within 24h of inclusion, and those who did not. Variables associated with C-peptide to insulin ratio were determined using a multivariate linear regression.

**Results:** Median age was 67 [59, 78] and 29 (58%) were male. Insulin was administered in 33 (66%) patients within 24h before inclusion. During the observation period, patients treated with insulin 24h before inclusion had higher daily glycaemic levels (day 1: 12 [10, 15] vs. 10 [6, 11] mmol/l; day 2: 12 [10, 15] vs. 10 [9, 15] mmol/l; day 3: 12 [10, 14] vs. 13 [9, 14] mmol/l, p<0.05), and lower C-peptide to insulin ratio (day 1: 3 [2, 8] vs. 35 [14, 48]; day 2: 5 [3, 13] vs. 18 [11, 31]; day 3: 5 [3, 15] vs. 16 [11, 30], p=0.04), compared to those who did not. Administration of insulin during the observation period was independently associated with a decrease in serum C-peptide to insulin ratio (-16±3 per 1 U/kg of exogenous insulin, p<0.01).

**Conclusions:** Administration of exogenous insulin impaired the endocrine physiologic response to hyperglycaemia in critically ill diabetic patients treated with a liberal glycaemic control strategy.
The effect of sepsis on insulinemia and c-peptide levels in critically ill diabetic patients

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Aim: Poor glycaemic control is classically considered as being associated with increased infection risk. C-peptide endogenous secretion is upregulated by hyperglycaemia and may be associated with immunomodulatory features in the setting of sepsis. We aimed to evaluate C-peptide levels and insulinemia in a critically ill diabetic cohort with sepsis.

Methods: We included 50 type 2 diabetic critically ill adult, after exclusion of those with acute diabetic complications. Glycaemia, serum C-peptide levels and insulinemia were measured at inclusion, and on the following 2 days. We recorded administered exogenous insulin doses. Univariate comparisons were performed between patients without or with sepsis, and in the septic group, between those receiving or not exogenous insulin. Parameters associated with C-peptide to insulin ratio were determined using a multivariate linear regression.

Results: Median age was 67 (interquartile range [59; 78]) and 29 (58%) were male. At inclusion, 42 (84%) were mechanically ventilated and 39 (78%) were receiving vasopressor support. Sepsis was present in 22 (44%) patients. At inclusion, compared to septic patients not receiving exogenous insulin (n=8), septic patients treated with exogenous insulin (n=14) had significantly higher glycaemia and insulinemia, and lower C-peptide to insulin ratios (5 [1.5; 9.8] vs. 48 [33.3; 72.3], p<0.01). Over the observation period (3 days), diabetic patients with sepsis treated by exogenous insulin had lower C-peptide levels and C-peptide to insulin ratio, compared to those who did not (p<0.05 and p=0.01, respectively). In multivariate analysis, only sepsis (positively) and exogenous insulin (negatively) were independently associated with the C-peptide to insulin ratio (p=0.03 and p<0.01).

Conclusions: In diabetic patients, sepsis is positively and independently associated with higher C-peptide to insulin ratios. Exogenous insulin administration is associated with a negative effect on this physiological response to sepsis.
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Performance of urinary cell cycle arrest biomarkers for the prediction of acute kidney injury in critically ill patients

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**Aim:** Adequate risk assessment of acute kidney injury (AKI) is mandatory before considering designing interventions aiming at altering its course. Urinary cell cycle arrest biomarkers (uCCAB – TIMP-2 and IGFBP-7) has shown promising performances in the prediction of AKI in various critically ill populations. We aimed to assess the performance of uCCAB in predicting early AKI in critically ill patients.

**Methods:** In this single centre prospective observational study, we enrolled critically ill adult patients presenting one of the following criteria after admission: vasopressor support, urine output <0.5 ml/kg/h during 4 hours, or a serum creatinine increase >8 µmol/L over 6 hours. We excluded patients with stage 2 or 3 AKI at enrollment. uCCAB was measured at inclusion. AKI was defined by KDIGO-based stage 2 or 3 AKI, and assessed after 12 hours of urine collection. uCCAB (absolute value and corrected by urinary creatinine concentration [uCr]) performance to predict AKI was assessed using area under the receiver operator characteristics curve (AUROC) and net reclassification index (NRI).

**Results:** We included 52 patients (age 61±16 years, 26 women), of whom 18 (35%) had sepsis, 27 (52%) required vasopressors, and 33 (63%) received mechanical ventilation. AKI occurred in 18 (35%) patients. At inclusion, uCCAB was 0.8±1.1 (ng/ml)²/1000 respectively, and did not differ between patients with and without AKI (p=0.28). uCCAB levels were >2.0 in 5 patients, 3 of which did not develop AKI. uCCAB had an AUROC to predict AKI of 0.68 (95% confidence interval [0.52; 0.84], p=0.03) and a NRI of 0%. uCCAB was positively associated with uCr (R²=0.33, p<0.01). uCr-corrected uCCAB had an AUROC to predict AKI of 0.59 (95%CI [0.42; 0.76], p=0.30).

**Conclusions:** The ability of uCCAB to predict AKI in a representative population of critically ill patients demonstrated poor performances, that were not improved after correction of uCCAB levels for urine concentration.
Impact of furosemide on urinary oxygenation in septic shock patients

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Aim: Renal medullary hypoxia plays a pivotal role in acute kidney injury pathogenesis, yet its detection in the clinical setting remains a challenge. Continuous monitoring of urinary bladder oxygen tension (PUO2) allows less-invasive estimation of medullary oxygenation. The impact of diuretic treatment on medullary hypoxia remains controversial. We aimed to evaluate the effect of an intravenous furosemide bolus on renal medullary oxygenation estimated by PUO2 in patients with septic shock.

Methods: In this single-centre prospective observational study, all ICU patients with a suspected diagnosis of septic shock were considered for continuous PUO2 monitoring. Intravenous furosemide bolus (20 or 40 mg) was administered as per the treating physician, and PUO2 was recorded during the subsequent 60 minutes. A diuretic response was considered present if urine output was above 2 ml/kg/h at 2-hour following furosemide administration.

Results: We evaluated 29 furosemide boluses administered to 7 patients with septic shock (median age 65 years [IQR 50; 80]; 2 males). The furosemide dose was 20 mg in 19 episodes, and 40 mg in 10. At baseline, PUO2 was 21 [18; 25] mmHg, but increased significantly at 20 minutes (26 [20; 30] mmHg, p<0.01) and 60 minutes (28 [24; 33] mmHg, p<0.01) after the furosemide bolus. In episodes followed by a diuretic response (n=16), PUO2 was significantly higher at 60 minutes, compared to non-responders (29 [28; 35] vs. 22 [20; 26], p=0.01).

Conclusions: We describe the first use of PUO2 monitoring in septic patients. This surrogate of renal medullary oxygenation was low at baseline, yet rapidly increased significantly after furosemide administration, suggesting that this treatment alleviated medullary hypoxia. A short-term diuretic response >2ml/kg/h was associated with higher levels of PUO2.
**Yanase F**1,2, Bitker L1, Cutuli S.L1, Wilson A1, Eastwood G.M1, Bellomo R1.

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**Title of abstract**
Comparison of the hemodynamic effects of a room temperature and warm 4% albumin fluid bolus after cardiac surgery.

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**Aim**
Fluid bolus therapy (FBT) performed with room temperature colloids is used to treat hemodynamic instability after cardiac surgery. However, little is known of the effects of FBT with warm 4% albumin. The aim of this study is to compare hemodynamic variables after warm 4% albumin FBT, compared to room temperature FBT, after cardiac surgery.

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**Methods**
In this single-centre prospective observational study, we included 12 adult patients in the ICU after cardiac surgery, and prescribed FBT for the treatment of hemodynamic instability. Patients received a 500 mL 4% albumin FBT, either warmed at 40°C by a fluid warmer at delivery (intervention, n=6), or at room temperature (control, n=6). Cardiac index (CI), mean arterial pressure (MAP) and blood temperature were recorded before, and at 0 and 30 minutes after FBT. Ventilation and intravenous drugs were kept unchanged during the observation period.

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**Results**
All patients (median age: 71 years, IQR [64; 77]) were mechanically ventilated and 4 required vasopressor support. FBT was administered to treat hypotension (n=8), low CI (n=3) or low filling pressures (n=1). In each study group, CI and MAP significantly increased at 0 and 30 minutes after FBT, compared to baseline. CI did not significantly differ between intervention and control at 0 minutes (0.4 [0.3; 0.6] vs. 0.5 [0.2; 0.5] L/min/m²), and at 30 minutes (0.4 [0.3; 0.5] vs. 0.3 [0.2; 0.5] L/min/m²). Likewise, no significant difference in MAP between groups was observed at 0 minutes (variation from baseline: 6 [4; 7] vs. 12 [6; 15] mmHg), and at 30 minutes (7 [-2; 9] vs. 5 [1; 11] mmHg). Blood temperature was significantly lower in the control group, compared to the intervention (p<0.01).

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**Conclusion**
Warm FBT prevents FBT-induced decreases in body temperature while delivering equivalent hemodynamic effects to room temperature after cardiac surgery.
Are patients with diabetes at greater risk for contrast induced nephropathy than those without diabetes?

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Introduction: Contrast-induced nephropathy (CIN) is an important cause of acute kidney injury (AKI) in inpatients. However, the prevalence and predisposing factors for CIN remain poorly documented. The aim of this study was to investigate the association between CIN, kidney function and diabetic status in inpatients.

Methods: We identified inpatients who received IV contrast prior to a computed tomography (CT) scan between July 2012 to March 2018 at Austin Health, Melbourne. Our study was restricted to patients > 54 years as all patients above this age who have a HbA1c measurement when admitted to our hospital as part of the Diabetes Discovery Initiative. Outpatients, patients <54 years, patients who had multiple CT scans with IV contrast and patients with a baseline estimated Glomerular Filtration Rate (eGFR) <30ml/min/1.73m² were excluded. We obtained creatinine measurements at baseline and 48 hours post contrast administration and defined CIN as an absolute rise in creatinine of ≥44mmol/L. Patients were divided into those with and without a history of diabetes and/or those with renal impairment (defined as an eGFR < or ≥ 60/ml/min/1.73m²). Firth logistic regression model was used for data analysis.

Results: Out of 1280 patients, 28.75% had a history of diabetes and 29.53% had baseline eGFR of <60/ml/min/1.73m² and 70.47% has baseline eGFR of ≥60/ml/min/1.73m². The overall prevalence of CIN was 3.2%. Pre-existing diabetes, degree of glycaemic control (assessed by admission HbA1c) or presence of renal impairment was not associated with an increased risk of developing CIN.

Conclusion: Patients with or without diabetes who had a CT scan with IV contrast appear to have a similar risk for the development of CIN after adjusting for other variables. A larger data set may yield different outcomes.

Words: 281.
A randomised controlled trial to assess the effects of initial triple versus sequential therapy on beta cell function in people with newly diagnosed type 2 diabetes

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AIM:
This pilot study is a randomized controlled trial aimed to determine whether triple therapy comprised of metformin, saxagliptin and dapagliflozin compared to sequential therapy with initial metformin is safe and tolerable and improves beta cell function.

METHODS:
Ten subjects with newly diagnosed type 2 diabetes (T2DM) were randomized to initial triple therapy of metformin, saxagliptin and dapagliflozin or to sequential metformin, saxagliptin and dapagliflozin therapy for 12 months (ACTRN12617000789369). Changes in beta cell function and insulin sensitivity were estimated following a mixed meal tolerance test at 0 and 12 months post randomisation.

RESULTS:
At baseline, subjects had a median HbA1c of 7.7% (IQR 6.8-8.9) with BMI of 36kg/m² (32-41). The median 2hr glucose was 12.5mmol/L (11.2-17.3). Compared to people without T2DM, insulin sensitivity was (i) 25% (21-31), as calculated by homeostatic model assessment 2-insulin sensitivity (HOMA2-S) and (ii) Matsuda index was 28% (1.4 (1.0-1.6)). Compared to people without T2DM, the median beta cell function was (i) 62% (39-94), as calculated by HOMA2-B and (ii) disposition index (DI), which is a measure of beta cell function adjusted for insulin sensitivity, was 60% (45-88). Preliminary results of the one year follow up of the first 5 participants suggest that either approach produces a median HbA1c decrement of 1.3% (1.2-3.0) with a 2hr glucose level of 10 (9-15.5). HOMA parameters of insulin sensitivity and beta cell function were 28% (21-53) and 79% (66-130), respectively. The change in DI was 27% (-22-185). No hypoglycaemic events were reported.

CONCLUSION:
Our preliminary data show that in people with newly diagnosed T2DM, triple therapy comprised of metformin, saxagliptin and dapagliflozin, given sequentially or as an initial combination, is safe and tolerable. Further study is required to determine whether initial combination of the above medications or their sequential addition provides the optimal approach to improving beta cell function in T2DM.
Assessing the efficacy of telemedical interventions in older people with diabetes: A systematic review and meta-analysis.

Aims:
The population is ageing, with greater numbers of older people with chronic and complex conditions requiring management and support. In response, there is increasing interest in the use of Telemedicine to deliver home-based health care to this population. This meta-analysis investigates the effect of telemedical interventions on key glycaemic outcomes, including HbA1c, fasting and post-prandial plasma glucose levels, in older adults living with diabetes.

Methods:
A search of 4 databases was conducted (MEDLINE, Embase, EmCare, and Cochrane CENTRAL) inclusive of papers between March 2008 until March 2018 for randomized controlled studies of telemedical interventions for people with type 1 and type 2 diabetes, with a mean age greater than 65 years. A total of 1582 studies were extracted and independently screened for eligibility criteria by two authors. Studies involving artificial pancreas systems or telemedicine interventions without the involvement of health care professionals were excluded.

Results:
Data from 7 randomized controlled trials (n= 3003, of which 1599 were randomized to a telemedical intervention and 1404 to usual care) were analyzed. Participant mean age was 69 ± 8 years and baseline HbA1c was 7.8% ± 1%. Only 1 study included participants with type 1 diabetes. Median follow-up time was six months. Telemedicine led to reductions in: (i) Mean HbA1c levels of 0.45% (95%CI: -0.68% to -0.23%), (ii) mean fasting plasma glucose 0.77mmol/l (95%CI: -1.31mmol/l, -0.24mmol/l) and (iii) mean post-prandial glucose 2.75mmol/l (95%CI: -5.20mmol/l, -0.31mmol/l).

Conclusion:
Despite the high rates of diabetes among older people, few studies have been undertaken in this age group. Telemedicine interventions
significantly improve glycaemic parameters in older adults living with diabetes. Further research is required to determine if these effects are cost-effective and durable, and if telemedicine could also improve cardiovascular risk factors, rate of hospitalisations and quality of life.
Exercise challenges faced by adults with type 1 diabetes: a cross-sectional study

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Background: Individuals with type 1 diabetes (T1D) are encouraged to undertake regular physical activity to complement their medical management. Undertaking this exercise, however, can be challenging due to unpredictable glucose responses and variable insulin requirements. Guidelines exist to assist adults with T1D to manage exercise, though their impact on exercise behaviour is not yet established.

Aims: To survey the exercise practices and guideline knowledge amongst adults with T1D.

Methods: Adults with T1D attending ambulatory services at St Vincent’s Hospital Melbourne were surveyed regarding their awareness and understanding of exercise guidelines, their perception of exercise barriers, and their individual physical activity and diabetes management practices undertaken during the preceding 7 days.

Results: The survey was completed by 110 adults (n=53 men, median [IQR] age 40 [31–53] years, T1D duration 21 [12–33] years, BMI 26.2 [23.6–30.1] kg/m² and HbA₁c 7.5 [7.0–8.5] % | 58 [53–69] mmol/mol; n=61 (55%) were using insulin pump therapy). Amongst our sample, 97% reported undertaking some exercise (22 [9–3] MET-hours). The Australian physical activity guidelines were correctly recalled by n=61 (55%) and successfully met by 51%. Exercise-associated hypoglycaemia was reported by 42%. Fitness level, health status and fear of hypoglycaemia were perceived as exercise barriers by 27%, 22% and 17% of participants, respectively; these barriers were associated with reduced physical activity (p<0.05). Strategies utilised to optimise glucose levels around exercise included insulin pump basal rate adjustments, prandial insulin bolus dose adjustments and supplemental carbohydrate intake. Awareness of T1D exercise management guidelines (n=39, 35%) was not associated with strategy use frequency or higher physical activity levels.

Conclusions: There is scope for improved awareness and implementation of exercise guidelines amongst adults with T1D with just over half our sample meeting Australia’s physical activity guidelines. Hypoglycaemia remains a major risk related to exercise, although numerous strategies are used to prevent it. Perceived fitness level may have a greater impact on physical activity behaviour than fear of hypoglycaemia. This should be considered by clinicians when promoting exercise.

Keywords: exercise, physical activity, type 1 diabetes, hypoglycaemia, insulin

**Cortex leads thalamus in tonic seizures of Lennox-Gastaut Syndrome**

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**Aim**

Tonic seizures and generalised paroxysmal fast activity (GPFA), characterised by diffuse fast activity on scalp EEG, are key features of Lennox-Gastaut syndrome (LGS), a severe epilepsy phenotype. Our prior imaging studies¹ have confirmed cortex and thalamus are both involved, but the role of these structures in initiation of epileptic activity has been controversial. We aimed to assess the relative role of cortex and thalamus (centromedian nucleus; CM) in epileptic activity of LGS. This is part of the larger ESTEL study (Electrical Stimulation of the Thalamus in Epilepsy of the Lennox-Gastaut phenotype; HREC/16/Austin/139).

**Methods**

Five patients with LGS undergoing bilateral CM deep brain stimulation electrode insertion had simultaneous, intra-operative EEG from scalp and thalamus (17-34 minutes). Remifentanil/Isoflurane anaesthesia permitted visualisation of epileptic activity. Onset of discharges was marked manually, at both scalp (‘cortex’) and thalamus.

**Results**

GPFA/tonic seizures were recorded in 4/5 patients. 55 GPFA/tonic seizures were analysed. GPFA was observed earlier on scalp 67.2% (37/55) samples. The average lag of thalamic to cortical discharges was $92.7 \pm 86.8$ msec. Three discharges were exclusively noted in cortical electrodes. 14 discharges had simultaneous onset in thalamus and scalp. Thalamic-only GPFA was noted in one sample.

**Conclusion**

Epileptic activity of LGS is detectable in CM of thalamus, confirming that the CM is part of the epileptic network of LGS. Scalp EEG discharges, representing adjacent cortical activity, usually precede or occur simultaneously with thalamic discharges. This is consistent with EEG-fMRI data and suggests that the cortex drives GPFA and tonic seizures in LGS patients. This finding is important to future studies using responsive stimulation, as they require that epileptic activity is expressed in the thalamus in order to sense and stimulate response in order to decrease GPFA and seizures.

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Aim: Cut homeodomain transcription factor CUX2 is essential to dendrite branching, spine development, and synapse formation in layer II-III neurons of the cerebral cortex. We identified a recurrent de novo CUX2 p.Glu590Lys, as a novel cause for developmental and epileptic encephalopathy (DEE).

Methods: Phenotyping was performed on 9 patients with CUX2 mutations identified by whole-exome sequencing (n=5) or targeted gene panel (n=4).

Results: 7 males and 2 females with the de novo CUX2 variant p.Glu590Lys (mean age 13 years, range 0.5-21 years) had median age of seizure onset of 6 months (2 months to 9 years) with myoclonic, atypical absence seizures with myoclonic components, and focal seizures. Seizures were drug-resistant (7) or controlled with valproate (2). Six had DEE: myoclonic DEE (3), Lennox-Gastaut syndrome (2) and West Syndrome (1). Two had static encephalopathy and genetic generalized epilepsy. One infant had multifocal epilepsy. Eight had severe cognitive impairment, with autistic features in six. p.Glu590Lys affects a highly-conserved glutamine residue in the CUT domain predicted to interfere with CUX2 binding DNA targets during neuronal development.

Conclusion: Patients with CUX2 p.Glu590Lys display a phenotypic spectrum of generalized epilepsy, including infantile-onset myoclonic DEE and generalized epilepsy with severe static developmental encephalopathy.
Investigating microstructural heterogeneity of white matter hyperintensities in Alzheimer’s disease using advanced diffusion MRI

Aim
White matter hyperintensities (WMH) are commonly observed on T2-weighted MRI (in particular, on FLAIR MRI) in Alzheimer’s disease (AD) patients. These lesions are known from pathology to be heterogeneous, but appear homogeneously bright on FLAIR. Advanced diffusion MRI methods could enable the underlying microstructural heterogeneity of WMH to be investigated non-invasively in vivo. In this study, we investigated WMHs in a cohort of AD and healthy elderly control (HC) subjects using this approach.

Methods
Diffusion MRI data (2.3mm³ voxels, 60 directions, b=3000²/mm²) and FLAIR images (0.9x1x1mm³) were collected from 48 AD patients and 94 HC subjects from AIBL (Australian Imaging, Biomarkers and Lifestyle study) on a 3T scanner. WMH segmentations were automatically performed using the HyperIntensity Segmentation Tool (HIST), and automatically classified into “periventricular” (PVWMH) and “deep” (DWMH). We computed a measure of relative white matter/grey matter/CSF (WM-GM-CSF)-likeness of the diffusion signal by obtaining compartments for each imaging voxel using a method called single-shell 3-tissue constrained spherical deconvolution (SS3T-CSD). We computed the mean WM-GM-CSF signal fractions within PVWMH and DWMH, and in normal-appearing WM (NAWM) in all subjects.

Results
AD patients exhibited significantly greater PVWMH, but not DWMH volume compared to HC. PVWMH and DWMH showed distinct compositions in terms of their relative WM-GM-CSF mean tissue fractions, with higher CSF-likeness in PVWMH, and higher GM-likeness in DWMH. WMH could be clearly distinguished from NAWM in their diffusion profile, and the different classes could be distinguished from one another. Moreover, heterogeneity was consistently observed within lesions.

Conclusion
Advanced diffusion MRI (SS3T-CSD) goes beyond the binary lesion segmentation provided by FLAIR MRI to reveal differences in diffusion signal profile within WMH classes, as well as microstructural heterogeneity within lesions. This will enable investigation of WMHs as heterogeneous entities when probing associations with histopathology and clinical progression of AD in the future.

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Brain Repair Requires A Collective Overhaul Of Research Methods: Recommendations From 1st Stroke Recovery and Rehabilitation Roundtable

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Background and aims: Thousands of stroke rehabilitation trials have been completed, yet we lack treatments to markedly alter expected stroke recovery trajectories. An international collaboration was established in 2015 to form consensus on how to develop and promote excellence in stroke rehabilitation and recovery research.

Method: The first Stroke Recovery and Rehabilitation Roundtable, convened in Philadelphia, USA 2016, included 60 members across four working groups. Key hurdles addressed across the stroke research pipeline were: translation of pre-clinical studies, biomarkers of stroke recovery, development and reporting of interventions, and measurement in clinical trials.

Results: A radical new vision of ‘brain repair’ emerged, which will necessitate commencement of recovery trials early after stroke and identification of acute biological targets relevant in animal models and human stroke survivors. Recommendations include standardised research time points, based on knowledge of neural repair, assessments and reporting. Six consensus papers are available open access http://journals.sagepub.com/page/wso/srrr.

Discussion: Stroke rehabilitation science is lagging that of our acute colleagues by 15 years. These new recommendations, with a focus on early stroke, will help us to understand the full pathway of stroke recovery. The second roundtable, October 2018, will draw together our recommendations to establish the next big trials required to progress stroke recovery.
Distinct functional properties of the posteromedial cortex reveal aberrant functional connectivity patterns in Alzheimer’s disease

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Aim: In Alzheimer’s disease (AD), the posteromedial cortex (PMC) is identified as a region of early metabolic change. Previous fMRI studies have treated this region as a functionally homogenous structure in the brain. However, recent work has demonstrated that a more fine-grained parcellation is possible (1), that characterises its distributed connectivity with multiple brain networks. Here, we aimed to characterise the functional properties of the PMC to determine if subregions may be more sensitive or selectively impacted for delineating the neural substrates of AD.

Methods: A constrained independent component analysis on the PMC region was performed using resting-state fMRI from 100 healthy participants in the Human Connectome Project. This analysis was applied to AD patients \((n=29)\) and healthy controls \((n=38)\) from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database. We further investigated whether similar PMC connectivity changes could be observed in Mild Cognitive Impairment (MCI) patients \((n=21)\) that converted to AD at follow-up.

Results: The PMC was found to subdivide into several functionally distinct subregions that are connected to multiple highly disparate brain networks. AD patients showed increased connectivity of the dorsal posterior cingulate (dPCC) \((p=0.03)\) (Fig 1A) and a decreased connectivity of the retrosplenial cortex networks \((p=0.01)\) (Fig 1B) compared to healthy controls. The ventral posterior cingulate network showed increased connectivity to frontal regions (ventromedial prefrontal cortex) in AD patients \((p=0.01)\) (Fig 1C). MCI patients that converted to AD showed similar connectivity cascades to AD patients with decreased connectivity of the anterior precuneus network to medial temporal lobe regions \((p=0.02)\) and increased frontal connectivity in the dPCC network.

Conclusion: Our findings demonstrate that highly integrated PMC subdivisions, such as the dPCC are preferentially affected in AD, and prodromal MCI patients. This work highlights the utility of the PMC for mapping cascading functional network changes during different stages of AD pathophysiology.

References
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Depletion of PAK1 increases survival via upregulating immune response in mouse pancreatic cancer model.

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Aim
Pancreatic cancer has the highest mortality rate of all major cancers with only 7% 5-year survival rate\(^1,2\) and this has not changed much in the past 40 years, due to low surgical eligibility with likelihood of recurrence and drug resistance. PAK1 has been shown to be overexpressed in many solid tumours including pancreatic cancer\(^3\). This study aims to investigate the potential role of PAK1 in tumour immune response using pancreatic cancer model.

Methods
The pancreatic cancer mouse model (KPC) with PAK1 gene knocked out were generated and housed in Austin BRF. The mice are monitored as the disease progresses. At the study endpoint, KPC mice survival was compared between the PAK1 wildtype (WT), heterozygous (Het) and knockout (KO) genotypes, the pancreas was collected, formalin fixed, embedded, sectioned and immunohistochemical staining was performed to analyse expression of immune markers such as CD8, FoxP3, CD4 and PD1.

Results
Depletion of PAK1 significantly increased survival of KPC mice carrying pancreatic cancer (p = 0.008). The number of infiltrating CD8+ and CD4+ effector T cells to pancreatic cancer was also markedly elevated in the PAK1KO mice compared to its wildtype counterpart.

Conclusion
Our novel PAK1KOKPC pancreatic cancer mouse model showed that PAK1 depletion significantly improved survival in the KPC mice possibly through upregulation of immune response reflected in the increased infiltration of effector CD8+ and CD4+ T cells to pancreatic cancer. This clearly demonstrates an essential role of PAK1 in the progression of pancreatic cancer and highlights its potential in immuno-therapy.

References
Abstract

Introduction

Immunotherapy with immune checkpoint inhibitors has achieved durable responses in a proportion of advanced melanoma patients. To minimise frequently occurring treatment-related adverse events for patients that are unlikely to respond, biomarkers for responses and patient stratification are urgently needed.

The immune system can be broadly categorised into the innate and adaptive immunity. The cells that comprise the former are the first responders to infection and foreign antigens (e.g. cancer antigens) and enable subsequent mounting of the adaptive immune response. The adaptive immunity recognises highly specific antigens and allows a more potent secondary response. Interestingly, certain subsets of immune cells like γδ T cells bear traits from both the innate and adaptive immune cells and may be key cells in anti-tumour immunity. In this study, we investigate if these cells are associated with immunotherapy outcomes.

Methods

Melanoma patient samples

Peripheral blood mononuclear cells (PBMC) were obtained before and during immunotherapy (ipilimumab) from 16 melanoma patients at the Austin Hospital. Written informed consent and approval of the Ethics Committee of the Austin Health (LNR/18/Austin/190) were obtained. Clinical response was determined with PET/CT scans. Clinical responders are defined as individuals who demonstrate overall reduction in tumour volume or exhibit stable disease. Non-responders are defined as individuals who demonstrate disease progression.

Monoclonal antibody staining

Cells were stained with antibodies against CD3 as T cell lineage marker. Vδ1 and Vδ2 TCR antibodies were used to identify the 2 main subsets of γδ T cells, and CCR7, CD62L, CD27 and CD45RO antibodies were used to determine their differentiation status. Data were acquired on a flow cytometer.

Results
Our results demonstrate differences in the changes of the frequencies and differentiation states of Vδ2 T cells subsets with immunotherapy between responders and non-responders.

**Conclusions**

Our results demonstrate differences in the frequencies and differentiation states of Vδ2 T cells subsets with immunotherapy between responders and non-responders. Monitoring the differentiation states of Vδ2 T cells may have the potential to serve as a biomarker. Findings from this pilot study are limited by a small sample size of patients but justify further studies.
Anti-metastasis therapy via nanoparticle mediated drug delivery

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Metastatic disease is the major cause of cancer-related death in patients with solid tumours such as breast cancer. The mainstay of current treatments for metastatic disease is chemotherapy (e.g. doxorubicin) that is often limited by systemic toxicity. To improve drug efficacy, there is an urgent need for a mechanism to target tumour cells with minimal damage to normal tissues. Preliminary data show that the Unfolded Protein Response (UPR) chaperone glucose-regulated protein 78 (GRP78) is overexpressed on the cell surface of multiple metastatic breast tumour tissues including spine, lung and heart. Targeting GRP78 on the surface of metastatic cancer cells with a GRP78 binding peptide fused to an apoptotic moiety exhibited promising effects in in vivo models of metastatic breast cancer. We have demonstrated previously that nanoparticles (NPs) can be targeted to colorectal cancer cells and doxorubicin-loaded NPs exhibited similar toxicity to treatment with doxorubicin alone in in vitro studies with SY5Y neuroblastoma cancer cells. The aim of my project is to develop and test a tumour specific drug delivery system using NPs that selectively target metastatic tumour cells by virtue of their high levels of surface-localised GRP78. The project will comprise the design, generation and characterization of a library of NPs with optimal size and binding affinities for selective uptake by tumour cells and for optimal drug releasing properties within cells. Furthermore, selectivity towards tumour cells of GRP78 targeting NPs containing doxorubicin and the mode of internalization and release of the doxorubicin will be tested. Having determined the biodistribution, toxicity and half-life of GRP78 targeting NPs, the efficacy in preclinical models of metastatic cancer, using either doxorubicin or an apoptosis-inducing peptide as the therapeutic agent, will be analysed.

To date, a library of multiple NPs of different sizes and containing different lengths of polyethylene glycol (PEG) side chains has been generated and chemically characterized. NPs were loaded with Cyanine5 (Cy5) to analyse their cancer cell attachment properties. PEGylated NPs that had a GRP78 binding peptide attached showed stronger tumour cell association with surface GRP78-positive murine 4T1.2 cells than NPs linked to a scrambled peptide or a PEG side chain alone. Replacement of Cy5 with doxorubicin or an apoptosis-inducing peptide will allow us to test cytotoxic properties of the NPs towards surface GRP78-positive breast cancer cell lines.

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2. Johnston, AP. ACS Nano 2012, 6, 6667-6674. 'Targeting cancer cells: controlling the binding and internalization of antibody-functionalized capsules'
Planning Study: Optimizing a brachytherapy plan by visualizing OARs on MRI imaging compared to optimizing to a HR- CTV volume.

Introduction

Brachytherapy is the gold standard treatment for cervical cancer. One of the considerations for patient care is the time in which it takes from applicator insertion to finishing treatment. At ONJWC a planning study was undertaken to trial the plan quality of an image based plan versus a plan to the HR CTV volume.

Aim

The aim of this planning study was to assess the acceptability of a brachytherapy plan without volumes and compare it with a plan with the HR CTV by comparing the DVH values for HR CTV coverage and OAR tolerances of the plans.

Method

10 cervical brachytherapy patients were selected to compare plans with and without HR CTV volumes contoured by the Radiation Oncologist. An experienced brachytherapist planned the treatment based on visually optimizing a plan based on the MRI images to avoid dose to the relevant OARs. An HR CTV was then contoured and the plan was then further optimized for coverage and compared to the initial plan. Data was collected on the DVH differences of the OARs.

Discussion

Preliminary data suggests visually planning is more conservative and spares OAR toxicities compared to HR CTV planning and optimizing for coverage.

Conclusion

This study indicates that an experience brachytherapist is able to visually plan a cervix treatment based on the imaging dataset and ensure OAR tolerances are achieved. Planning to HR CTV has demonstrated improved coverage to the tumour volume.
Androgen deprivation therapy (ADT) use with post-prostatectomy radiotherapy (PPRT) in the Prostate Cancer Outcomes Registry Victoria (PCOR-Vic)

ABSTRACT

Introduction: The aim of this study is to evaluate the use of androgen deprivation therapy (ADT) use with post-prostatectomy radiotherapy (PPRT) in a population-based cohort of Australian men.

Methods: This is a prospective cohort of men with localised prostate cancer captured in the Prostate Cancer Outcomes Registry Victoria (PCOR-Vic), who received PPRT between January 2010 and December 2015. The primary outcome is ADT use with PPRT. Multivariate logistic regressions were used to identify patient-, tumour- and institutional factors influencing ADT use.

Results: 485 men were included in this study – 115 (24%) had pT2 disease, 231 (48%) pT3a, 134 (28%) pT3b and 5 (1%) pT4. Eighteen (4%) men had ISUP grade 1 disease, 139 (29%) ISUP grade 2, 170 (35%) ISUP grade 3, and 158 (33%) ISUP grade 4/5, while 267 (64%) men had positive surgical margin. Median time from prostatectomy to PPRT was 8.1 month (IQR=5.3-13.9). Sixty-six (14%) patients had ADT with PPRT. In multivariate analyses, increased age (OR=1.06; 95%CI=1.01-1.11), seminal vesicle involvement (OR=3.81; 95%CI=1.63-8.91) and men treated in regional centres (OR=2.17; 95%CI=1.08-4.33) were more likely to have ADT with PPRT.

Conclusion: We reported 14% of men treated with PPRT received ADT in a population-based cohort of Australian men, which was less than half of the proportion of ADT use with PPRT in the US. It will be of interest to evaluate the uptake of ADT with PPRT in the coming years following recent publications of level 1 evidence confirming overall survival benefits of ADT with PPRT.
Symptoms and Solutions for cancer patients receiving chemotherapy

BACKGROUND/OBJECTIVES: Upper gastrointestinal symptoms including taste changes, nausea, dry retching and vomiting are common in patients receiving certain chemotherapy regimens. This study was devised to determine which symptoms chemotherapy patients experience and can those who develop symptoms of taste changes, nausea and vomiting be predicted by genetics of taste and if any mouth wash solutions benefit symptomatic patients.

SUBJECTS/METHODS: Thirty-two patients (27 breast cancer, 5 colorectal cancer) programmed to receive cyclophosphamide or 5-FU regimens were recruited from a tertiary hospital chemotherapy day oncology department. Twenty-seven patients (24 breast, 3 colorectal) completed the study. Prior to chemotherapy commencement, genetic characteristics of participants taste were tested and number of taste buds counted. After 2 cycles of chemotherapy participants rated their symptoms for appetite, taste changes, nausea and vomiting. Sixteen (53%) of patients suffered excessive symptoms. Eleven patients trialled 6 simple mouthwashes: water, salt, sodium bicarbonate, sugar, ginger and peppermint, in a random order for 1 day each following cycle 3 of chemotherapy. Participants rated the effectiveness of each mouthwash in reducing symptoms via a questionnaire.

RESULTS: Of the 27 patients completing the study 20 (74%) reported anorexia, 16 (59%) taste changes, 19 (70%) nausea and 7 (26%) dry retching or vomiting. All solutions trialled in 11 patients improved symptoms in some of the patients. Peppermint water and sodium bicarbonate gave the greatest improvement in mouth feel and symptom control.

CONCLUSION: This study provides evidence that gastro-intestinal symptoms of chemotherapy can be relieved or eliminated with simple mouth wash solutions.
Changes in weight, nutritional intake and symptoms in breast cancer patients receiving chemotherapy

BACKGROUND/OBJECTIVES: Chemotherapy (CThx) is one of the most widely used treatment options for breast cancer patients. Adjuvant CThx is associated with weight changes in breast cancer. Weight gain is thought to be common and associated with decreased quality of life and increased comorbidity risk. This study aimed to determine whether chemotherapy regimens for breast cancer influence body weight and to assess the relationship between weight changes, nutritional intake and symptoms.

SUBJECTS/METHODS: An audit of weight changes of 39 breast cancer patients receiving CThx regimens of cyclophosphamide was completed. Twenty-seven breast cancer patients (n=27 female, age 52±10 years) were prospectively recruited to investigate causes of weight changes, 25 completed the study. Weight, symptoms and dietary intake were recorded on recruitment, at cycle 3 and after treatment completion.

RESULTS: The audit demonstrated 12 (31%) patients gained weight, 7 (18%) remained weight stable and 20 (51%) lost weight from commencement to treatment completion. Of the 25 patients prospectively recruited, eleven (44%) gained one kilogram (kg) or more (4.2±1.9 kg), ten patients (40%) lost 1 kg or more (3.5±2.7 kg) and four (16%) remained weight stable. Patients who gained weight tended to be lighter and pre-menopausal compared to those who lost weight. Of the 24 patients with complete food records, 10 gained weight, nine lost weight and four remained weight stable. In the weight gain group, energy and protein intake increased during cycle 3 then fell below baseline after treatment completion. Patients that lost weight tended to be post-menopausal, experience more symptoms and both energy and protein intake decreased over the treatment period.

CONCLUSION: Breast cancer patients undergoing chemotherapy were as likely to experience weight loss as weight gain, with post-menopausal women experiencing greater weight loss. A decrease in energy and protein intake and more symptoms were accompanied by weight loss.
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Introduction of huddles during nursing shifts to promote teamwork, staff development and patient outcomes

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Aim
The aim of this project was to develop, implement and evaluate the introduction of a “check-in” huddle designed to enhance teamwork and identify immediate learning (foundational and specialty-based) and support needs of nursing staff working on 7 South.

The large geographical layout, limited communal work spaces for staff and use of COWs means that nurses spend much of their shift isolated from their nursing colleagues as well as medical and allied health teams. An unintended consequence of this has been a reduction in: experiential learning (the most common method of learning for post-registration nurses working in oncology/haematology); identification of patient care needs by staff with limited specialty knowledge, and; (re)allocation of resources to support nurses who need help during their shift.

Methods
The introduction of huddles followed a review of the literature and consensus of the ward leadership team. The wider nursing team were consulted and feedback via meetings and survey were sought during the planning, implementation and evaluation phases.

Results
The huddles were introduced January 2018 by pairing a more senior staff with a more junior staff member. Staff uptake was initially high, however, by June nurses were no longer engaging in huddles routinely. Nursing staff reported that they while they agreed with the concept the burden of responsibility on senior staff was high. Key changes to the huddle were made including: teams of three +/- ANUM/NUM, set time and set questions.

Conclusion
The implementation of structured “check-in” huddle during each shift has improved the timeliness of support as well as identified key learning needs of nursing staff, irrespective of skill level. The impact of the second iteration of the huddles is currently being evaluated, however, preliminary findings suggest that this version is meeting the support needs of the least experienced members of the nursing team and supplementary staff but more work is required to ensure support is extended to staff needing to develop their specialist knowledge.
Impact of the National Disability Insurance Scheme on a spinal outreach service.

Ms K. Macdonald and Ms E. Garner.


Introduction: The National Disability Insurance Scheme (NDIS) is rolling out incrementally to provide care, equipment and services for Australians with permanent disabilities. The Spinal Outreach Service (SOS) at Austin Health offers expertise in spinal cord injury and appears to have experienced an increase in service demand since the NDIS commenced. The project aimed to assess and analyse this impact, and to provide recommendations to Austin Health on how best to address this in the future.

Methods: A qualitative survey was developed and distributed to SOS staff. Episodes of direct contact with service users was also analysed, and a comparison between pre and post-NDIS data completed.

Results: 6 out of 7 staff completed the survey. Emerging themes included the perception of increased workload since NDIS commenced, the need for further education around the scheme and additional administrative support. Reviewed quantitative data showed an increase of 30% in overall contacts, and 38% more clinical time spent with clients since NDIS commenced. 71% of SOS clients will be eligible by roll out completion.

Conclusion: This project concluded by providing recommendations to Austin Health, regarding moving forward with the SOS in the context of NDIS. These included the potential registration of the SOS, in order to ensure that clients with spinal cord injuries continue to receive care from clinicians with expert skills and experience in this field.
Rees L

Telehealth – connecting specialist health services to Victorians with spinal cord injury.


Aim
Telehealth has been identified as an innovative channel to support community based clients living with SCI. Introducing Telehealth into healthcare settings relies on acceptance to deliver a new health care model; drive to implement changes from those who will be at the face of delivery; and, well informed and engaged participants. Multidisciplinary health surveillance reduces the incidence of secondary complications due to SCI, therefore this project aimed to introduce a sustainable and successful Telehealth program to the Victorian Spinal Cord Service (VSCS).

Methods
A literature review, benchmarking, and stakeholder surveys (clients and clinicians) were completed, to identify core pilot components.
Feedback identified two opportunities:
- Regional surveillance pre-screening
- Routine use of Telehealth with Spinal Community Integration Service clients

Results
Trial of Telehealth commenced in May 2017, with clinicians and clients embracing the new communication method. Clinicians have shown innovation regarding Telehealth’s use, including equipment prescription for remotely based clients, and incorporating Telehealth training as part of inpatient rehabilitation.

Conclusion
Telehealth uptake has been positive, highlighting ways to build capacity with community health services, improve time and resource management, and offer a broader delivery of health surveillance to VSCS clients.

References
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Nerve transfers in Tetraplegia - a worldwide perspective

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The introduction of nerve transfers (NT) has resulted in a paradigm shift for upper limb reconstructive surgery in tetraplegia offering new hope in upper limb reanimation. Combinations of nerve and traditional tendon procedures have the potential for superior long-term outcomes, however uptake of these new techniques worldwide is unknown and in its infancy.

Aim
To undertake an online international survey to investigate the uptake and experience of clinicians using nerve transfers for the Spinal Cord Injury (SCI) population.

Method
412 surgeons and therapists known to be working in upper limb reconstructive surgery for SCI were targeted. “Snowballing” was used to broaden the respondent base. Respondents completed a 20 minute survey comprising 85 questions – half specific to surgeons and half to therapists.

Results
57 people responded from 23 centres worldwide (30 surgeons and 27 therapists). Beginning with 1 surgeon in 2011; now 22 surgeons and 20 therapists report working in this specialized field in 2018. The key reasons for not offering NT surgery were lack of training, support and evidence base. 100% (n=22) of those undertaking NT surgery believe it should be offered in the first year post injury with 90% (n=17) undertaking the SPIN procedure for hand opening. Only 30% (n=6) currently offer NT for grasp or pinch. There was little consensus on use of outcome measures, postop protocols or ongoing therapy techniques. Therapists noted an increased workload with longer therapy involvement, greater shared care with community therapists and the need to provide more education following NT.

Conclusion
Uptake of NT surgery for SCI is growing worldwide with apparent agreement on timing, prerequisites of surgery and its use in hand opening. Further evidence is required to establish the benefits of NT for grasp and pinch and to establish consensus on outcome measurement and post-operative management. We aim to repeat the survey in 2021.
A framework for stroke rehabilitation facility design: A multi-disciplinary approach

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5. The Hopkins Centre Research for Rehabilitation and Resilience, QLD

Background: Many stroke patients require inpatient rehabilitation to re-learn skills or abilities. Hospital design can impact patient outcomes, but most hospital design research has been in acute healthcare settings. Rehabilitation facilities are unique because they are both a healthcare space and a learning space. The priorities for the design of stroke inpatient rehabilitation facilities are therefore likely to be different from acute healthcare settings.

Aims: The aim of this project was to determine what experts think is important in the design of inpatient stroke rehabilitation facilities.

Methods: A Value-Focused Thinking expert-elicitation methodology was carried out over 2 workshops which were attended by selected experts, including: Past stroke patients; clinicians with experience in stroke rehabilitation; healthcare environments academics; learning environments academics; architects and designers of healthcare or learning environments; and health policy-makers. These experts used Value-Focused Thinking to iteratively identify what they considered important in the design of rehabilitation facilities, and to structure these values into a hierarchical framework.

Results: Twenty-eight experts attended workshop 1, and 16 attended workshop 2. The final framework of values suggested that an optimal stroke rehabilitation building should: 1) maximise the efficiency of the facility; 2) maximise the effectiveness of the facility, i.e., maximise patients’ outcomes; 3) foster emotional well-being of all users; and 4) maximise safety for all users. The hierarchy provided new insights into how potentially conflicting values (e.g., safety vs. practicing physical function) could coexist.

Conclusions: Value-Focused Thinking provided a creative yet systematic methodology for a multi-disciplinary question in healthcare design. The framework developed in this study can be used to structure evaluation of existing facilities and to inform the design of new facilities and refurbishments.
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Use of polyethylene-glycol hydrogel in novel stem cell therapies for Hirschsprung Disease

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Aim
Hirschsprung Disease is characterised by a defect in the enteric nervous system, resulting in a lack of innervation to the distal gut. Stem cell therapies have been proposed as a potential adjunct to surgical approaches. Serosal application, whereby a synthetic membrane carrying neural stem/progenitor cells (NSP) is wrapped around the affected gut, has been proposed as a safe and effective method of NSP delivery. These cells would then reach their final position via trans-serosal migration. A potential candidate for this membrane is the polyethylene-glycol (PEG) hydrogel. This study aimed: (1) To characterise the ability of PEG hydrogels to support adhesion, growth and migration of neural cells; (2) To compare the PEG hydrogels with the RGD-PEG hydrogel, containing a cell adhesion amino-acid moiety cross-linked to the membrane surface.

Methods
Neural tubes, containing NSP were dissected from embryonic day 2 quail. These were transferred to PEG hydrogel, RGD-PEG hydrogel, or control fibronectin coated plates, immersed in culture medium and incubated for 48 hours. Samples were then assessed immunohistologically for NSP cells and cell adhesion molecules.

Results
After 48 hours, neural tubes were observed to adhere to PEG hydrogel, RGD-PEG hydrogel and control fibronectin plates. Those neural tubes that adhered to the PEG hydrogel showed no signs of NSP migration. Conversely, NSP cells were immunologically demonstrated to have migrated away from neural tubes on both the RGD-PEG hydrogel and control fibronectin plates. Those on fibronectin coated plates migrated further and in greater numbers when compared to those on RGD-PEG hydrogel.

Conclusion
This study shows that whilst the PEG hydrogel is inadequate, the RGD-PEG hydrogel membranes may support the growth and migration of neural cells. However, it is likely that further modifications to the surface of PEG hydrogels would be of benefit in ensuring greater neural cell adhesion and migration.
Abstract

**Background:** Monocytes in the circulation expressing both the CD14+ and CD16+ monocytes antigens are known to be pro-inflammatory and elevated in a number of autoimmune conditions. Patients undergoing total knee replacement (TKR) are in a number of occasions known to have residual pain post TKR despite the operation. This is frequently associated with inflammation and pain. The question is whether circulating CD14+/CD16+ monocytes might identify this patient population pre-operatively. It is recognised that subclinical fibromyalgia is also a contributor to non-inflammatory post-operative pain.

**Methods:** A prospective, observational study with a follow up of three months was conducted. We measured 15 participants’ CRP and CD14+/CD16+ monocyte population as an overall percentage of CD14+ monocytes prior to their surgery. Their level of subclinical fibromyalgia was also assessed. Participants’ change in pain was assessed using validated questionnaires and statistical analysis was carried out using R Studio.

**Results:** At time of submission, seven patients have completed their follow up. It was found that patients with higher CD14+/CD16+ monocyte percentages experienced significantly less pain reduction. Pearson’s correlation coefficient was calculated to be -0.82 (p < 0.05). A linear regression model for prediction of percentage pain reduction based on monocyte percentages and subclinical fibromyalgia scores showed that for every 10-fold increase in CD14+/CD16+ monocyte percentage, participants will experience a 30% less pain reduction.

**Conclusion:** Our findings suggest that CD14+/CD16+ monocyte population is potentially a valid predictor of chronic pain post TKR. It is a significant predictor of chronic pain, likely of inflammatory nature. A sufficiently powered study may be required to further confirm this.
Reducing early morning falls; it's in the timing.

1Austin Health, Heidelberg, VIC

Aim
The overall aim is to reduce the number of falls in the Palliative Care Unit, falls has been identified as one of the major clinical risks for patients in the Palliative Care Unit. A review of the data for a 12-month period (February 2016 - February 2017) highlighted a peak time of 0600-0700 for patient falls, with a total of 16 falls occurring at this time. This time period is when patients are waking up and starting to get up and go to the toilet. Nursing staff at this time are usually attending to pain medication for patients; this takes two nurses to check, leaving only one nurse in the patient clinical area, and unable to constantly supervise patients.

Methods
A six month trial of changing the Health Assistant in Nursing (HAN) starting time to 0600 to assist with all daily living activities (ADL’s) of patients was negotiated and started in early June. The HAN role includes assisting patients with attending to daily living activities, under the guidance of registered nurses in particular; this includes escorting patients to the bathroom.

Results
There have been 42 falls in the 6 month trial period. Only 2 of these falls occurred between 0600 and 0700, and one of these were on days that the HAN was not working. This is a 73% reduction in falls for the morning period and an overall reduction of falls of 20%.

Conclusion
By identifying the peak time of falls on the ward and likely contributing factors, we were able to introduce an earlier additional staff member to address the likely issue of patients needing to go to the bathroom when they get up. The significant reduction in falls over this period has resulted in a permanent change of starting time for the HAN on our unit.
Title of abstract: Implementing a delirium framework into a Palliative Care setting

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3. Palliative Care Consultant, Austin Health

Aim
The overall aim was to trial and introduce the most appropriate delirium assessment tool for the inpatient palliative care unit to assist nursing, medical staff and allied health to recognise early signs of delirium and implement an appropriate care pathway relevant to each individual patient’s goal of care. To reduce variation in care, a clear pathway was developed that recognises, assists with diagnoses, and manages the delirium specific to our patients and relative to their stage of illness.
A recent analysis of falls data had found that at least fifty per cent of patients with falls had cognitive impairment; this provided further impetus to improve recognition and management of delirium.

Methods
A multi-disciplinary working group was established to identify a suitable assessment tool that worked within our model of care and incorporated prevention strategies. Once identified, this tool was implemented on the ward. A care pathway and related guidelines were also developed.

Results
The Nursing Delirium Screening Scale (NuDESC) rating tool was successfully implemented and is completed at least twice daily on every patient. Auditing of assessment and adherence to guideline has been undertaken with positive results.

Conclusion
Introducing this tool has allowed for earlier and more accurate detection of delirium, with greater awareness amongst staff and rapid implementation of management strategies, thus improving patient care.
RETROSPECTIVE REVIEW OF 27 CASES REPORTED AS LOW GRADE SEROUS OVARIAN CARCINOMA

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Background
Understanding of serous carcinoma involving the ovary has changed greatly over recent decades. Serous ovarian carcinoma involving the ovary was previously graded using a three-tier system. Low grade serous ovarian carcinoma (LGSOC) and high grade serous carcinoma (HGSC) are now recognized as distinct and separate entities, neither of which are graded. These entities have different pathogenesis, with HGSC involving the ovary being an aggressive neoplasm, commonly originating from the fallopian tube. By comparison LGSOC is an uncommon malignancy, often occurring in the setting of a borderline serous tumour, encountered in a younger population, with a typically prolonged survival compared to HGSC. Specific prognostic variables for LGSOC are not established.

Aims
Our study aims to identify cases of LGSOC using current diagnostic criteria enabling subsequent prognostic analysis of this cohort.

Methods
A retrospective histological review of cases clearly diagnosed as LGSOC over a 12 year period (2005 – 2016) was performed. World Health Organization (WHO) 2014 criteria were used for final classification.

Results
From the database search, 27 cases were identified to have been clearly diagnosed as LGSOC, with slides available for review. An additional 8 external cases were excluded as slides were not available for review. Of 27 cases reviewed by the authors, 23 met current diagnostic criteria for LGSOC, and 4 (17%) were reclassified (3 HGSC, and 1 FIGO G1 endometrioid adenocarcinoma). In two confirmed LGSOC cases, seromucinous carcinoma was also considered. All cases either reclassified, or considered for reclassification were reported prior to 2014, and reclassification was assisted by immunohistochemistry.

Conclusions
Histological review of slides with current criteria (WHO) resulted in reclassification of 17% of cases previously diagnosed as LGSOC. Diagnostic challenges occasionally exist between LGSOC and HGSC, and with some forms of serous borderline tumour. Separation of LGSOC and HGSC is essential given the very different prognostic and treatment implications, and reflects the differing pathogenesis of these tumours.
Claire Keith¹, Jane Booth², Parnaz Aminian¹

Finding the needles in a haystack – automated detection of Adverse Drug Reactions through ICD-10 coding

Aim: Amongst Australian experts it was felt ICD-10 coding held largely untapped potential to improve adverse drug reaction event reporting rates¹. We designed a pilot study (December 2016 to November 2017) exploring this hypothesis.

Method: An ICD-10 coding report was run monthly; discharge episodes with predetermined codes were flagged for review. Codes were refined with input from Health Information Services.

Results: During the intervention period, an additional 256 ADR events were detected through ICD-10 coding (compared to 319 through parallel standard voluntary reporting). Sub-types included 14 cases of anaphylaxis, 7 cases of angioedema, 8 cases of severe immune reactions to checkpoint inhibitors. 223 additional reports from ICD-10 coding were submitted to Therapeutic Goods Administration; 97 patients received an individualised alert letter (with companion letter to their general practitioner). For 117 patients, their drug allergy alert in the Cerner electronic medication management system was amended.

Challenges included an increased pharmacist workload, and unfamiliar IT processes. A strength of our project was the combination of automated ADR screening techniques with individualised case follow-up.

Conclusion: ICD-10 coding offered a valuable opportunity to identify, document and follow-up significant adverse drug reaction reports, which were otherwise missed by formal voluntary clinician reporting. Benefit is expected to both individual patients, as well as the community through enhanced macro pharmacovigilance.


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2. Pharmacy Department, Monash Health
Imported medicines: a pre-emptive approach to procurement, striving to enhance point-of-care medication safety

Use of imported medicines (via Special Access Scheme, “SAS”) has become an accepted part of Australian tertiary care. Reasons for this are multifactorial – local supply shortages, discontinuation of low usage off-patent medicines, and niche prescribing for complex patients.

Sourcing medicines outside our regulatory system brings theoretical pharmaceutical quality risks of counterfeit items or contaminants. Purchasing items through countries with comparable regulatory standards (North America, European Union, United Kingdom) is preferred. Independent to this, new medication risks can be introduced including foreign language labelling, and packaging not compliant to our national standards\(^1\). The SAS stock procurement cycle involves a range of staff (e.g. the prescriber, pharmacists and purchasing officers) both at hospitals and Australian-based wholesalers. Decisions can be made based on availability or price, without full consideration of the clinical safety implications.

Our pre-emptive upstream approach includes:

- Awareness training of staff
- Requesting quotes to include English labelled products among cost comparisons for new product lines. Photographs of stock labelling is helpful
- Investigation of the manufacturer for listings on other regulated markets
- Pharmacist checking stock upon arrival for labelling and quality issues
- Strategies to mitigate risks – including review of intravenous guideline text, additional package labelling, consideration of clinical alternatives

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\(^1\) Medicines Shortages in Australia – a snapshot of shortages in Australian Hospitals. SHPA 2017

\(^2\) Graudins LV, Treseder R, Hui C, Samuel T, Dooley M. A proactive quality strategy to decrease the risk of error associated with medication procurement. Journal of Pharmacy Practice and Research (2016); 46:145-51
Special handling required! Implementing a guideline for hazardous medication handling at a major tertiary hospital

Procedures around handling of chemotherapy, a subset group of hazardous medications, have been widely described and well-regulated at Australian organisations. What are the guidelines where APF label 21 ‘Special handling and disposal required – ask your pharmacist,’ is recommended?

We describe the roll out of an evidence-based handling of hazardous medicines guideline to our institution; this guides hospital staff on the safe handling of non-cytotoxic medicines that may pose a risk to the health worker. Medicines included in the guideline fall into three groups; those that are known hazardous non-cytotoxic medicines; those that primarily pose a risk to health workers actively trying to conceive, are pregnant or breastfeeding; and those that are irritant to mucosal membranes or airways. The guidelines give stepwise personal protective equipment measures based on the degree of risk of exposure (e.g. administering a whole, intact tablet vs. preparation of an injectable product).

Implementation of the guideline needs a multi-modal strategy, with widespread education and engagement of nursing, pharmacy and medical staff. The strategies include: presentations via the clinical nurse educators; internal intranet campaigns; pharmacy education sessions, and additional content within the electronic Medication Management System. A sensitive approach is required to address any potential concerns of staff that previous practices may have allowed dangerous exposure.

Education and awareness of the guideline will allow staff confidence in knowing how to protect themselves when administering hazardous non-cytotoxic medicines. It also delivers a consistent in approach for patients under their care.
To tell or not to tell? How we do open disclosure.

Background:

Open disclosure is the open communication that takes place between health practitioners and their patient after an adverse event. It is a process that seeks to provide compassion for the patient during a tumultuous time with the aim of re-establishing trust and allowing the provision of good and safe medical care to continue. The Australian Open Disclosure Framework was released by the Commonwealth of Australia in 2013 and defines open disclosure as an open discussion with a patient about an incident(s) that resulted in harm to that patient while they were receiving health care.

Objective:

To determine the rate of open disclosure documentation in incident severity reports (ISR) 1 and 2 in 2016 following delivery of educational sessions in open disclosure by the Austin Health Quality and Patient Safety Unit.

Design:

ISR 1 and 2 clinical incidents reported in VHIMS were reviewed over the 2016/2017 calendar year. In looking for documentation of open disclosure data was sourced from the Riskman reporting system (Riskman), the Scanned Medical Record (SMR) and the medical records documented on the Cerner system (Cerner).

Conclusion:

This process acknowledges the experience of the patient and/or significant others following an adverse event. Comprehensive documentation at the time is noted to contribute significantly to successful open disclosure. Further education across all available modalities and dynamic review of clinician understanding of Open Disclosure is required.

Authors: Melanie Stephenson, Amanda Charles, Kathryn Law, Joe Rotella
Never wait to escalate! (Cases of failure to escalate at Austin Health)

Background:
A review of cases presented at the Clinical Review Panel (CRP) at Austin Health from January 2017 to June 2018 was performed. Anecdotally, concerns had been raised by senior clinical staff that there may have been issues with a failure to escalate care of patients resulting in adverse outcomes. Following the review of 26 cases that had been presented to CRP, there was identification of 5 cases where failure to escalate care was a factor in an adverse outcome.

Objective:
To review cases of FTE and analyse potential failures to escalate in the 10 days prior to their adverse event.

Design:
Of the 26 cases reviewed at CRP over 2017/2018 5 cases were identified where FTE contributed to poor outcome. A standardised audit tool was created. Scanned Medical Records and Medical Records documented on Cerner were utilized to identify and analyse potential failures in escalation in the 10 days prior to patient adverse event. Potential barriers to escalation were identified and compared to current literature.

Variables reviewed included:
- the number of MET/MER/UCR calls made;
- day and time of day the calls occurred;
- was there alteration to the call criteria;

Conclusion:
All the patients identified were older than 60 years and had length of stays > 10 days. All of the MET/MER/UCR calls were after hours. Only 3 had documented Consultant discussions. Number of changing of escalation criteria ranged from 0 to 6. Ongoing MET calls despite altered criteria was present in all 4 cases where the patient died during admission. Barriers to escalation at Austin Health align with current literature. These include lack of familiarity with escalation pathways, professional hierarchies and expectations of adverse interpersonal or clinical outcomes.

Authors: Melanie Stephenson, Amanda Charles
Sellars M,1,2 Morton RL,3 Clayton JM,1,4 Tong A,5,6 Mawren D,2 Silvester W,2 Power D,7 Ma R,8 Detering KM,2,9

A case-control study of end-of-life treatment preferences and costs following advance care planning for adults with end stage kidney disease.

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8. Clinical Costing, Austin Health, Melbourne, Australia;
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Aim
To examine the efficacy of advance care planning (ACP) to improve the likelihood that end-stage kidney disease (ESKD) patient’s preferences will be known and adhered to at end-of-life.

Methods
A case-control study of a nurse-led ACP program in adults with ESKD from a major tertiary hospital, Austin Health, Melbourne, Australia. The primary outcome was the proportion of patients whose preferences were known (by substitute decision maker and/or clinicians) and adhered to by their treating doctors. Secondary measures were health system resource use and costs ($AUD) for a nurse-led ACP intervention in the last 12-months of life.

Results
In total, 57 cases (38 men, mean age 73.8 years) and 57 historical controls (38 men, mean age 74.0 years) were included. Cases (38/57, 67%) were significantly more likely than controls (15/57, 26%) to have their preferences known and adhered to by their treating doctor at end-of-life (p<0.001). Cases (33/40, 83%) were also significantly more likely to withdraw from dialysis in accordance with their preferences than controls (11/33, 33%) (p<0.001). For cases, the average hospital costs in the last 12 months of life was AUD $99,077 (SD = $71,002) per patient. The total cost of the ACP program in 2010/11 was AUD $26,821.

Conclusion
ACP was associated with improvements in end-of-life care preferences being known and adhered to for people with ESKD.
Authors: Marnie Graco, 1,2 Sally E Green, 3 Sandra Henderson, Alyssa Rigoni, 1 Carmel Nicholls, 1 Julie Tolson, 1 Bronwyn Stevens, 1 Maree Barnes, 1 David J Berlowitz. 1,3

Title: Burden versus benefit of continuous positive airway pressure therapy for the treatment of obstructive sleep apnoea in chronic tetraplegia: a mixed methods study.

1 Institute for Breathing and Sleep, Austin Health, Melbourne, Victoria, Australia
2 The University of Melbourne, Department of Medicine, Melbourne, Victoria, Australia
3 Monash University, School of Public Health and Preventive Medicine, Melbourne, Victoria, Australia
4 The University of Melbourne, Department of Physiotherapy, Melbourne, Victoria, Australia

Introduction
Continuous Positive Airway Pressure (CPAP) therapy is the recommended treatment for obstructive sleep apnoea (OSA). Adherence to CPAP may be worse in tetraplegia than in the non-disabled due to additional physical and psychosocial issues. The aim of this study was to estimate CPAP adherence in people with tetraplegia and OSA, and to explore barriers and facilitators to CPAP use.

Methods
People with chronic tetraplegia and OSA were implemented with autoset CPAP and supported for one month. Semi-structured interviews were conducted with participants at one month and analysed thematically. CPAP usage data were collected at one and six months, with “adherent” defined as achieving more than four hours average per night.

Results
Sixteen patients completed the study (80% male; mean age 56(SD=15)). Mean nightly CPAP at 4 weeks was 3.07 hours (SD=2.53) with 38% adherent, and at 6 months was 2.6 hours (SD=2.8), with 25% adherent. Whether the benefits from CPAP were perceived to be relatively greater than the burdens strongly influenced ongoing use. Burdens were common, and included mask discomfort, physical and emotional problems. Participants were motivated by the immediate daytime benefits to mood, alertness and sleepiness. They tended not to recognise their symptoms of OSA until after they were treated.

Conclusion
CPAP use is challenging for people with tetraplegia, who experience substantial burden from using the device. When tolerated, the proximate benefits are substantial. People with tetraplegia need more intensive support for longer to help them overcome the burdens of CPAP.
Authors: Marnie Graco,1 2 David J Berlowitz,1 3 Sally Green4

Title: Understanding the clinical management of obstructive sleep apnoea (OSA) in tetraplegia: a qualitative study using the theoretical domains framework (TDF).

Affiliations:
1 Institute for Breathing and Sleep, Austin Health, Melbourne, Victoria, Australia
2 The University of Melbourne, Department of Medicine, Melbourne, Victoria, Australia
3 The University of Melbourne, Department of Physiotherapy, Melbourne, Victoria, Australia
4 Monash University, School of Public Health and Preventive Medicine, Melbourne, Victoria, Australia

Background: Clinical practice guidelines recommend further testing for people with tetraplegia and signs and symptoms of obstructive sleep apnoea (OSA), followed by treatment with positive airway pressure therapy. Little is known about how clinicians manage OSA in tetraplegia. The theoretical domains framework (TDF) is commonly used to identify determinants of clinical behaviours. This study aimed to describe OSA management practices in tetraplegia, and to explore factors influencing clinical practice.

Methods: Semi-structured interviews were conducted with 20 specialist doctors managing people with tetraplegia from spinal units in Europe, UK, Canada, USA, Australia and New Zealand. Interviews were audiotaped for verbatim transcription. OSA management was divided into screening, diagnosis and treatment components for inpatient and outpatient services, allowing common practices to be categorised. Data were thematically coded to the 12 constructs of the TDF. Common beliefs were identified and comparisons were made between participants reporting different practices.

Results: Routine screening for OSA signs and symptoms was reported by 10 (50%) doctors in inpatient settings and eight (40%) in outpatient clinics. Doctors commonly referred to sleep specialists for OSA diagnosis (9/20 in inpatients; 16/20 in outpatients), and treatment (12/20; 17/20). Three doctors reported their three spinal units were managing non-complicated OSA internally, without referral to sleep specialists. Ten belief statements representing six domains of the TDF were generated about screening. Lack of time and support staff (Environmental context and resources) and no prompts to screen for OSA (Memory, attention and decision processes) were commonly identified barriers to routine screening. Ten belief statements representing six TDF domains were generated for diagnosis and treatment behaviours. Common barriers to independent management practices were lack of skills (Skills), low confidence (Beliefs about capabilities), and the belief that OSA management was outside their scope of practice (Social/Professional role and identity). The three units independently managing OSA were well resourced with multidisciplinary involvement (Environmental context and resources), had ‘clinical champions’ to lead the program (Social influences).

Conclusion: Clinical management of OSA in tetraplegia is highly varied. Several influences on OSA management within spinal units have been identified, facilitating the development of future interventions aiming to improve clinical practice.
**Background**
Drug-induced interstitial lung disease (DILD) is the most common form of drug-induced pulmonary toxicity. Early detection of DILD has the potential to improve outcomes, however studies which have examined the accuracy of pulmonary function testing (PFT) in patients being monitored for DILD have shown conflicting results. This is the first systematic review to investigate the sensitivity and specificity of PFT for an early detection of DILD caused by various drugs known to be associated with DILD. A broad systematic review was conducted which included both chemotherapeutic and non-chemotherapeutic agents. In this report the results for non-chemotherapeutic agents will be presented, and the results of chemotherapy studies will be presented in a separate report.

**Methods**
Ovid MEDLINE and EMBASE were searched through 9th of February 2018, for literature that evaluated PFT for the detection of DILD using MeSH terms. We used Google Scholar to search for conference abstracts. Prospective and retrospective cohort studies and randomised clinical trials that utilised any form of PFT during treatment with a prespecified list of drugs known to cause DILD, including, but not limited to, Amiodarone, methotrexate and nitrofurantoin. Studies were excluded if they included participants who had concurrent chest or mediastinal radiotherapy or were <18 years of age or had fewer than 10 participants. Two independent reviewers extracted data using pre-defined criteria and evaluated the quality of included studies using established criteria.

**Results**
There were 4,065 citations (after removal of duplicates) identified, 195 full text articles were then reviewed, and 42 studies were included in our qualitative synthesis. Out of these, 15 articles evaluated non-chemotherapeutic agents, however only 9 articles (7 for Amiodarone, 1 for low dose Methotrexate and 1 for Rituximab) provided sufficient quantitative data. Included studies were clinically heterogeneous and therefore meta-analysis was not performed. Study quality of the included studies were variable. The majority of studies reported changes in diffusing capacity for carbon monoxide (DLCO) and a few reported spirometry. Sensitivity for monitoring changes in DLCO while on Amiodarone ranged between 20-100% in individual studies and specificity varied between 54-83%.

**Conclusion**
The current evidence base does not support the routine use of PFT for the early detection of DILD. For some clinical settings future studies, if large enough and well conducted, may provide more precise and valid estimates of the value of PFT. Further research into alternative methods for early detection is needed. Methodological quality of included studies was often limited by the lack of a gold standard approach to the diagnosis of DILD and the development of internationally accepted consensus guidelines for the diagnosis of DILD will facilitate further research in this field.
Respiratory function in people with neuromuscular disease: characteristics and association with past history of respiratory tract infection

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4. Department of Physiotherapy, Austin Health, Heidelberg, Vic., Australia.

Aim
People with neuromuscular diseases (NMD) have reduced lung volumes, weaker coughs and an increased risk of respiratory tract infections (RTI). This study examined associations between lung function measures and their relationship with RTIs.

Methods
Cross-sectional observational study of Victorian Respiratory Support Service patients with NMD and respiratory involvement (vital capacity (VC) <80% predicted). Spirometry, lung volumes, total respiratory system compliance (Crs), respiratory muscle strength and cough were measured. History of RTI defined as a hospital admission or general practitioner diagnosis plus antibiotic use during the past year was recorded. Descriptive statistics (mean±SD), associations (Pearson’s correlation coefficients) and group comparisons between those with/without a RTI (Student’s t-tests) were performed. The relationships between respiratory function, peak cough flow (PCF) and RTI were examined using linear and logistic regression modelling.

Results
Sixty participants with severe restriction (VC 39±18% predicted) are reported. Significant correlations existed between Crs and lung volumes (inspiratory capacity (IC) r=0.63) but not with respiratory muscle strength. Peak cough flow was associated with VC (r=0.59, p<0.001), IC (r=0.65, p<0.001), Crs (r=0.48, p<0.001) and maximal expiratory pressure (MEP, r=0.47, p<0.001). The IC and MEP explained 69% of the variability in PCF (p<0.001). Participants with a RTI in the previous year had lower VC (32±17% vs 45±16%, p=0.003) and PCF (154±51 vs 200±76 L/min, p=0.009). Only IC was significant in the regression model for RTI (standardised OR (95% CI) = 2.19 (1.08,4.47), p=0.03).

Conclusion
Respiratory system compliance is an important factor in severe respiratory restriction; lung volumes are related to Crs but not respiratory muscle strength. Compliance and lung volumes are associated with cough flow generated, however the most important factors are IC and expiratory muscle strength. Inspiratory capacity is also related to a history of RTI. Therapies that improve IC and Crs may prove beneficial in people with NMD.
Hatch M,^1 Goh NSL,^2,3 Khor YH^2,3

Baseline Inflammatory Markers and Survival in Patients with Interstitial Lung Disease

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2. Institute for Breathing and Sleep, Vic.
3. Department of Respiratory and Sleep Medicine, Austin Health, Vic

Aim
The interstitial lung disease (ILD) constitutes a broad array of rare lung diseases of varying prognoses. As part of the initial assessment of patients with ILD, serum C-reactive protein (CRP) and albumin levels are collected as part of a prospective protocol. We aimed to determine the association between these levels and survival in our patients.

Methods
We undertook a retrospective audit of patients seen in the ILD clinic at Austin Health over two years. Data collected included patient demographic and diagnosis, baseline albumin and CRP levels, respiratory function tests, and six-minute walk tests. Patients were excluded if they did not have blood tests at diagnosis or if their blood tests were performed during hospitalisation.

Results
161 patients were identified (male n= 78 (65%); mean age= 65.9 (±13.6); deceased =34 (21%)). The median follow up was 25 months (range = 1 to 107). One patient received lung transplantation, and was included in the deceased group. The survivor group was younger and had better lung function and exercise capacity compared to the deceased group (Table). A range of diagnoses were present within both groups, with idiopathic pulmonary fibrosis and connective tissue disease-related ILD being the common ones. Compared to the survivor group, the proportion of patients with low albumin levels (p=0.03), combined low albumin and elevated CRP levels (p<0.0005) were significantly higher than the deceased group.

Table. Serum CRP and albumin levels in the survivor and deceased groups

<table>
<thead>
<tr>
<th></th>
<th>Survivor Group</th>
<th>Deceased Group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated CRP</td>
<td>55 (43%)</td>
<td>21 (62%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Low Albumin</td>
<td>21 (17%)</td>
<td>12 (35%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Dual Abnormalities</td>
<td>12 (9%)</td>
<td>10 (29%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Dual normal</td>
<td>64 (50%)</td>
<td>11 (32%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)*</td>
<td>64.5 ± 14.2</td>
<td>71.2 ± 9.8</td>
<td>0.01</td>
</tr>
<tr>
<td>FVC (% predicted)*</td>
<td>82.2 ± 18.1</td>
<td>64.4 ± 17.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>DLCO (% predicted)*</td>
<td>57.9 ± 19.5</td>
<td>37.2 ± 12.0</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

* Results expressed as mean ± standard deviation

Conclusion
In a cohort of ILD patients of varying diagnoses, our preliminary analyses suggest that abnormal baseline albumin and CRP levels appear to be associated with survival.
Background:
The use of smartphone-based communication applications amongst clinicians in Victorian hospitals is pervasive. The demands of modern medicine, with its heavy reliance on instant messaging services with the ability to support multimedia content have made applications such as Whatsapp® indispensable. Despite the availability of a competing platform which complies with Australian privacy regulations, Whatsapp® has remained the most popular application amongst Victorian clinicians.

Aim:
To analyse the patterns of usage, media types and message contents of a dedicated Whatsapp® channel within a Colorectal Unit, despite privacy and data security concerns.

Methods:
Communication within a Whatsapp® chatgroup of a Colorectal Unit over a six-month period was analysed. The number, content, author and timing of messages were noted.

Results:
A total of 5764 messages were transmitted during the 6 month period. The multimedia platform support of Whatsapp® was utilised, with a substantial amount of multimedia messages or photographs transmitted within the chatgroup (655, 11%). The majority of messages sent were clinically relevant to patient care (5222, 77%). Most communication occurred during working hours, however there was significant after-hours communication as well (1337, 23%). The trend of Whatsapp® usage has been increasing over the study period, with a peak of usage in December, with 1527 messages transmitted.

Conclusion:
Text and multimedia support by Whatsapp® meets the communication demands of clinical practice of a surgical unit. Its ability to support multimedia format has significant advantage over traditional communication tools, such as Short Message Service (SMS), paging systems and telephone calls. Despite privacy and data security concerns, its usage has increased over time. Potential drawbacks of substantial after-hour communication and non-clinically related messaging could impact clinicians despite its advantages.
Australian and New Zealand colorectal surgeons in the modern era: the rise of social media

Radojcic M¹, Smits M¹, Wickramasinghe N²,³, Lawrentschuk N⁴, Smart P⁵

Background: Social media encompasses multiple forms of electronic communication where users create online communities to share ideas, information and other content. Social media use has grown rapidly, becoming important in surgical practice by providing opportunities for medical education and interaction with patients and colleagues. No study to date has looked at the uptake and prevalence of social media use amongst colorectal surgeons in Australia and New Zealand (NZ).

Aim: To assess the use of websites and social media by all practicing colorectal surgeons in Australia and NZ.

Methodology: All members of the Colorectal Surgical Society of Australia and NZ (CSSANZ) were identified. Comprehensive searches of websites and social media platforms (Facebook, Twitter, LinkedIn, YouTube and ResearchGate) were undertaken to record the presence of a private website or social media account. Factors that were examined included the sex of the surgeon, years in practice and geographical location of the surgeon.

Results: There were 230 practicing colorectal surgeons in Australia and NZ as of December 2017. 80% of surgeons had a private website, of which 20% were ‘single surgeon’ websites. 68% of surgeons had at least one type of social media account. The most widely-used social media platform was LinkedIn (55% of surgeons). 25% of surgeons had a Facebook account and 31% had a ResearchGate profile. Nine percent of surgeons were on Twitter whilst less than 2% were on YouTube. There was no difference between the sexes in use of websites or uptake of social media. NZ surgeons were more engaged with LinkedIn than their Australian peers. Younger surgeons were more likely to use social media.

Conclusion: Colorectal surgeons in Australia and NZ are users of multiple social media platforms and have a strong online presence. There is potential for further uptake of social media which could enhance surgeon-patient and surgeon-surgeon interaction and education.
A Systematic Review of Stenting for Bowel Obstruction for Extracolonic Malignancies – a data deficit?

Malachy Feeney¹, Amanda Nikolic¹, Anthony Lamanna¹, Philip Smart¹,²

BACKGROUND
Self expandable metallic stents (SEMS) for obstructing colon cancer (CRC) is well established. Limited data suggest stenting for large bowel obstruction (LBO) due to extracolonic malignancy (ECM) has a worse outcome than primary CRC.

AIM
To perform a systematic review with subgroup analysis of randomised controlled trials (RCTs) comparing stenting and surgery for outcomes in ECM vs. CRC.

METHOD
A detailed electronic search was carried out from the following databases: Cochrane Central Register of Controlled Trials, MEDLINE, Embase and PubMed. The search was performed using the terms ‘colonic obstruction’, ‘intestinal obstruction’, or ‘large bowel obstruction’, ‘stent’ or ‘colorectal stent’, or ‘bridge’. No language limitation was applied to the search. All studies published from 1990 to 2018 were considered.

Abstracts of potentially relevant publications based on the titles were read and comparative studies of SEMS vs. emergency surgery retrieved. A hand-search of the references of all comparative studies retrieved was undertaken for any further potential studies; these were then reviewed.

Patient subgroups were examined to extract ECM cases to evaluate outcome. RCTs deemed relevant were then screened using the assessment tool as shown in Fig 1. Studies that scored 2 or less were excluded from the review.

RESULTS
None of the studies retrieved for this systematic review included data of sufficient quality enabling measurement of outcome in LBO due to ECM vs. CRC.

DISCUSSION
Limited lower quality evidence in the form of cohort studies or retrospective reviews suggest outcome of SEMS in ECM has a worse outcome than CRC. Possible reasons include bulkier tumours, increased fibrosis secondary to radiotherapy, or the presence of peritoneal carcinomatosis.

Whilst the RCTs assessed in this review report the complication rates for SEMS vs. surgery for CRC, it is worth noting that the complication rate of endoscopic stenting for ECM may be similar to the surgical complication rate.

CONCLUSION
Currently no available Level 1 data exists to allow for subgroup analysis comparing the efficacy or safety of SEMS in ECM. An RCT comparing SEMS vs. surgery for LBO due to ECM is needed to clarify the efficacy and safety of stenting in patients with ECM.
The Use of Communication Applications in the Australian Health Care System

Amanda L Nikolic¹, Nilmini Wickramesinghe, Damien Claydon-Platt, Vikram Balakrishnan², Philip Smart¹²

Background: The use of communication applications (Apps) on smartphones offers an efficient, unobtrusive, and portable mode of communication for medical staff. The potential enhancements in patient care and education appear significant, with clinical details able to be shared quickly within multidisciplinary teams, supporting rapid integration of disparate information and more efficient patient care. However, sharing patient data in this way also raises legal and ethical issues. No data is currently available demonstrating how widespread the use of these apps is, doctor’s attitudes towards them, or what guides clinician choice of app.

Objective: To quantify and qualify the use of communication apps among medical staff in clinical situations, their role in patient care, and knowledge and attitudes towards safety, key benefits, potential disadvantages, and policy implications.

Methods: Medical staff in hospitals across Victoria (Australia) were invited to participate in an anonymous 33-question survey. The survey collected data on respondent’s demographics, their use of communication apps in clinical settings, attitudes towards communication apps, perceptions of data ‘safety’, and why one communication app was chosen over others.

Results: Communication apps in Victorian hospitals are in widespread use from students to consultants, with WhatsApp™ being the primary app used. The median number of messages shared per day is 12, encompassing a range of patient information. All respondents view these apps positively in quickly communicating patient information in a clinical setting, however all had concerns about the privacy implications arising from sharing patient information in this way. 67% considered patient data was ‘moderately safe’ on these apps, and 50% are concerned the use of these apps was inconsistent with current legislation and policy. Apps were more likely to be used if they were fast, easy to use, had an easy login process, and were already in widespread use.

Conclusion: Communication app use by medical personnel in Victorian hospitals is pervasive. These apps contribute to enhanced communication between medical staff, but their use raises compliance issues, most notably with Australian privacy legislation. Development of privacy-compliant apps such as MedX™ needs to prioritise a user-friendly interface and market the product as a privacy-compliant comparator to apps previously adapted to healthcare settings.
Internal seton for supralevator Sepsis: An effective technique for complex fistulae
Amanda Nikolic1,2, Corina Behrenbruch1, Benjamin Fleming1, Philip Smart1,2, Rodney Woods1

BACKGROUND
The majority of supralevator sepsis results from superior extension within the intersphincteric plane (Fig 1). The basis of management of these patients is drainage of sepsis and subsequent definitive repair. Drainage of supralevator sepsis is challenging, as achieving sustained drainage of this anatomical space can be difficult. Drainage techniques include:
- Insertion of internal latex mushroom drainage catheters. This is first step management in our institution (Fig 2).
- External drainage with mushroom catheters through the perirectal skin.
- Incision over the abscess with drainage into the anal canal combined with partial internal sphincterotomy.

Definitive management options for supralevator fistula include:
- specialty procedures such as flap repairs
- long term internal mushroom catheter placement, or
- long term management with external setons or drains.

Management of supralevator fistula with internal setons has not previously been described. We present a novel technique to insert an internal seton into supralevator fistula-in-ano as a definitive management option.

SURGICAL TECHNIQUE
Patients are placed in lithotomy. Skin preparation used, and antibiotics administered at the discretion of the operating surgeon.
Using a Hill-Ferguson anal retractor, the site of supralevator extension is identified via examination under anaesthetic (EUA). A gently curved Lockhart-Mummery probe is used to intubate the tract through the opening at the dentate line. The index finger of the surgeon’s non-operating hand is placed the rectum. The probe is guided to the apex of the tract and the index finger palpates the tip of the probe through the rectal wall for proximity. The probe is then perforated back into the anorectal lumen through the rectal wall (Fig 3). An 0 silk tie is then tied to the tip of the probe, and the probe withdrawn to advance the tie through the tract and back through the opening at the dentate line. The silk tie is then tied to the end of a silastic seton, which is guided into the tract by withdrawing the other end of the tie. A further 0 silk tie is then used to secure the seton with the two ends of the silastic seton lying parallel (Fig 4).

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PROCTOTOMY

The authors acknowledge there may be reluctance by colorectal surgeons to perforate the rectum. Internal drainage however is logical due to the proximity of the abscess cavity and fistula tract to the rectal wall. Precedence to healing of a sinus by internal drainage exists, such as in the use of Endosponge for anastomotic leak(8). In addition, we believe it is preferable to external drainage, which requires perforation through the pelvic floor and creation of complex fistula.

IN PRACTICE

This simple and cost effective technique of internal seton for definitive management of supralelevator fistula has been used in our institutions since 2000 in a range of Chron’s and cryptoglandular fistula patients. To date, no significant intraoperative or post-operative complications related to this technique have been noted. Internal seton drainage is an effective, sphincter preserving, low morbidity procedure for definitive management of supralelevator sepsis in selected cases.
Twenty years of research output by Australasian colorectal surgeons; more clinical trials are needed

Mat (Matija) Radojcic¹, Adele Lee¹, Lynette Lau², Pith Beh Soh¹, Philip Smart¹,³

BACKGROUND
Well-designed and well-conducted research has a tangible impact on the scientific community and can optimise medical decision-making. Assessment and benchmarking of research is necessary for the practice of evidence-based medicine and is also important in securing funding and grants for future studies. To date, there has been no evidence regarding the quantity and quality of research output of colorectal surgeons in Australia and NZ. Such information is valuable as it may help guide directions for future research.

AIM
To quantify the amount and type of research published by current members of the Colorectal Surgical Society of Australia and New Zealand (CSSANZ) over the last 20 years.

METHOD
All current members of the Colorectal Surgical Society of Australia and NZ (CSSANZ) were identified in December 2017. A search of the Scopus database was conducted to quantify each surgeon’s research output from the past 20 years (1998 - 2017). The year of publication, topic of each paper and type of study conducted (randomised control trial, case report, etc) were recorded.

RESULTS
A total of 4105 papers were published in the 20 year period studied. Of the major colorectal pathologies, the most popular topic was colorectal cancer, followed by pelvic floor disorders and inflammatory bowel disease (32%, 4% and 3.5% of all papers published, respectively). Approximately one quarter of all research output (24%) was unable to be categorised while 19% of publications were on non-colorectal topics. The most popular type of studies were audits/case series, comprising 21% of all studies. Randomised control trials made up 7% of total research volume, while only 56 papers (1.4%) described novel surgical techniques.

CONCLUSION
Colorectal surgeons have contributed greatly to the medical literature over the past 20 years. Colorectal cancer is the most published research topic and this has been consistent over 20 years. Randomised control trials are lacking and measures need to be put in place to improve this aspect of research output.
Ethics Applications in Australian Health Services: a novel scoring system

Creski M Gilong¹, Nikolajs Zeps³, Philip Smart¹,4

BACKGROUND
Ethics approval is an essential prerequisite to conducting a human research study, as required by the Declaration of Helsinki. While there is a need for a thorough review process to prevent unethical research, the resulting administrative workload required for applications is substantial and this is often multiplied in multi-centre studies.

AIM
To assess research ethics application processes across all Health Services in Australia

METHOD
All Australian health service websites were systematically assessed for Ethics requirements. Data collected included application types and processes, meeting dates and timeframes. The ethics application process of each health service is objectively scored using our novel scoring system (Table 1).

RESULTS
Whilst most hospitals run HREC only (53.8%), there are also a few hospitals without any meetings (7.7%), hence relying on the HREC from other hospitals to provide ethics approval (Figure 1). The number of documents requested for the same category of research (Full Ethics/HREC vs SSA vs LNR vs QA) varied widely between health services despite (Figure 2). In particular, there are health services requiring more than 5 documents simply to conduct Quality Assurance activities. Most health services organise 7 to 11 HREC meetings a year.

CONCLUSION
The research ethics application process in Australia is widely variable between health services. We propose a scoring system which objectively describes the current status of research ethics applications across Australia.
Efficient Surgical Research Projects - Concept to Completion In 12 weeks

Jason Kong¹, Amanda Nikolic², Michael Smits², Mat Radojcic², Philip Smart¹,²

BACKGROUND
Involvement in research and successful output is a key and increasingly important component in resident training, which is becoming more competitive at an accelerating rate. It is a crucial component in a successful specialty training application and beyond.

Research has typically been performed using significant personal time investment, with no guarantee of any successful research output. However, we believe that a different paradigm will be necessary in the future, with potential trainees needing to demonstrate an ability to do more in a shorter period of time.

AIM
To create a framework for surgical research projects to be performed that optimises time investment by the researcher and includes a method to ensure successful research output.

Methods:
Various researchers were consulted about their research experiences. A 12-week research framework was designed to train researchers to learn to utilise any resources available to them and develop a managerial mindset. The key idea was to ensure parallel progression of project design, project implementation and research output phases.

A book containing this framework as well as information about common pitfalls, barriers to success, and useful project management techniques and technologies was also published to be used as a reference and instructional text.

Results
Several simple projects were attempted using the framework. These led to a number of peer-reviewed publications and international poster presentations. A number of ongoing projects utilising this framework are also currently in progress. Overall the framework was shown to be an effective method of managing a research project.

CONCLUSION
A new research paradigm for potential trainees is needed that maximises research involvement and output while minimising any personal time investment. The mechanism for achieving this is detailed in our book, but essentially involves a managerial mindset, outsourcing work, and effective project management in order to ensure parallel progression of design, implementation and output phases.
Golnaz Sharafi1, Hong He1, Mehrdad Nikfarjam1

The effects of CBD and THC on pancreatic cancer cell proliferation

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Aim
Pancreatic cancer is one of the leading causes of cancer-related death in current society. In recent years, cannabinoids the active components of Cannabis sativa and their derivatives, have drawn renewed attention because of their diverse pharmacologic activities such as cell growth inhibition, anti-inflammatory effects, and tumour regression. The aim of the current study is to assess the effect of CBD (Cannabidiol), THC (Tetrahydrocannabinol), the combination of them and the combination of CBD or THC with Gemcitabine on pancreatic cancer cells.

Methods
The effects of CBD and/or THC on pancreatic cancer cell proliferation were determined by Sulforhodamine B (SRB) Assay using. 4 human and 2 murine pancreatic cancer cell lines used in this study. After 24 hours serum-starvation, the cells were incubated with CBD and/or THC alone or in combination with different ratios of CBD: THC. The combined effects of gemcitabine with CBD or THC on 2 human and 2 murine cancer cell lines were also determined by SRB. The cells were pre-treated with Gemcitabine (at the IC50 for each cell lines) for 24h followed by either CBD or THC treatment for another 24h.

Results
Both CBD and THC does-dependently inhibited cell proliferation. The combination of CBD and THC at 1:1 ratio (among the ratios tested) had maximal inhibitory effect on cell proliferation. Among all the cell lines tested, pre-treatment of Gemcitabine dramatically enhanced the inhibitory effects of CBD and THC on these cells.

Conclusion
CBD and THC inhibited the proliferation of pancreatic cancer cells alone or in combination with maximal inhibition achieved at 1:1 ratio of CBD: THC. Gemcitabine enhanced the inhibitory effects of both CBD and THC.
Aim: Therapeutic resistance is the major contributor to the low survival or poor prognosis of pancreatic cancer (PC). PC progression is a complex process reliant on interactions between tumor and tumor microenvironment (TME). A unique chemokine family, CXCLs, seems to play important roles in regulating PC progression in pancreatic TME as well as PC stem cells. Therefore, it is important to identify the roles of members of the CXCL family in PC and the mechanism(s) involved to overcome chemoresistance.

Methods: To access expression levels of CXCLs and selected CSC genes in PC cells, predict any correlation between PAK1, investigate possible involvement of a CXCL or CSC gene in chemoresistance, CXCLs and selected CSC genes, and determine whether a selected CXCL plays a role in chemoresistance in PC, RT-PCR, regression analysis and immunohistochemistry were conducted.

Results: Expression of CXCL5 were sharply increased in a panel of human PC cell lines, suggesting an important role of CXCL5 in PC. In contrast, CXCL10 expression had significant reductions in the both human and mouse cell lines. Similarly, the selected CSC genes, ALDH1, CD24, CD44 and CD133 also increased expression in most the cell line. CXCL5 and the selected CSC genes were found to positively correlate with
gemcitabine resistance while CXCL10 had the opposite trend. In the presence of the chemotherapeutic reagent, the reduction of CXCL5 expression in the human cell lines was less pronounced than in the GEM\textsuperscript{R} ones. However, from the immunohistochemical results, gemcitabine along or combined treatments led to increased CXCL5 protein expression while CXCL10 was unaltered, suggesting a role of CXCL5 in chemoresistance of PC.

Conclusion: CXCL5 mediates resistance to gemcitabine in PC.
Regulation of hypoxia inducible factor-1 alpha and its biological significance in prostate cancer PC3 cells.

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BACKGROUND AND AIM

The aim of this study was to determine whether metal ions (Cu²⁺, Zn²⁺, Fe²⁺, Mg²⁺, Mn²⁺), anti-oxidants (two superoxide dismutase/catalase mimetics EUK134 and MnTmPyP) and FG4592 (a prolyl hydroxylase inhibitor) modulate the expression of hypoxia inducible factor 1 alpha (HIF-1α) in prostate cancer cells and whether changes in HIF-1α expression affects proliferation or survival of prostate cancer cells. HIF-1α is a protein upregulated under hypoxic conditions and triggers many adaptive survival mechanisms within cells.

METHODS

Changes in HIF-1α levels were measured using Western Blot analysis. Cell proliferation was measured using colorimetric MTT assays. PC3 cell survival was measured following the treatment of PC3 cells with cytotoxic concentration of hydrogen peroxide.

RESULTS

Zn²⁺, Mn²⁺, EUK-134 and FG4592 increased HIF-1α expression in a dose dependent manner. Cu²⁺, Mg²⁺, MnTmPyP did not change HIF-1α expression. Although Fe²⁺ ions decreased the expression of HIF-1α and the survival of PC3 cells under oxidative stress, they increased the proliferation of PC3 cells. Even though the combination of Fe²⁺ ions and FG4592 treatment led to an increase in HIF-1α expression it did not increase the cell survival.

CONCLUSIONS

There are a number of pathways that regulate the expression of HIF-1α in PC3 cells, most of which act by decreasing the breakdown of HIF-1α via the PHD pathway. Further it is unclear whether increased levels of HIF1α is the only pathway via which PC3 cell survive under oxidative stress. Therefore, further research is needed to elucidate the role of HIF1α in cell survival and its potential use as a therapeutic tool.
**Comparison of risk factors in patients undergoing mitral valve surgery**

**Introduction:** It is not currently known if the status of mitral regurgitation is independently associated with early post-operative complications in patients undergoing mitral valve surgery (MVS). We sought to determine if patients undergoing MVS for functional ischaemic mitral regurgitation (FIMR) were at a higher risk of post-operative complications, and further risk factors contributing to poorer outcome after mitral valve surgery.

**Methods:** 574 patients who underwent MVS for mitral valve regurgitation from January 2001 to November 2017 were identified from the St Vincent's ANZSCTS database. Patients with mitral stenosis only, undergoing a salvage or redo procedure, or have had a previous sternotomy were excluded. We then compared post-operative complications between patients with FIMR vs NIMR.

The primary endpoint was a composite criteria defined as ≥2 post-operative adverse outcomes including: new onset cardiac arrhythmia, new renal failure, prolonged ICU stay ≥3 days and prolonged intubation ≥7 days. Secondary endpoint was mortality.

**Results:** 516 (89.9%) patients had NIMR and 58 (10.1%) had IMR. Of the 20 (3.5%) patients who died in the post-operative period, 12 (2.3%) were in the nIMR group and 8 (13.8%) in the FIMR group. Logistic regression demonstrated that FIMR (OR: 2.96; 95% CI: 1.53 – 5.7; p=0.001) and red blood cell transfusion (OR: 14.57; 95% CI: 5.68 – 37.44; p=0.001) were independently associated with the primary endpoint. FIMR (OR: 4.57; 95% CI: 1.74 - 12; p=0.002) and red blood cell transfusion (OR: 6.05; 95% CI: 1.34 – 27.24; p=0.019) were also independently associated with mortality.

**Conclusions:** Compared to those with nIMR, patients with IMR undergoing mitral valve surgery are at higher risk of early post-operative complications and mortality. Red blood cell transfusion is a strong predictor of adverse outcomes and all efforts made to mitigate transfusion should be performed.
The effect of Renin Angiotensin System (RAS) inhibition on liver regeneration

G Kastrappis, T Fifis, R Paolini, K Walsh, G Riddiough, D Ardila, M Perini, C Christophi

Background:

Liver resection surgery has been used to remove benign and malignant growths and is currently the best treatment available for patients with liver cancers including colorectal liver metastasis (CRCLM) and hepatocellular carcinoma. Over 90% of CRC related deaths are due to metastatic disease and liver is the most common organ of CRC metastasis. Between 40-60% of patients that have successfully undergone liver tumour resection will relapse within five years. Studies have shown that the cytokines/growth factors released during the liver regeneration process contribute to tumour regrowth and metastasis. Recent research, including ours, has shown that inhibition of the Renin Angiotensin System (RAS) classical pathway reduces tumour growth. We also have shown RAS inhibition enhances liver regeneration by reducing inflammation.

Aims: To determine the effect of Captopril (a RAS inhibitor) on the cytokines released during liver regeneration.

Methods: CBA mice are subjected to 70% liver resection by removing the median lobes and the left posterior lobe. Mice in both the control and treatment group are injected with saline or 750mg/kg captopril daily starting from 4 days before surgery and on the day of surgery. Mice are culled at various time-points starting at 1 hour and up to day 6 after liver resection surgery. Sera and remnant liver tissues are collected. Several cytokines including TNF-a, IL-6 and MCP-1 in the sera and liver lysates are analysed using multiplex cytometric bead assays.

Preliminary Results: IL-6 shows a significant decrease in the treatment group compared to control group at the 3 and 4-hour time points post resection. MCP-1 also showed a significant decrease in the treated group compared to the control at the 3-hour time point post resection. Additional cytokines and time points are currently under investigation.

Conclusion: Reduction in pro-inflammatory cytokines could contribute to enhanced liver regeneration and inhibit tumour progression.
Background and Aim
In Australia, colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second commonest cause of cancer death. Advances in primary cancer treatment have led to the emergence of metastases as the major cause of cancer deaths. Traditionally, murine models of CRLM have consistently induced widespread liver tumours via splenic injection. Emerging evidence suggests that following partial hepatectomy (PH) for CRLM, the liver’s innate regenerative responses paradoxically drive micrometastasis activation and favour disease progression. Subsequently, this laboratory sought to create a model of CRLM that induces solitary or dual tumours to facilitate the study of PH and liver regeneration on the progression of disease.

Methods
The appropriate animal ethics was granted and experiments were performed within the Austin BRF. Mouse colorectal cancer (MoCR) cells are passaged subcutaneously in CBA mice and are routinely used for tumour induction. Cells were counted to provide four concentrations as follows; 2x10^6 cells/ml (50,000 cells), 1x10^6 cells/ml (25,000 cells), 4x10^5 cells/ml (10,000 cells) and 2x10^5 cells/ml (5,000 cells) in Ringer’s solution. Diluted tumour cells were added to an equal volume of Matrigel to provide a final volume of 50µl per injection. Under general anaesthetic, a laparotomy was performed and 50µl of cancer cell Matrigel suspension was injected under the liver capsule of the mice at the required concentrations. The tumours were allowed to grow for 18 days following which the mice were culled and the tumour progression was assessed. The feasibility and advantages of a smaller cell delivery volume is currently under investigation.

Results
Tumours developed in proportion to the concentration of tumour cells directly injected into the liver parenchyma. Injections of 5,000 and 10,000 cells produced tumours of around 2-3mm and 7-8 mm respectively.

Conclusion
Direct injection of CRC cells into the liver produces solitary and confined CRLM whilst maintaining macroscopically normal liver parenchyma peripherally. This confirms proof of the principle and this novel method of tumour induction will facilitate study of the liver’s regenerative response on tumour growth following PH.
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The effects of zinc on ischemia-reperfusion injury in the liver in a global ischemia rat model

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Aim
Liver ischemia-reperfusion injury (IRI) is a challenging problem in liver transplantation and liver resection. Various treatments have been studied but there are currently no treatments that have been able to be transitioned into clinical practice. This study aims to assess whether zinc can ameliorate the effects of liver ischemia-reperfusion injury.

Methods
The effect of zinc was studied in a rat model of liver ischemia-reperfusion injury with 30 minutes of global (100%) liver ischemia via clamping of the portal triad. The treatment group (n=5) was given 10mg/kg subcutaneous injection of zinc chloride, 24 hours and 4 hours before the surgery while the control group (n=5) was given normal saline subcutaneous injection at the same timing. Blood was taken at 1, 2, 4, 24, 48, 72, 96 and 120 hours of reperfusion. Liver injury was assessed by serum alanine transaminase (ALT) and aspartate transaminase (AST) levels. Animals were culled after 7 days and then the liver was harvested for histological analysis.

Results
Following 30 minutes of liver ischemia in rats, zinc preconditioning reduced ischemia-reperfusion injury as evidenced by lower AST and ALT serum concentrations and histological liver damage scores. These differences were most significant at 24 hours reperfusion with both ALT (341.2 ± 107.52 vs 2863.5 ± 828.27, p=0.011) and AST (606.4 ± 78.78 vs 3591.8 ± 948.1, p=0.009) in zinc treated groups showing marked reductions compared to control. Zinc preconditioned rats also showed greater weight gain post-surgery compared to controls (10% vs 3% weight gain from baseline).

Conclusion
Zinc preconditioning reduces the overall level of hepatocellular injury from liver ischemia-reperfusion injury with significant reduction especially at 24 hours and facilitates better recovery with greater weight gain post-surgery. Further studies are warranted to assess the benefits of zinc preconditioning in larger animal studies and to determine the possible mechanisms involved.
**Background**
Endovascular Clot Retrieval (ECR) is the standard of care for acute ischaemic stroke due to a large vessel occlusion. It is a time critical and complex process involving many specialised care providers and resources. Maximising patient benefit while minimising cost of this service requires optimisation of human and physical assets.

**Aim**
The aim of this study was to develop a computational model of an ECR service, designed to optimise resource allocation.

**Methods**
Using Simmer-an R-based Discrete Event Simulation (DES) package- as frequently employed in complex logistical operations, we have developed a comprehensive computational model that closely mimics the environment of an ECR service from presentation to emergency department to the angio suite.

This model was tested using real data collected from a quaternary institution with ECR service.

**Results**
Our model assesses the impact of available services, and aids optimisation of resource distribution and access, allowing comparison of various competing strategies.

In this simulation, the numbers of different human or capital resources such as stroke physicians, neuro-interventionists, and angiography equipment can be varied to assess the impact on efficiency and availability of service delivery.

Other factors and variables such as equipment breakdown, servicing or times taken during components of an individual stroke management pathway can also be integrated, to identify sources of systemic delay and cost-points, with a view to service improvement.

**Conclusion**
A novel computation model is proposed to help existing ECR services, in targeting optimum service delivery and best patient outcomes.
Audit of routine colonoscopy following an episode of acute diverticulitis diagnosed by CT: What is the value and clinical implications?

Routine colonoscopy has been recommended following the diagnosis of acute diverticulitis to detect colonic neoplasia, due to perceived higher risk in these populations. However, recent large studies report the neoplastic risk in this group to be similar to the general population and that routine colonoscopic follow-up is not recommended, unless other risk factors are present.

Purpose:
To assess the proportion of patients that obtained a colonoscopy following a CT diagnosis of acute diverticulitis, median time to colonoscopy, and rate of colonic neoplasia (including carcinoma, advanced neoplasia and polyp formation).

Methods and Materials:
Retrospective single centre review. All patients with a CT diagnosis of acute diverticulitis were identified using an in-house database program (PRaISE) between January 2010 to December 2016. Patient records were assessed, and the following data recorded: patient demographics, presence/absence of a colonoscopy, time to colonoscopy, colonoscopic/histological results, and risk factors/alarm symptoms for colonic neoplasia. Qualitative analysis performed. Rates of colonic neoplasia were compared to the published literature.

Results:
1214 patients were identified with a CT diagnosis of acute diverticulitis (62.87 years, SD14.71; male: female ratio (M: F) 48.3: 51.7). Of these, 303 patients (25%) underwent post diverticulitis colonoscopy (59.77 years, SD13.33, M: F 48.1: 51.9), with the remaining 911 patients (75%) having no colonoscopy recorded at our institution (63.9 years, SD14.94, M: F 48.2: 51.8). 54 patients (4.4%) had a colonoscopy within the preceding 12 months of the CT diagnosis of acute diverticulitis. Median time to colonoscopy (MTC) from CT was 95 days [IQR 57-223 days]. Of patients who underwent a colonoscopy, 3 were diagnosed with carcinoma (0.9%; 59.02years, SD 14.57; MTC 4 days [IQR 3.5-4]), 8 were diagnosed with advanced neoplasia (2.64%; 60.12years, SD 13.05; MTC 230 days [IQR 94-426]) and 103 diagnosed with polyps (33.9%; 59.08years, SD 13.35; MTC 101 days [IQR 55.5-246.5]).

Conclusion:
A significant proportion (75%) of patients did not have a colonoscopy at our institution following a CT diagnosis of acute diverticulitis. Amongst those undergoing colonoscopy, the colon cancer prevalence was 0.99% - slightly higher than the published rates in Australian screened asymptomatic group aged 50-75years (0.36% [Australian National Bowel Cancer Screening Program (NBCSP)]) U.S. Census data (0.68%; age >55) but less than pooled meta-analysis prevalence data (5%) . This supports recent literature suggesting patients with acute diverticulitis are at similar risk to asymptomatic average-risk individuals and the recommendation of routine colonoscopy following a CT diagnosis of acute diverticulitis may not be warranted.

References:
Endovascular flow-diversion of visceral and renal artery aneurysms using dual-layer braided nitinol carotid (CASPER) stents

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Abstract

Purpose

Visceral and renal artery aneurysms (VRAAs) are uncommon but are associated with a high mortality rate in the event of rupture. Endovascular treatment is now first line in many centres, but embolization and preservation of the parent artery may be difficult in tortuous or unfavourable anatomy at arterial bifurcations. Flow-diversion is used in neurovascular intervention to treat intracranial aneurysms but is less often utilised in the treatment of VRAAs. The CASPER stent is a dual-layer braided nitinol stent designed for carotid stenting.
with embolic protection and flow-diversion properties. We report the novel use of the CASPER stent for the treatment of VRAAs.

Materials and Methods

We present a case series describing the treatment of six patients with VRAAs using the CASPER stent for flow-diversion.

Results

Six patients with unruptured VRAAs were treated electively. There were three splenic aneurysms, two renal aneurysms and one hepatic aneurysm. Aneurysms were treated with flow diversion using the CASPER stent, with or without loose aneurysm coil packing depending on the size. All procedures were technically successful with no immediate or periprocedural complications. Cases with repeat imaging show aneurysms are either reduced in size or completely occluded.

Conclusion

Preliminary experience with the CASPER stent suggests its suitability, safety and efficacy for use in the treatment of VRAAs.
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Use of CT and MRI for occult neck of femur fractures: the Austin Health experience

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Aim
The aim of our study is to review the use of computed tomography (CT) and subsequent magnetic resonance imaging (MRI) studies for suspected neck of femur fractures (NOFs) in patients with negative or equivocal x-rays. Timely diagnosis of NOFs is required to decrease morbidity and mortality.\textsuperscript{1} Guidelines suggest that MRI be performed if a suspected NOF is not visible on x-ray.\textsuperscript{2} Although MRI is the gold standard, access out-of-hours is challenging and CT is often used instead\textsuperscript{3}.

Methods and Materials
Institutional Board ethics committee approval obtained. A retrospective review of adult patients with negative or equivocal x-rays with suspected NOFs between 1 July 2016 and 30 June 2017 was performed. Review of CT and subsequent MRI studies was performed with documentation of reported findings and time intervals between scans.

Results
393 CT studies were reviewed. 101 CT studies in 98 patients met inclusion criteria. Median age was 83 years (interquartile range, IQR 69-90 years) with 37 male (37.8\%) and 61 female (62.2\%) patients. CT reported 6 occult NOFs (5.9\%). 13 patients with a negative CT proceeded to MRI. 4 of these patients had a NOF on MRI. 1 patient with a negative CT with no follow-up MRI had a NOF on x-ray 9 days later.

Median time (hours) from x-ray to CT, then MRI was 74:06 (IQR 45:09-100:56). This is 18.2 times longer than the median time from x-ray to CT (4:07, IQR 2:09-8:49). Median time from request to MRI was 23:14 (IQR 4:30-27:52), 19.1 times longer than time from request to CT (1:21, IQR 0:52-1:58).

Conclusion
Access to CT for evaluation of NOF is much quicker compared to MRI. Thus, CT is more practical and useful in detecting an occult NOF. If CT is negative and a NOF is still suspected, a timely MRI should be performed.

References:
Yates S¹, Graham J¹, Weinberg L¹, Nazareth J¹

Clinical Audit: Preoperative Ordering of HbA¹C in Upper Gastrointestinal and Endocrine Surgical Patients

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Aim
Diabetes and higher HbA¹C are independently associated with a higher risk of adverse outcomes after surgery. We aimed to establish the compliance of the Austin Hospital Upper Gastrointestinal and Endocrine Surgery (UGIS) Unit to the Austin Hospital and ANZCA recommendation for preoperative HbA¹C testing. A clinical audit guideline published by ANZCA recommends all patients undergoing major elective surgery should, if possible, have their HbA¹C tested preoperatively. This recommendation is in line with local policy at Austin Hospital.

Methods
After research Ethics Committee approval (LNR/17/Austin/556) we performed a retrospective clinical audit to ascertain adherence to these recommendations. All patients undergoing elective major surgery (defined as requiring ≥2 night stay) under the UGIS were audited for the 2016/17 financial year.

Results
We studied data from 191 consecutive patients undergoing major surgery. Of these patients, 25 (18%) had diabetes based on HbA¹C testing. 113 (59%) had a preoperative HbA¹C checked. Of the 78 patients who were not tested, 33 patients had their HbA¹C ordered in the immediate postoperative period as part of an automated system which operates at Austin Health. This system ensures that all patients aged ≥54 years who have a >24-hour admission and have not had an HbA¹C ordered within three months have an automated order for HbA¹C created. Of this group of 33 patients, 6 (18%) returned an HbA¹C result of ≥6.5%. Breakdown by surgery type in 78 patients not checked for HbA¹C preoperatively is summarised here graphically.

Conclusions
In our audit population, 41% of patients did not have HbA¹C checked preoperatively. Further, a small percentage of these patients proceeded to major surgery with undiagnosed diabetes. Additional education and more reliable mechanisms for checking HbA¹C preoperatively are required. Implementation of an automated system for the ordering of preoperative HbA¹C in surgical patients may increase adherence to current recommendations, improve patient outcomes and would likely be applicable to many healthcare services across Australia.
Audit of use of sublingual ketamine at Austin Health 2012 - 2017
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Abstract
We retrospectively audited use of sublingual ketamine for Austin inpatients and outpatients for the period January 2012 to December 2017. Using Pharmacy records, 46 patients were identified. Four dominant groups of use were identified: 1) patients with difficult personalities who were opioid-seeking or dependent – 8 patients; 2) patients who used sublingual ketamine as a medication of last resort – 13 patients; 3) patients with difficult pain due to intensely inflammatory states - 11 patients 4) patients did not persist with sublingual ketamine due to lack of efficacy, excessive side effects, or death – 10 patients. The duration of use ranged from days to multiple years. The maximum dose permitted was 150 mg per day. No severe adverse effect nor drug diversion was identified. Sublingual ketamine was considered to be a useful part of the therapeutic armamentarium due to improving analgesia and/or lessening opioid escalation.
Background: The efficiency of lung gas exchange deteriorates after induction of general anaesthesia due to increased ventilation-perfusion (V/Q) scatter. Blood gas data from some previous studies suggests that propofol TIVA may preserve V/Q matching better than inhalational agents. We compared V/Q matching in patients under relaxant general anaesthesia randomized to either propofol TIVA or sevoflurane maintenance anaesthesia, using both Bohr deadspace and shunt fraction measurements and the MIGET (Multiple Inert Gas Elimination Technique) for characterization of V/Q distributions.

Methods: Patients with clinical evidence of underlying lung disease were excluded. Baseline arterial blood sampling and collection of mixed expired gas was done before induction and repeated after 1-2 hours of relaxant general anaesthesia, supine with controlled ventilation at an FiO₂ of 0.3 and a target end-tidal PCO₂ of 30-35 mmHg and bispectral index range of 40-60. Blood samples for MIGET were processed by headspace equilibration in 20mL gas tight glass syringes at 36°C, with measurement of partial pressures in expired and headspace gas samples by gas chromatography. The primary endpoint was comparison of the two groups in the change from baseline of absolute difference between log standard deviation of ventilation and blood flow distributions ($\partial(\sigma_V-\sigma_Q)$).

Results: Data from 20 patients (10 in each group) was suitable for analysis. There were no significant differences between the two groups in baseline demographics or lung function indices. Deadspace fraction increased and PaO₂/FiO₂ ratio decreased across both groups overall, with anaesthesia, but change in deadspace was not significantly different between groups (mean [SD] sevo 21.8 [11.7]% versus TIVA 20.5 [10.6]% p = 0.601). The change in PaO₂/FiO₂ ratio was also similar between groups (mean [SD] sevo -51.9 [69.1]mmHg versus TIVA 78.3 [76.9, mmHg] p = 0.43), as was change in shunt fraction ($\delta Qs/Qt$ mean, [SD] sevo -5.1 [12.6]% versus TIVA 0.4 [7.7]%, p = 0.174). The primary endpoint $\partial(\sigma_V-\sigma_Q)$ was not different between sevoflurane and propofol TIVA groups (mean [SD] 0.17 [0.81] versus 0.17 [0.29], p = 0.94).

Conclusions: We found no evidence that TIVA preserved V/Q matching in patients with normal lung function undergoing anaesthesia with controlled ventilation compared with sevoflurane.
Attitudes of anaesthetists attending the funeral of patients they care for: a cross-sectional survey amongst Australian and New Zealand anaesthetists

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Background: A patient’s death can pose significant stress to the family and the treating clinician. The attitudes, benefits and barriers of attending a patient’s funeral as perceived by anaesthetists is unknown. Therefore, we performed a prospective cross-sectional study ascertaining the rate of, and facilitators and barriers of anaesthetists attending a patient funeral.

Methods: After Human Research Ethics Approval, we performed a cross-sectional mixed method study using validated survey methodology. We surveyed registered Fellow anaesthetists actively practising in Australia and New Zealand. The primary aims were to ascertain the attitudes of anaesthetists towards attending their patient’s funeral. Further, we examined the perceived benefits of and barriers to attending the funeral, and explored the rate of formation of special bonds between anaesthetists and patients and their families. NVivo v.12. was employed to extract the principle themes. Descriptive statistical analysis was performed using STATA/IC v.13.

Result: 424 participants completed the survey (response rate 21.2%). 268 respondents (65.8%) were male, 257 (63%) aged 40-60 years, and the majority (77.9%) practising for >5 years. 77% and 23% of participants practiced in Australia and New Zealand, respectively. 5.9% of anaesthetists had attended a patient’s funeral. 364 participants (85.9%) rarely formed special bonds with patients or their families. 233 (55%) anaesthetists believed that formation of a special bond increases the likelihood of their attendance. Showing respect to patients or their families was the most common perceived benefit of attending a patient’s funeral. Participants found expression of personal grief and caring for the patient beyond life beneficial to themselves and the family. Fear of their attendance being misinterpreted or not warranted, and time restraints were common barriers of anaesthetists’ attendance at a patient’s funeral.

Conclusion: Most anaesthetists practising in Australia and New Zealand have never attended their patient’s funeral. Few anaesthetists form close relationships with patients or families. Respect, expression of grief and caring beyond life were commonly perceived benefits of attendance. Families misinterpreting or not expecting their attendance and time restraint were common perceived barriers. Future studies could focus on the family’s perspective on anaesthetists’ attendance at a patient’s funeral.
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Analgesia Pathway following Trans Arterial Chemo Embolisation

Aim

Patients can develop severe pain after Trans Arterial Chemo Embolisation (TACE) procedures. These can be difficult to manage in radiology recovery and some require Acute Pain Service (APS) involvement. The aim of this project was to establish a safe and effective analgesia pathway for patients following (TACE) procedures.

Method

In January – April 2017, we audited patient’s analgesia after TACE procedures – medications used, pain scores, duration in radiology recovery, APS involvement. The analgesia pathway was implemented in November 2017. This involved preoperative multi-modal analgesia, post-operative titration of intravenous oxycodone in radiology recovery and escalate to APS if required. Another audit was done between January – April 2018 to compare these same outcomes.

Results

40 patients and 35 patients had a TACE procedure in January – April 2017 and 2018 respectively. There was 94% (33/35) compliance to the analgesia pathway in 2018. Multi-modal analgesia was used 92% and 100% of cases in 2017 and 2018 respectively. There was no difference in the duration in radiology recovery between the two groups (median 45 minutes for both groups, interquartile range 34.25-60 in 2017 and 45-60 in 2018). Fewer patients left recovery with pain scores of 7 or higher in 2018 compared to 2017 (5.7% [2/35] vs 12.5% [5/40], P = 0.44). More patients had decreasing pain while in radiology recovery in 2018 compared to 2017 (75.0% [6/8] vs 42.8% [3/7], P = 0.31). No patients required APS and PCA (patient controlled analgesia) in 2018 compared to 7.5% (3/40) in 2017 (P = 0.25). There were no adverse events attributed to the introduction of this analgesia pathway.

Conclusion

The implementation of TACE Analgesia Pathway has improved patient analgesia in radiology recovery without adverse outcomes.
Intubation in the Emergency Department: do we need to improve and how?
Lois Mackley, Fiona Desmond, Joseph Ghaemi

Introduction: At least one in four major airway events are known to occur in urgent airway management in the Emergency Department (ED) or the Intensive Care Department (ICU) (1). The outcome of these events can lead to permanent harm or death (1). Case analysis highlighted that common areas of deficit include poor identification of at-risk patients, incomplete planning and failure to use or interpret capnography as a basic tool (1). Management of the emergency airway via endotracheal intubation is known to be a low frequency, high-risk procedure in the ED (2) and Austin hospital is no exception. The use of a peri-intubation checklist in ED is advised by the Difficult Airway Society (DAS) for intubation outside of the theatre environment (3) and has been shown to decrease airway complications (4). One such checklist was introduced in Austin Hospital ED in May 2016. We have conducted an audit of this intervention in order to assess the efficacy of this checklist, and what improvements are needed in order to improve this intervention further.

Methodology:
- A retrospective audit was performed during 2 six-month periods preceding and following the introduction of a peri-intubation checklist in May 2016.
- Ethical approval was sought and provided by Austin Health Human Research Ethic Committee (REF: LNR/18/Austin/321).
- The population was identified via those patients who were prescribed standard intubation drugs; alongside patients who were discharged from ED to ICU, theatre or the mortuary between November 2015 and April 2016 and November 2016 and April 2017.
- Identified documents were screened for attempted endotracheal intubation in the emergency department.
- De-identified data was collected from ED discharge letters and emergency nursing assessment forms (M6.1) on SMR regarding patient characteristics and indication for intubation, staff present, assessment of predictors of difficult intubation, intubation attempts, peri-intubation adverse outcomes and documentation of Cormack and Lehane airway grade.

Data was audited against five international standards:
- a) an airway assessment should be performed and recorded prior to induction in 100% of cases in ED (1, 6).
- b) Failed intubation (defined as requiring a second dose of short acting paralytic) should occur in less than 1% of RSI cases in ED (6).
- c) Greater than four attempts at laryngoscopy should not be attempted outside of the operating room (3).
- d) Greater than two attempts at laryngoscopy are known to be associated with significant increased risk of hypoxia, oesophageal intubation, regurgitation, aspiration and cardiac arrest (1).
- e) 100% of patients intubated in ED should be monitored with continuous capnography (1, 6).

Results:
- 1023 notes were screened and 66 presentations were identified for inclusion (44 vs. 22).
- The baseline characteristics of the procedures within each audit period was comparable with the most common indications for intubation being complication of drug overdose (23% vs. 36%), persistent seizures (27% vs. 14%) and decreased conscious level of non-toxicological cause (25% vs. 14%).
- The majority of procedures occurred out-of-hours (61% vs. 56%) and occurred in patients with evidence of physiological disturbance prior to induction (71% vs. 76%).
- Supervision by a consultant was more varied. (36% vs. 59%)
- First pass success rate was frequent (86% vs. 86%). Few intubation attempts in ED were performed by anaesthetists, 81% vs. 60% were performed by an ED registrar, 13% vs. 25% by an ED consultant and 9% vs. 6% by an anaesthetist. However documentation of who intubated could be vague and need improving.
- No notes in either audit period met the audit standard of a recorded airway assessment and only 4.5% in both groups had documented evidence of a partial airway assessment.
- Failed intubation did not occur in any cases, nor did greater than 4 attempts at laryngoscopy.
- An equally low rate of 4.5% for greater than 2 attempts at laryngoscopy was observed in both groups.
- Confirmation with continuous capnography occurred in 91% of cases prior to the introduction of a checklist and this did not improve in the second audit period (91%).
- Documentation of an airway grade post intubation was not universal (80% vs. 68%).
- Adverse events were reported in 52% vs. 46% cases with transient hypoxia and hypotension being the most common, comparable to other published studies in Australian EDs (5).
- There were no peri-intubation deaths and one case of oesophageal intubation that was recognized promptly.

Conclusion: The majority of intubation attempts in Austin ED occur out-of-hours, in physiologically compromised patients and are performed by non-anaesthetists. First-time success rates are high and while adverse events are common this is comparable to previous published data (5). However improvements are needed in particular with documentation of planning and assessment and universal capnography monitoring. The introduction of mandatory documentation via Cerner is predicted to address several of these issues.

2) Endotracheal intubation in the pediatric emergency department, Paediatric Anesthesia, Elliot Long, Stefan Sabato, Franz E. Babi.
3) A Preprocedural Checklist Improves the Safety of Emergency Department intubation of Trauma Patients. Academic Emergency Medicine. 2015: 22(8)
Rapid Response Team activations after major hip surgery: can we catch you before you fall?

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Background: Rapid Response teams (RRT) are a critical care resource that review deteriorating patients within the hospital environment. Whilst the contemporary literature has focused on outcomes and impact of RRTs, little is known about the detailed perioperative course of patients who require RRT activation after major hip surgery.

Aims: We aimed to describe the demographic, preoperative, surgical, anaesthetic and postoperative characteristics of patients who required RRT activation after major hip surgery. We also sought to assess if these characteristics affected mortality during the index hospital admission.

Methods: After Human Research Ethics Committee approval, we reviewed a dedicated RRT electronic database of adult patients undergoing orthopaedic surgery at a university teaching hospital. We retrospectively reviewed the electronic medical records to extract a-priori defined patient, preoperative, surgical, anaesthetic and postoperative data of major hip surgery admissions between September 2014 and December 2017. Patients who survived the indexed hospital stay were compared to those who died.

Results: There were 187 patients with postoperative RRT activations. The mean (SD) age was 82.1 (11.6) years; 125 (67%) were female and they had significant comorbidity (mean [SD] Charlson Comorbidity Index [CCI] 5.6 [2.1]). The majority of patients (68%) were frail, ASA class 3 or greater (91%) and underwent non-elective surgery (88%). 26 (14%) of patients did not survive the index hospital admission. In comparing the patients who survived and died, there were no differences in mean time to surgery (24.7 hours [13.8;38.7]), type of operation, surgical approach, type of anaesthesia (regional vs general) or median (IQR) duration of anaesthesia (128 minuets [99;163]). Similarly, there were no differences in median (IQR) epochs of intraoperative hypotension (3.5 [1;9]), severity of hypotension, use of intraoperative vasoactive medications or inotropes. Furthermore, in the post anaesthesia care unit, there were no differences in temperature (36.2° [36,37]), haemodynamics, analgesia, vasopressor or inotrope use. The median (IQR) time from surgery to RRT activation was 29.4 hours (11.3;75.0), and 25 (13%) patients had unplanned admissions to ICU/HDU. The median (IQR) hospital stay was 9 days (6;14). Of those that did not survive, the median (IQR) time to death after RRT activation was 2.9 days (0.2;8.9). These patients also displayed higher comorbidity (CCI 6.5 vs 5.5; p=0.02), received less total IV morphine equivalent analgesia in theatre (5.83mg vs 11.7mg; p=0.03), and more frequently had an Urgent Clinical Review prior to RRT activation (40% vs 62%; p=0.05).

Conclusions: Death after RRT activation occurred in 1 out of 7 patients who had undergone major hip surgery. Common characteristics amongst these patients included advanced age (>80 years), frailty, high CCI and emergency surgery. These risk factors may facilitate timely recognition of those who will require RRT activation postoperatively. Our findings suggest that surgical factors (type or duration of surgery) and anaesthesia factors (type of anaesthesia, intraoperative haemodynamics, opioid use, vasopressor use) did not differentiate between patients who died or survived after RRT activation. Further studies investigating the role of enhanced postoperative surveillance teams in identification of the deteriorating patient after major hip surgery are warranted.
Thillainadesan T¹, Lee C¹, Mandaleson A¹, Tan CO², Weinberg L²

“Rebound Pain” after Interscalene Brachial Plexus Blockade in Shoulder Surgery – How Often, How Bad?

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Aim

“Rebound Pain” (RP) is a sudden, significant pain following regional nerve blockade regression. When interscalene brachial plexus blockade (ISB) is used for shoulder surgery, RP is well-recognised, but poorly quantified. Primary endpoints were to describe the incidence, time of onset, severity and opioid requirements for the duration of RP. Secondary endpoints included identification of factors influencing adverse pain outcomes.

Methods

From a 2010-2012 database of 102 patients who had undergone shoulder surgery, 67 had received ISB analgesia. Descriptive statistics and univariate analyses were used for parameter point estimates whilst binary logistic and linear multivariate regression analyses used to identify surgical, patient and anaesthesia factors affecting adverse pain outcomes.

Results

Of the patients who underwent procedures under ISB, RP occurred [mean (SD)] at 12.3 (5.8) hrs, at intensity of Numerical Rating Scale-11 (NRS-11) scores of 3.4 (3.3) and requiring 4.3 (4.5) hrs with IV morphine equivalents of 16.2 (15.4) mg during this time to resolve. (See Fig. 1). 20% of ISB patients had no RP, 27% had NRS-11 scores 6+, and 3 patients suffered 10/10 RP. Independent factors related to 6+ scores were Open Procedure, Arthroscopic Acromioplasty, high pre-emptive Sustained Release IV morphine equivalents, and Patient Controlled Analgesia (PCA) prescription.

Figure 1. Proportion of patients per group at time of event.

Conclusion

RP is variable in timing, intensity and duration, but can be severe, requiring high opioid utilization with prolonged time to resolution. Operative type is a predictor of significant RP, whilst use of PCA prescription shortens time to resolution. Aggressive pre-emptive and reactive management of RP is mandatory, along with monitoring side effects of acute opioid loading.
Peak serum potassium levels during reperfusion in adult patients undergoing primary cadaveric liver transplantation

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Introduction: Reperfusion during cadaveric liver transplantation is associated with significant biochemical, physiological and haemodynamic derangements. Hyperkalaemia during reperfusion is common and can be associated with significant cardiac arrhythmias including cardiac arrest. Monitoring of serum potassium, particularly at the time of reperfusion is therefore paramount. The literature to date is very scarce regarding the exact timepoint where serum potassium peaks post reperfusion of the donor graft. Therefore, we performed an observational study to identify the timepoint of peak serum potassium levels after reperfusion of the donor graft during cadaveric liver transplantation.

Methods: After Human Research Ethics Committee approval, we assessed the serum potassium levels during reperfusion of 30 consecutive adult patients undergoing cadaveric liver transplantation. Between August 2017 and April 2018, patients were recruited at Austin Health, a quaternary university teaching hospital with a dedicated liver transplant service. All patients had two arterial lines inserted (femoral line for continuous haemodynamic monitoring, and a radial line for dedicated blood sampling), as part of routine care. Arterial blood was drawn from the radial arterial line immediately before reperfusion, every 20 seconds for 2 minutes, then every 30 seconds until 5 minutes post-reperfusion. Arterial blood gases measuring serum potassium levels were analysed on an ABL 800 Blood Gas Analyser (Radiometer, Copenhagen, Denmark) with a fully automated micromode eliminating risk of user-induced bias or loss of accuracy with very small samples. Changes in potassium levels were analysed over these timepoints. We assessed the correlation between changes in potassium levels, and MELD score, cold and warm ischaemia time, total vasopressor use at the time of reperfusion, and potassium effluent levels of the donor liver.

Results: The median (interquartile (IQR) age and Model for End Stage Liver Disease score was 58 years (46,64.5) and 21 (15.5, 26.3) respectively. The median (IQR) warm and cold ischaemia times were 46 minutes (41, 55.7) and 365 minutes (240, 407.3) respectively. Mean (IQR) durations of surgery for the dissection and anhepatic stages were 150 minutes (124, 195) and 70 minutes (60, 78) respectively. 28 patients (93%) were receiving noradrenalin at the time of reperfusion (median (IQR) dose 15ug/min (8, 20). The median (IQR) serum potassium immediately prior to reperfusion was 4.1 mmol/L (3.8, 4.5). Compared to baseline values, potassium values peaked at 100 seconds post-reperfusion [median (IQR) of 5 mmol/L (4.7, 5.7)]; p <0.0001. By 5 minutes serum potassium levels had returned to baseline values. There was a modestly strong association between pre-reperfusion potassium levels and peak potassium values at 100 seconds (Spearman R=0.38; p=0.04). Peak serum potassium levels did not correlate with cold ischaemia time, duration of anhepatic stage, noradrenalin use at the time of reperfusion, or effluent potassium levels.

Conclusion: Serum potassium levels peak at 100 seconds after reperfusion during cadaveric adult liver transplantation, normalising to baseline by 5 minutes post-reperfusion. Hyperkalaemia is severe in approximately 20% of patients. A high serum potassium level prior to reperfusion was associated with higher potassium level after reperfusion. Results of this study have implications in guiding prevention i.e. proactively treating high potassium values pre-reperfusion, vigilance during, and optimal timing to sample serum potassium values, as part of an anaesthetic liver transplantation protocol.
Anoop N Koshy; Francis J. Ha; Paul J. Gow; Hui-Chen Han; FM Amirul-Islam; Han S Lim; Andrew W. Teh; Omar Farouque

Computed Tomographic Coronary Angiography and Coronary Artery Calcium Score in Perioperative Risk Stratification prior to Noncardiac Surgery: A Systematic Review and Meta-Analysis

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Aim
Cardiovascular complications after noncardiac surgery can lead to significant morbidity and mortality. Predicting events in individual patients remains a challenge. The prognostic value of computed tomographic coronary angiography (CTA) and coronary artery calcium (CAC) score in cardiovascular prevention is well described. However, there is no consensus on its utility in perioperative risk stratification. We performed a systematic review and meta-analysis evaluating preoperative risk prognostication of CTA and CAC score in noncardiac surgery.

Methods
We searched MEDLINE, EMBASE & PubMed databases for studies of preoperative CTA and CAC reporting perioperative major adverse cardiovascular events (MACE) with at least 30 days follow-up. Summary odds ratios (OR) for degree of coronary artery disease (CAD) and associated MACE were pooled using a random-effects model.

Results
Eleven studies were included. Two hundred and forty-six (7.1%) MACE occurred in 3480 patients. Risk of perioperative MACE rose incrementally with the severity and extent of CAD on CTA (no/nonobstructive 3.1%; obstructive single-vessel 7.1%; obstructive multivessel 23.1%, p<0.001- Figure top panel). Multivessel disease demonstrated the greatest risk (OR 8.88 95%CI 5.14-15.34, p<0.001, Figure bottom panel). Increasing CAC score was associated with higher perioperative MACE (by CAC score: ≥100 OR 5.08, ≥1000 OR 10.42, all p<0.01). In a cohort deemed high risk by established clinical indices, absence of multivessel disease on CTA demonstrated a negative predictive value of 96% (95%CI 92.8-98.4) for predicting freedom from MACE.

Conclusion
Severity and extent of CAD on CTA conferred incremental risk for perioperative MACE in patients undergoing noncardiac surgery. The ‘rule-out’ capability of CTA is comparable to other non-invasive imaging modalities and may be a viable alternative in perioperative risk stratification.
Assessing the prevalence of familial hypercholesterolaemia in coronary artery disease patients

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Aim
Familial hypercholesterolaemia (FH) is a dominantly inherited genetic disorder with an estimated population prevalence of 1/200 – 1/300. Mutations affect genes related to LDL cholesterol, leading to disruption in cholesterol removal from the circulation. This results in congenitally elevated LDL cholesterol levels and, if untreated, severe and premature cardiovascular disease. FH is likely to be over-represented in patients presenting to hospitals with coronary artery disease. Despite this, there has been little research into the prevalence of this severe but treatable condition within an Australian population. The aims of this study were to assess the prevalence of FH within a population of coronary artery disease patients.

Methods
This cross-sectional study assessed consecutive patients < 70 years old presenting to Austin Health from Feb-June 2018. Patients were included if they presented with: acute coronary syndromes, elective coronary angiography requiring percutaneous intervention or coronary artery bypass graft surgery. Diagnosis of familial hypercholesterolaemia was made utilising the full Dutch Lipid Clinic Network score. Other cardiovascular risk factors (hypertension, diabetes, smoking status, elevated lipoprotein(a)) were also recorded. The Wilcoxon rank-sum test was used to analyse continuous variables and Fisher’s exact text was used to analyse categorical variables.

Results
214 patients were assessed within this time period with 177 being eligible for analysis. 19 patients were diagnosed with “definite” or “probable” FH, resulting in an estimated prevalence of 10.7% (95% confidence interval 6.6% - 16.3%). 94.7% of patients with FH were taking statins prior to admission. When analysing patients less than 60 years of age, the prevalence of FH rose to 17.7% (95% confidence interval 10.0% - 27.9%).

Conclusion
This study has demonstrated the over-representation of familial hypercholesterolaemia in an at-risk population of patients. Its high prevalence and association with significant morbidity and mortality indicates a recommendation for screening. Diagnosis allows referral to specialist lipidology for appropriate treatment and cascade screening of undiagnosed family members.
Delivering heart failure system change through quality improvement initiatives

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⁵. Heart Foundation, Victoria, Australia

Background: Heart failure (HF) is a costly, complex chronic condition with high readmission rates and poor clinical outcomes. Care that is consumer-centred, driven by evidence and organised for safety has proved challenging to implement and deliver. There is large variance in HF readmission rates across healthcare services. In 2016, The Victorian Cardiac Clinical Network (VCCN) funded the Heart Foundation to develop a Heart Failure Toolkit to provide health services with a clinical redesign framework to address readmission rates and care variation. In 2017 our aim was to implement the Toolkit to improve access to timely and appropriate HF care through system redesign.

Method: We employed the quality improvement model with associated plan-do-study act-cycles to: 1) map the HF patient journey; and 2) improve care transition flow and access to HF specialty care.

Results: 95 Plan-Do-Study-Act cycles were undertaken; 93 complete and two incomplete. The improvement activities did not reduce 30 day readmission rates (2016: 21%; 2017: 30%). Improved outcomes included reduction in clinic waitlist by 23%; reduction in HF outreach wait times by 83%, and improvement in time to first contact by 96%. Multi-disciplinary policy for community access to HF specialty cardiology, standardised process for identifying readmitted outreach patients and for accessing client medical records in the community were developed.

Conclusions: System redesign is possible using the quality improvement model and the HF toolkit provides an effective framework for undertaking this work. It is not surprising that 30 day readmissions were not impacted as project timeframes and funds were limited. (250 words)
Feasibility of Undertaking Standardised Patient Reported Outcome Measures in those with Heart Failure

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⁵. Heart Foundation, Victorian, Australia

**Background:** As health budgets are strained and care becomes more patient-centred, governments, funders and providers are focusing on value as defined by outcomes. Patient-Reported Outcomes Measures (PROMs) are reports by patients about how they feel or function in relation to their health condition and management. The Victorian Cardiac Clinical Network (VCCN) funded the Heart Foundation to support collection of the HF PROMs standard set as described by International Consortium for Health Outcomes Measurement (ICHOM).

**Method:** Patients presenting to the HF outreach clinic, from August to September 2017, with a confirmed HF diagnosis were invited to complete the HF PROMs. The set included the Kansas City Cardiomyopathy Questionnaire (KCCQ), the Patient Health Questionnaire-2 (PHQ-2), two functional health questions (PROMIS), number of hospital readmissions and appointments.

**Results:**

There were 189 patients across the 11 clinic sessions. 119 consented; 67% male; median age 72yrs (IQR: 60-80). Missed questions were 5 for both PHQ2 and PROMIS; and 29 regarding number of hospital admissions and outpatient appointments. 16 (13%) were at high risk of 6 month readmission and/or death (KCCQ score <25); 42 (35%) had a high probability (>75% on PHQ-2) of being depressed; 67 (56%) had >1 admission in preceding 12 months; 25 (21%) had three to five admissions.

**Conclusion:** Overall the PROMs questions were relatively easy for patients to complete in the outpatient environment and the resulting data is aligned with the literature. There needs to be a process by which PROMs information can be effectively drawn upon in consultations with clinicians. (249 words)
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Cyclosporin Dosing and Toxicity and Posaconazole Interactions Following Allogeneic Transplantation
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Introduction
Cyclosporin (CSA) is commonly used as GVHD prophylaxis in allograft recipients. The recommended oral dose at switching from IV in the pre-posaconazole era was 3mg/kg BD. Posaconazole is now commonly used as antifungal prophylaxis in this context; it increases CSA levels through inhibition of the cytochrome involved in CSA metabolism. We evaluated CSA-related toxicity after switch from IV to oral CSA in alloHSCT recipients receiving posaconazole with the aim of defining the optimal weight based oral dose.

Methods
A retrospective audit of adult alloHSCT patients between October 2015 - October 2017 switching from IV CSA to oral CSA and who received concomitant posaconazole (300mg IV daily then 300mg oral daily or 200mg oral BD). Two groups were analysed: those with starting oral CSA doses ≥ 2.8mg/kg BD ('higher dose') and < 2.8mg/kg BD ('lower dose'). Exclusion criteria included continuation of IV CSA beyond day 30 or CSA taper before day 40 due to relapse. Data collected included CSA doses at transition from IV to oral CSA, day 40 and day 60, and dose reductions due to various toxicities: renal impairment (fall in eGFR >15), new/worsening hypertension, hypomagnesaemia (<0.60 mmol/L despite IV replacement), nausea and/or headache not attributable to other causes and miscellaneous (thrombotic microangiopathy and PTLD).

Results
Twenty eight of 44 patients allografted during this period were eligible with a median age of 43 (19-68) years. All received CSA/methotrexate as GvHD prophylaxis with T cell depletion in 20 (71%). The majority continued posaconazole at day 40 (71%) and day 60 (68%).

<table>
<thead>
<tr>
<th></th>
<th>Higher dose group: N=12</th>
<th>Lower dose group: N=16</th>
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<tr>
<td>Transition IV CSA to oral CSA</td>
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<tr>
<td>Median dose*</td>
<td>2.90 (2.86 – 3.33)</td>
<td>2.35 (1.75 – 2.78)</td>
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<td>eGFR*</td>
<td>91 (40 – 91)</td>
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<td>Day 40</td>
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<tr>
<td>Number of pts remaining on CSA</td>
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<td>N = 16 (11 on posa)</td>
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<td>Median CSA dose overall</td>
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<td>2.03 (1.33 – 2.76)</td>
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<tr>
<td>Median CSA dose pts on posa</td>
<td>2.46 (1.43 – 3.33)</td>
<td>2.19 (1.34 - 2.28)</td>
</tr>
<tr>
<td>Day 60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of pts remaining on CSA</td>
<td>N = 9 (6 on posa)</td>
<td>N = 16 (11 on posa)</td>
</tr>
<tr>
<td>Median dose overall</td>
<td>2.15 (0.87 – 3.33)</td>
<td>1.53 (0.79 – 2.57)</td>
</tr>
<tr>
<td>Median dose pts on posa</td>
<td>1.84 (0.86 – 2.25)</td>
<td>2.02 (0.79 – 2.57)</td>
</tr>
<tr>
<td>No. pts with CSA dose reduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transition to day 40</td>
<td>8 (67%)</td>
<td>8 (50%)</td>
</tr>
<tr>
<td>Day 40 – day 60</td>
<td>9 (75%)</td>
<td>10 (63%)</td>
</tr>
<tr>
<td>At any time point</td>
<td>10 (83%)</td>
<td>12 (75%)</td>
</tr>
</tbody>
</table>

Values expressed as median (range) * CSA doses in mg/kg BD * eGFR in ml/min/1.73m²
¥ Posaconazole levels in mg/L; posa = posaconazole

Toxicities requiring adjustment were: renal impairment (51%), nausea (43%), hypomagnesemia (43%), hypertension (14%), headache (11%), and miscellaneous (6%). Four patients were admitted to hospital due to toxicity. Acute GvHD (grade 3-4) occurred in 1 patient.

Conclusion
The 3mg/kg BD oral CSA dose in alloHSCT patients on concomitant posaconazole is associated with frequent toxicity. We are prospectively evaluating whether 2.5mg/kg BD reduces toxicity without compromising the risk of GvHD, particularly in patients receiving T cell depletion.
Diffuse Large B cell lymphoma (DLBCL) Presenting with synchronous CNS and systemic disease at diagnosis: Results from an international collaborative study

Background:

DLBCL presenting with both CNS and systemic disease at first diagnosis is rare. Such patients are excluded from most clinical trials; thus, the optimal treatment is unknown and clinical outcomes are poorly described.

Aim:

To describe the treatment and outcomes of patients with synchronous CNS and systemic DLBCL at first diagnosis.

Methods:

Multicentre retrospective international study (6 Australian & UK sites). Cases were identified from clinical and pharmacy records. Eligible patients had histologically proven DLBCL, with radiological, histological, or CSF evidence of synchronous systemic & CNS disease, treated with combination chemotherapy and rituximab. Patients with relapsed disease were excluded. Primary Endpoint: OS. Secondary endpoints: CR rate, PFS, toxicity. P values of <0.05 were considered significant.

Results:

Of 59 patients, 71% were male and the median age was 66yrs (range 17-86). 45 (76%) had NCCN-IPI ≥4. Median number of extranodal sites outside the CNS was 2 (range 0-8). 10% were double-hit by FISH, and 35% of those with data available were double-expressors of MYC and BCL2 protein. CNS disease was leptomeningeal only in 24 (41%); 35 (59%) had parenchymal disease, 8 (14%) had both. 34 (58%) received systemic therapy (predominantly R-CHOP, n=31) plus a CNS-directed treatment (group A). 25 (42%) underwent intensified MTX and/or Ara-C containing therapy: hyper-CVAD n=14, CODAX-M/IVAC n=10, DHAC=1 (group B). CNS-directed therapy in group A included: IV HD-MTX in 19 (56%), HD-MTX + Ara-C in 2 (6%), intrathecal therapy (IT) only in 10 (29%), radiotherapy (RT) only in 2 (6%). Specific CNS therapy was omitted in one patient due to early PD.

Additional consolidative therapy included CNS RT in 18 (31%) (whole brain in 8, site-specific in 10), and autologous SCT in CR1 in 8 (13%) using BEAM (n=4) or BCNU + thiotepa (n=4) conditioning. All SCT patients were from group B. 23 (39%) required dose reductions and 23 (39%) required early cessation of therapy. Treatment-related mortality was 14% for the whole group (4 in each group, including 2 during transplant).

End of treatment CR rate was 58%; 62% for group A and 57% for group B (p=0.69). 25% were primary refractory; 26% in group A and 20% in group B (p=0.68). Site of relapse was: CNS only in 14, systemic only in 8, both in 6. Incidence rate of CNS progression at 2 years was 40%. 19/20 patients with CNS relapse died with median OS of 7.2 months (mo). Of the CNS relapses, 12 occurred in group A and 8 in group B (p=0.79). The estimated 2yr OS for those without CNS relapse was 74%.

Median OS: Whole cohort=11.1 mo, group A=11 mo, group B=11.8 mo (p=0.82). Median PFS: Whole cohort=10.1 mo, Group A=9.6 mo, Group B=10.6 mo B (p=0.65). The OS of transplanted vs non-transplanted was similar (p=0.18); 5/8 transplanted patients remain disease free with >1 year of follow-up. There was no survival difference between parenchymal vs leptomeningeal disease (p=0.56). The estimated 2yr PFS and OS was 41%, and 52% respectively, with no significant differences between groups (p=0.64, figure).

Conclusion:

Among this large cohort of synchronous + systemic DLBCL, intensified regimens and additional consolidation therapy were not associated with clinical benefit. The CNS is the most common site of treatment failure, which is associated with a dismal prognosis. OS is comparable to PCNSL (Ferreri, 2009), but those who achieve CNS control have 2yr outcomes similar to systemic DLBCL (Cunningham, 2013). Future efforts should focus on preventing CNS relapse. Biomarker tissue analysis is underway.
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Association of diabetes and HbA1c with outcomes for people hospitalised with influenza

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Aim
The relationship between diabetes and non-pandemic influenza outcomes is poorly defined. We aimed to investigate the association of the presence of diabetes and HbA1c levels with outcomes following hospitalisation for inpatients with influenza.

Methods
As part of the Austin Health Diabetes Discovery Initiative, all inpatients aged ≥54 years had their HbA1c measured between January 2013 and December 2017 in this prospective observational study. We examined outcomes in those admitted with influenza.

Results
Of 608 people admitted with influenza during the study period, 38% had diabetes. 10% of people with diabetes were newly diagnosed during their admission with influenza. There was no difference in gender, smoking status, admission unit, or influenza subtype between patients with and without diabetes. Compared to inpatients without diabetes, those with diabetes had higher (i) HbA1c (median=6.85%; IQR=6.2-7.9% vs median=5.6%; IQR=5.3-5.8%, p<0.01), and (ii) Charlson comorbidity index after excluding diabetes (median=5; IQR=4-6 vs median=5; IQR=3-6, p<0.01). After adjusting for a) gender, b) Charlson comorbidity index excluding diabetes but incorporating age, c) smoking status, d) whether influenza was contracted during the admission, and e) whether antivirals were administered within 48 hours of symptom onset, neither the presence of diabetes, nor higher HbA1c levels, were associated with mortality, ICU admission, mechanical ventilation, readmission, hospital length of stay, pneumonia, myocardial infarction or increased admission severity.

Conclusions
In this observational study, the presence of diabetes or increasing HbA1c levels were not associated with worse outcomes of hospitalisation with influenza. Studies with larger sample sizes may be necessary to define the associations between diabetes and outcomes following influenza infection requiring hospitalisation.
Fernando HKDH ¹, Angus PW ¹,², Herath CB ¹

Advanced glycation end products (AGEs) derived from diets have more impact on the progression of fatty liver disease than endogenously derived AGEs

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Aims
Non-alcoholic fatty liver disease (NAFLD) affects up to 30% of the Australian adult population and is a major cause of liver disease related deaths. Advanced glycation end products (AGEs), formed when reducing-sugars react with proteins, has been implicated in driving NAFLD to steatohepatitis. AGEs can be formed both endogenously or during food processing. We therefore, investigated and compared the effects of dietary and endogenously derived AGEs on NAFLD progression.

Methods
C57BL/6 mice were fed either a standard diet or a high fat high cholesterol (HFHC) diet for 40 weeks. Third group of mice was fed the HFHC diet for 30 weeks, followed by baked HFHC diet to increase dietary AGE intake for the remaining 10 weeks. Another three groups of mice fed on the HFHC were injected daily with varying doses of AGEs to mimic increased endogenously derived AGEs, similar to that occurs in diabetes, starting at week 30. Gene expression of RAGE, profibrotic and proinflammatory cytokines, hepatic stellate cell (HSC) activation marker (αSMA) and collagen 1 was determined. Hepatic fibrosis was quantified by picrosirius red staining.

Results
AGE administration caused an increased (p<0.05) gene expression of αSMA, RAGE, TNF-α, MCP-1, IL-1β, CTGF, TGFβ1 and collagen I, which was accompanied by increased (p<0.05) liver fibrosis compared to those in mice fed the standard diet. In contrast, gene expression and the level of fibrosis were much higher (p<0.05) in mice fed the baked diet to increase the dietary AGE intake compared to those in mice injected with AGEs. This was associated with increased (p<0.05) gene expression of liver endotoxin responsive protein TLR4.

Conclusion
The progression of NAFLD to steatohepatitis and liver fibrosis is triggered by activation of HSCs. We conclude that increased dietary AGE intake is more detrimental on NAFLD progression than those derived endogenously as that occurs in diabetes.
Fernando HKDH ¹, Rajapaksha DIG ¹, Leung C ², Angus PW ¹,², Herath CB ¹

Marination of food with vinegar offers a simple and effective approach to prevent advanced glycation end products (AGEs)-induced NAFLD progression

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Aims
Non-alcoholic fatty liver disease (NAFLD) affects up to 30% of the Australian adult population. Advanced glycation end products (AGEs), formed by non-enzymatic reaction between reducing-sugars and proteins, acting via RAGE (receptor for AGEs), have been implicated as a second hit that drives NAFLD to steatohepatitis. Western diets often contain high AGES due to preparation of food at high temperatures. However, the impact of high dietary AGEs on NAFLD progression in diabetes is unknown. Therefore, we investigated the role of dietary AGEs and diabetes on NAFLD progression.

Methods
C57BL/6 mice were fed a high fat high cholesterol (HFHC) diet or baked HFHC diet to increase dietary AGE content. Another two groups of mice fed the HFHC or baked-diet were made diabetic. In addition, a group of diabetic mice was fed a vinegar marinated and baked-diet. At 40 weeks, animals were sacrificed to harvest liver. Gene expression of RAGE, profibrotic and proinflammatory cytokines was determined by qPCR. Liver fibrosis was determined by picrosirius red staining.

Results
High dietary AGE intake significantly (p<0.05) increased liver gene expression of RAGE, TNF-α, MCP-1, IL-6, IL-1β, αSMA, CTGF, TGFβ1 and collagen 1 in diabetic mice compared with HFHC fed mice without diabetes. Moreover, the livers of high AGE fed mice showed increased (p<0.05) gene expression of endotoxin responsive proteins, CD14 and TLR4. Whilst diabetes or baking alone increased (p<0.05) liver fibrosis, diabetic mice fed the baked-diet had worse liver fibrosis, which was significantly (p<0.0001) reduced by marinating the diet. Treatment of Kupffer cells with AGEs increased (p<0.05) expression of proinflammatory cytokines.

Conclusion
Although both increased dietary AGEs and diabetes drive NAFLD progression to liver fibrosis, the effect of dietary AGEs, possibly acting via Kupffer cells, are more important. We also conclude that a simple vinegar marination of the diet is effective in reducing NAFLD progression.
Background

Falls and falls-related injuries are leading contributors to mortality and disability in the geriatric population. This burden of falls is even greater within residents living in residential aged care facilities (RACFs) due to increased frailty, multiple comorbidities, polypharmacy and lower functional baseline. Furthermore, RACF residents have high rates of hospital admission, inpatient complications, mortality and longer inpatient stays after a fall. We sought to characterise falls presentations to the Emergency Department (ED) from RACFs, to determine the proportion of minor or non-injurious falls presenting to hospital, and identify modifiable factors associated with injury.

Methods

Retrospective audit of all falls presentations to the ED from RACFs to the Austin Hospital between July 2016-January 2017. Data from the included presentations were obtained through patient discharge summaries, inpatient notes and RACF transfer notes. Chi-square and Mann-Whitney U test were used to compare groups with no/minor and severe injury using IBM SPSS.

Results

From the 1204 ED presentations that were recorded over the 6 months period, 235 (19.5%) presented as falls. People with falls had a median age of 88 and a median of 6 comorbidities and 8 medications. 86 (36.6%) residents presented with fractures and 111 (47.2%) presented with soft-tissue injuries. 12 (5.1%) residents presented with no injuries, 123 (52.3%) presented with mild injuries and 100 (42.6%) presented with severe injuries. Falls most commonly presented in the morning (44.7%) followed by evening (30.2%) and afternoon (25.1%). Of all the variables collected, only a past history of falls and prescription of dementia medication were associated with more severe injury.

Conclusion

Falls are common within the RACF population, with almost 20% of their hospital presentations attributed to falls. Observed correlations between past history of falls and prescription of dementia medication with severe injuries are intriguing and warrants further investigations.
Are brain changes found on MRI associated with presence of frailty in a memory clinic?

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Aim
Frailty and its aetiology have been studied extensively; however, only a few studies have assessed the associations between frailty and neuroimaging biomarkers. The aims of this study were to construct a cumulative-deficits Frailty Index (FI)\(^1\) and compare it to the validated Edmonton Frailty Scale (EFS)\(^2\); to measure the prevalence of frailty in a memory clinic; and to examine the associations between frailty and brain changes found on magnetic resonance imaging (MRI) in memory clinic attendees.

Method
A 54-item FI was retrospectively assessed for all clinic attendees from 2014. Frailty was defined as FI > 0.25. To confirm validity of this retrospective approach, prospective measures were also collected from 53 clinic patients (February-June 2018). Agreement between frailty scales was assessed using kappa-statistic. All available MRI from 2014 were analysed for stroke, cerebral small vessel disease (CSVD, including cerebral microbleeds, cortical superficial siderosis (CSS), white matter hyperintensity [WMH]) and neurodegenerative changes (hippocampal atrophy, positron emission tomography [PET] and single-photon emission computed tomography [SPECT]), blind to clinical findings. Chi Square tests were used to determine associations between brain imaging findings and frailty.

Results
There were 209 (age 35-93 years) attendees in 2014 and MRI were available for 121 patients. The prevalence of frailty in the memory clinic was 38.3% (using FI) in 2014. There was moderate agreement between frailty measured using FI and EFS (Kappa coefficient=0.54, p>0.001). Frailty was also found to be associated with all-cause dementia (p=0.02). In those with MRI, frailty was associated with increased severity of periventricular WMH and presence of CSS.

Conclusion
The findings of this study agree with previous publications showing an association between frailty and imaging evidence of CSVD. Further longitudinal studies are warranted in order to derive causality and account for important confounders.

References
Liver directed angiotensin converting enzyme 2 (ACE2) gene therapy for chronic biliary fibrosis and NAFLD

1. Department of Medicine, The University of Melbourne, Austin Health, Heidelberg, Vic., Australia;
2. Department of Gastroenterology, Austin Health, Heidelberg, Vic., Australia

Aim
Non-alcoholic fatty liver disease (NAFLD) and chronic biliary fibrosis are recognized as major indications for liver transplantation with no established medical therapy. We have successfully developed a gene therapy strategy and showed that liver-specific adeno-associated viral (AAV) vector carrying angiotensin converting enzyme 2 (ACE2) markedly reduced steatohepatitis and biliary fibrosis in short-term mouse models NAFLD and biliary fibrosis. ACE2 is a major enzyme of the alternate renin angiotensin system that generates antifibrotic peptide angiotensin-(1-7) from pro-fibrotic peptide, angiotensin II. The aim of this study was to investigate the antifibrotic effect of ACE2 therapy in a long-term dietary NAFLD model in the presence of diabetes, and in multiple drug resistant protein 2 knockout (Mdr2-KO) mice that develop progressive biliary fibrosis, closely resembling those seen in human patients.

Methods
A single intraperitoneal injection of liver-specific ACE2-AAV was administered to diabetic NAFLD mice and Mdr2-KO mice at two stages of disease progression. Liver biochemistry, fibrosis and gene expression of pro-inflammatory and pro-fibrotic mediators were determined. To evaluate the effect of angiotensin-(1-7), the peptide was directly infused to Mdr2-KO mice.

Results
In chronic biliary fibrosis, ACE2 increased ACE2 gene expression and protein activity, which has led to increased (p<0.0001) breakdown of potent pro-fibrotic peptide angiotensin II with a concomitant increase (p<0.05) in the production of hepatic angiotensin-(1-7). Moreover, ACE2 significantly (p<0.05) reduced the profiles of pro-inflammatory and pro-fibrotic cytokines and activation of hepatic stellate cells. Consistent with these results, the infusion of angiotensin-(1-7) markedly reduced (p<0.0001) biliary fibrosis in Mdr2-KO mice and showed similar changes on other parameters as in ACE2 injected animals. Consistent with biliary fibrotic model, ACE2 therapy significantly (p<0.05) reduced liver fibrosis in diabetic NAFLD mice.

Conclusion
Liver-specific over-expression of ACE2 markedly improves progressive biliary fibrosis and NAFLD in mice. Thus, we conclude that ACE2 gene therapy has potential to treat patients with chronic liver diseases such as biliary fibrosis and NAFLD.
Mas related G-protein coupled receptor type-D (MrgD) is a novel therapeutic target to reduce splanchnic vasodilatation in portal hypertension.

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Aims
Splanchnic vasodilatation which leads to an elevated portal venous inflow in cirrhosis plays an important role in the pathogenesis of portal hypertension (PHT). In this study, we therefore investigated whether chronic blockade of the vasodilatory receptors, Mas (MasR) and Mas-related G-protein coupled receptor type-D (MrgD), produce a clinically significant reduction of portal pressure (PP) in cirrhotic animals.

Methods
Liver disease was induced in Sprague-Dawley rats by bile duct ligation (BDL) surgery or twice-weekly carbon-tetrachloride (CCl4) injections. Two weeks after BDL and 8-weeks after CCl4 injections, rats received either MasR antagonist A779 or MrgD antagonist D-Pro-7-Ang-(1-7) (D-Pro) (28µg/kg/hr) for 2-weeks via subcutaneously implanted osmotic mini-pumps. Healthy, sham-operated, BDL and CCl4 animals receiving saline infusion served as controls. After treatment, the rats were cannulated to measure PP and mean arterial pressure (MAP). Coloured microsphere technique was used to calculate splanchnic vascular resistance (SVR), hepatic vascular resistance (HVR) and mesenteric blood flow (MBF). Mesenteric resistance vessels isolated from separate groups of rats were used in myographs to study their vasodilatory properties.

Results
D-Pro and A779 significantly (p<0.05) reduced PP in both models compared to saline-infused controls. In CCl4 rats this reduction was larger with D-Pro than A779. Treatment with both drugs significantly (p<0.05) increased SVR and HVR in both models. However, in the CCl4 model, increased SVR with D-Pro was greater than that of A779, leading to a marked reduction in MBF by 51% and 40%, respectively. D-Pro profoundly reduced (p<0.01) vascular relaxation of first order (45%) as well as 2nd/3rd order (13%) vessels in response to acetylcholine, whereas the vessels treated with A779 failed to inhibit acetylcholine-induced vascular relaxation.

Conclusion
These findings demonstrate profound effects of MrgD blockade on SPVR, MBF and PP. MrgD but not MasR blockade has splanchnic vasculature-specific effects in cirrhotic rats. We conclude that the novel receptor, MrgD, is a potential therapeutic target for the design of drugs that can specifically block splanchnic vasodilatation in cirrhotic PHT.
Splanchnic vasodilatation is associated with a reduced activity of the classic axis of the renin-angiotensin system in a rat model of non-cirrhotic portal hypertension

Aim:
Portal hypertension (PHT) is a life-threatening complication of cirrhosis, resulting from pathological vasodilatation of the splanchnic circulation. The renin-angiotensin system (RAS) is a major contributor to splanchnic vasodilatation in cirrhotic PHT; however, its contribution to non-cirrhotic PHT is largely unknown. We therefore investigated the development of PHT in an animal model of non-cirrhotic PHT and the RAS related changes in the mesenteric vasculature and the gut.

Methods:
PHT was induced in Sprague-Dawley rats by partial portal vein ligation (PPVL). Portal pressure (PP) was measured 2, 10 and 14-days after PPVL by cannulating the portal vein under anaesthesia. Gene expression of the RAS components including angiotensin converting enzyme (ACE), ACE2, Mas receptor (MasR) and angiotensin-II type-1 receptor (AT1R) was determined in mesenteric vascular bed (MVB) and gut tissues by qPCR. Ex-vivo perfused MVB preparations of PPVL and sham-operated rats were used to investigate the perfusion pressure response to angiotensin-II and angiotensin peptide metabolism.

Results
PP was increased (p<0.001) from day-2 post-PPVL compared with sham-operated rats. qPCR analysis showed, whilst ACE2 gene expression was reduced in MVB (p<0.0005), the AT1R expression was downregulated (p<0.005) in both gut and MVB of PPVL rats. However, MasR and ACE expression were not altered by PPVL in both vasculatures. There was a significant (p<0.05) reduction in splanchnic vascular resistance in PPVL rats compared with sham controls. Perfusion pressure response to angiotensin-II and ex-vivo angiotensin-(1-7) production from angiotensin-II were significantly (p<0.05) reduced in MVB preparations of PPVL rats compared to sham controls.

Conclusion
The Gut and MVB respond to portal vein stenosis by downregulating AT1R expression, leading to attenuation of angiotensin-II mediated vasoconstriction which results in increased mesenteric blood flow. Decreased expression of ACE2 in MVB is responsible for reduced Ang-(1-7) production from angiotensin-II. We conclude that decreased angiotensin-II mediated vasoconstriction in the gut and MVB contributes to the development of non-cirrhotic PHT.
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Targeting the receptors of the renin-angiotensin system to improve splanchnic vascular resistance in cirrhosis

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Aim
Portal hypertension (PHT) resulting from splanchnic vasodilatation is a major cause of morbidity and mortality in patients with cirrhosis. The renin-angiotensin system (RAS) plays an important role in the splanchnic vasodilatation. We hypothesized acute blockade of the vasodilatory RAS receptors, the Mas (MasR) and Mas related G-protein coupled receptor type-D (MrgD) improves PHT and counteracts systemic hypotension associated with angiotensin-II type-1 receptor (AT1R) blockers.

Methods
Liver disease was induced in Sprague-Dawley rats by bile duct ligation (BDL) surgery or twice-weekly carbon tetrachloride (CCl4) injections. Four weeks after BDL or 10-weeks after CCl4 injections, anaesthetized rats were cannulated for continuous measurement of portal pressure (PP) and mean arterial pressure (MAP). MasR antagonist A779, MrgD antagonist D-Pro-7-Ang-(1-7) (D-Pro) or AT1R blocker losartan were administered as an intravenous bolus injection. Separate groups of rats received a combined treatment in which a bolus of A779 or D-Pro was given 20-minutes after losartan.

Results
Treatment with A779 and D-Pro significantly (p<0.01) reduced PP in both models. However, reduction in PP was prominent in the first 5-minutes after the bolus of receptor blockers. In contrast, losartan resulted in a persistent and significant (p<0.05) reduction of PP in the CCl4 but not in the BDL model. This contrasted with MAP which was markedly (p<0.01) reduced with losartan in both models. However, the combined treatment with A779 or D-Pro failed to counteract the hypotensive effect of losartan. Radioimmunoassay of rat plasma showed that the peptide blockers, A779 and D-Pro, have a very short half-life in the rat circulation.

Conclusion
The use of A779 and D-Pro to increase vascular resistance in the splanchnic (thus, reducing PP) and systemic (thus, increasing MAP) circulation is hampered by their short half-life in the circulation. Therefore, development of non-peptidal receptor blockers would be a promising therapeutic approach for PHT, and systemic hypotension associated with AT1R blockers.
Grigg S¹, Sarri G¹, Gow P², Yeomans N¹

Tumour recurrence and survival outcomes with mTOR-inhibitor based immunosuppression following liver transplantation for hepatocellular carcinoma: a meta-analysis

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Aim:
Calcineurin-inhibitors (tacrolimus/cyclosporine) have been associated with an exposure related increase in tumour recurrence following liver transplantation for hepatocellular carcinoma (HCC)¹. Mammalian target of rapamycin (mTOR) inhibitors (sirolimus/everolimus) are a separate class of immunosuppressants that have been reported to reduce recurrence rates and improve survival in these patients². This study aims to clarify this effect through a meta-analysis of existing data.

Methods
A systematic search was conducted in three databases up until 6/6/18. The inclusion criteria were observational or interventional study designs reporting the effect of early initiated (<6 months post-transplant) mTOR-inhibitor-based immunosuppression on survival or tumour recurrence in patients transplanted with HCC, compared to a control arm of calcineurin-inhibitor-based therapy. The primary outcome was recurrence-free-survival. Secondary outcomes were tumour recurrence rate, and acute rejection rate. A sub-analysis of studies stratified by Milan-criteria was performed. Pooled risk-ratios (RR) were calculated using the random-effects-model.

Results
4793 studies were retrieved, of which 26 were included. Recurrence-free-survival was significantly increased with mTOR-inhibitor-based therapy at 1-year (RR: 1.09, 95%CI: 1.01-1.18) and 3-years (RR: 1.1, 95%CI: 1.01-1.21) post-transplant, with a non-significant increase at 5-years (RR: 1.15, 95% CI: 0.99-1.35). Recurrence rate was lower in the mTOR-inhibitor arm (RR: 0.67, 95%CI: 0.56-0.82), with no significant increase in acute rejection (RR: 1.1, 95%CI: 0.94-1.28). In a sub-analysis stratified by Milan-criteria, a 3-year recurrence-free-survival benefit with mTOR-inhibitor therapy was found for those with HCC within the Milan-criteria (RR: 1.13, 95%CI: 1.03-1.23), but not beyond it (RR: 0.95, 95%CI: 0.83-1.1). There were insufficient data to include 5-year recurrence-free-survival in this sub-analysis.

Conclusions
mTOR-inhibitor-based immunosuppression in patients transplanted with HCC improved recurrence-free-survival up to 5 years, and reduced the recurrence rate compared with standard calcineurin-inhibitor-based therapy, with no significant increase in the rate of acute rejection. Future research should aim to clarify the effect in higher versus lower risk cohorts.

References
Counting the cost of critical antibiotic shortages

Authors: Khumra S, Mahony AA, Devchand M, Garrett K, Grayson ML, Trubiano JA

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3. University of Melbourne

Aim: Shortages of common antibiotics pose challenges to prescribers and antimicrobial stewardship (AMS) teams. The AMS and economic consequences of these shortages in Australian hospitals are ill-defined. We aim to evaluate the impact of piperacillin+tazobactam and gentamicin shortages on antibiotic usage and associated costs.

Methods: A retrospective review comparing the inpatient use (excluding hospital-in-the-home) and costs of alternative antibiotics, 3 months pre-shortage (Jul-Sept, 2017) and 3 months during the shortage (Oct-Dec, 2017), was undertaken at Austin Health. A hospital-wide contingency plan recommended alternatives to piperacillin+tazobactam, mainly intravenous amoxicillin-clavulanate and cefepime, and to gentamicin, primarily amikacin, based on clinical indication. Antibiotic use data, expressed as days of therapy (DOT) per 1000 occupied bed days (OBD), was obtained from the electronic medication record. Associated costs were determined from drug acquisition costs. Percentage change in the use of each alternative antibiotic was categorized as either ‘minor; 1-10%’, ‘intermediate; 11-30%’ or ‘large; >30%’ increase. Percentage change in total antibiotic costs was also determined.

Results: There were large increases in the use of amikacin (261.7%), cefepime (233.3%), intravenous amoxicillin+clavulanate (190.5%), ciprofloxacin (52.9%) and ceftazidime (42.9%) with proportional cost increases. There were intermediate increases for ampicillin, cefazolin, metronidazole, clindamycin, meropenem and vancomycin, and a minor increase for ceftriaxone. The percentage increase for total antibiotic costs was 21.8% ($37,762.06).

Conclusion: Piperacillin+tazobactam and gentamicin shortages were accommodated by increases in high-cost and less desirable antibiotic use. Intravenous amoxicillin-clavulanate or anti-pseudomonal cefalosporins provide potentially narrower-spectrum alternatives however, the impact on patient safety and clinical outcomes because of increased prescribing of these agents requires further evaluation.
Outcome and safety of targeted liver biopsies for indeterminate lesions in patients with chronic liver disease – a single centre experience

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ABSTRACT:
Aim: To evaluate the histopathological and safety outcomes of indeterminate lesions in patients at high risk for developing hepatocellular carcinoma (HCC) and underwent ultrasound-guided biopsies.

Methods: Ultrasound-guided targeted liver biopsies for indeterminate lesions performed in a 10-year period at our institution were reviewed retrospectively for lesion characteristics, biopsy techniques, histopathological results and post procedural complications.

Results: A total of 172 biopsies were performed in 152 patients. Most common background liver disease included hepatitis C, hepatitis B, alcoholic and non-alcoholic steatohepatitis. 65.1% of patients had known cirrhosis at time of biopsy. HCC was the most common histopathological finding accounting for 55.8% of all biopsies, followed by cholangiocarcinoma, dysplastic nodule and metastasis. Rarer lesions including lymphoma, neuroendocrine tumour and angiomyolipoma were also encountered. No mortality, clinically significant bleeding or tumour seeding detected.

Conclusions: Ultrasound-guided liver biopsies of indeterminate lesions in patients at high risk of HCC yield important histopathological findings, important for management options including the provision of curative treatments and assisting future novel therapies such as immunotherapy and targeted therapies. The low complication rates confirm its safety and the procedure should not be avoided for fear of complications.
Abbott DF\textsuperscript{1,2}, Fleming SW\textsuperscript{1}, Jackson GD\textsuperscript{1,2}

Multiband fMRI and simultaneous EEG

1. The Florey Institute of Neuroscience and Mental Health (Austin campus), Melbourne, Australia;  
2. The University of Melbourne, Melbourne, Australia

Aims
- To verify efficacy of a fast (sub-second) whole-brain simultaneous multi-slice functional MRI acquisition with a lower than optimum flip angle (a parameter that governs both signal to noise ratio and energy deposition).
- To validate the safety of this acquisition sequence with simultaneous EEG, including carbon-fibre artefact detection loops that we developed.

Methods
To validate the efficacy of multiband fMRI with a low flip-angle (approximately half the optimum Ernst angle), 4 subjects (one healthy control and 3 epilepsy patients) completed block-design language tasks of duration approximately 4.5 minutes in a Siemens 3T Skyra MRI. Participants were imaged with a conventional (single band) fMRI sequence (3s per whole brain), and in a separate run they were imaged with a simultaneous multi-slice acquisition with a multiband factor of 6 (yielding 0.5s per whole brain).
To validate safety with simultaneous EEG, a Neoptix 4-channel fibre-optic temperature probe system monitored temperature of 32 and 64 channel EEG electrodes and 3-channel carbon-fibre loops. Initial testing was performed on a head-shaped saline-doped agar gel phantom. Tests were then undertaken on a healthy human volunteer, at electrode positions that had the maximum temperature rise in the phantom experiments.

Results
The multiband sequence substantially outperformed the conventional imaging sequence, despite use of a low flip angle. Indeed if one analysed only 6 of the 10 task/rest blocks in the multiband study (i.e. just 2.3 minutes of acquired data), the result remained superior to the conventional imaging.

The scanner-estimated radio-frequency (RF) specific absorption rate (SAR) at the head for the low-flip-angle multiband sequence was less than half that of the standard fMRI sequence.
Absolute temperature rise during a 52min scan of a human volunteer with 32-channel EEG cap and carbon-fibre motion loops was less than 1°C, and rise above a reference probe positioned on the neck was less than 0.5°C.

Conclusion
Use of a low flip angle can more than halve SAR whilst maintaining adequate fMRI contrast to noise. Indeed, the increased power evident with multiband acquisition allows one to also considerably shorten overall study time for task-based fMRI. Temperature probe measurements verified that simultaneous EEG-fMRI as tested here (including insulated carbon fibre artefact detection loops) appears safe.
ABSTRACT

Introduction
As interventional radiology (IR) adopts an increasingly pivotal role within therapeutic medicine, it is essential that medical students gain exposure to IR so as future doctors, they can fulfil the growing demand for interventional radiologists (IRs) and make appropriate referrals to IRs. Nonetheless, several international studies have reported no or little representation of IR in medical school. Our study aims to assess the current awareness, exposure, knowledge and attitudes about IR amongst Australian medical students, as to provide preliminary data on whether IR teaching in Australian medical schools needs improvement.

Methods
A prospective cross-sectional study was conducted via web-based and in-person distribution of a voluntary, anonymous questionnaire.

Results
237 complete responses were received from approximately 1400 clinical-based students (17% response rate). 38% of respondents had never witnessed an IR procedure, 39% witnessed 1-2, and the remainder 3-5. Few students reported adequate teaching or knowledge in IR (7% and 5% respectively). Of the 32% of students considering a career in IR, males predominated (25% of females vs 59% of males, OR=0.48, 95%,CI=0.27-0.83,p=0.008). Most students agree IR should be in the university curriculum (59%) and is key to improving healthcare (74%). Senior students were more likely to report adequate teaching (p<0.001) and believe IR teaching is important (p=0.001).

Conclusions
Australian medical students have a strong appreciation for IR despite having suboptimal teaching, exposure and knowledge in IR. In order to complement and sustain the rapid uptake of IR techniques in modern medicine, university curricula require a greater focus on IR.
Blennerhassett JM, 1,2 Janssen H, 3 Bernhardt J, 4 and Spratt N.3

The demography of patients admitted for stroke rehabilitation has changed.

1. Physiotherapy Department, Austin Health.
2. Health Independence Program, Austin Health.
3. Centre of Research Excellence in Stroke Rehabilitation and Brain Recovery: Hunter Medical Research Institute, University of Newcastle; NSW.

Aim
To report the demographical change for people admitted for stroke rehabilitation at Austin Health Royal Talbot campus between 2013 and 2018.

Methods
Two studies screened consecutive patients with stroke at Royal Talbot between January 2014 and June 2018, providing demographic data [age and pre-stroke level of disability using the modified Rankin Scale, (mRS)] over three successive time-periods: 1) “GAIT”, an outcome audit (January 2013 to December 2014); and 2) Altering Rehabilitation Environment to Improve Stroke Survivor Activity [AREISSA]1 involving two phases: “AREISSA-pre” (November 2014 to June 2016) and “AREISSA-post” (October 2016 to June 2018). Data were analysed to determine the change over time in demography of patients.

Results
The number of patients screened were: GAIT (n=136, over 24-months); AREISSA-pre (n=141, over 20-months); and AREISSA-post (n=146 over 21-months). Mean (SD) ages were 61(15) years [GAIT], 70(14) years [AREISSA-pre] and 70(15) years [AREISSA-post], with patients admitted during GAIT found to be significantly younger (p< 0.001). Days between stroke onset and admission to rehabilitation were comparable across time-periods. Median (IQR) number of days between onset and rehabilitation admission were 8 (5-15) [GAIT], 7 (5-14) [AREISSA-pre] and 8 (5-14) [AREISSA-post]. Over time, there was a significant change towards admitting people with higher levels of pre-stroke disability. Median (IQR) mRS scores were 0(0-1) [GAIT], 1(0-2) [AREISSA-pre] and 1(0-3) [AREISSA-post] (p=0.001). Furthermore, the proportion admitted who had minimal pre-stroke disability (defined as mRS ≤2) reduced over time from 93% (GAIT), 83% (AREISSA-pre) to 71% (AREISSA-post).

Conclusion
Over recent years, there has been a shift towards admission of people for stroke rehabilitation who were older or whom had a higher pre-stroke disability. This shift has implications when establishing goals, planning service delivery, and future research.

References
**Effectiveness of a submaximal cycle test to prescribe cycle based exercise training intensity**

Leona Dowman¹,²,³, Kerri Gergely¹, Cade Ringin¹, Catherine Hill¹,³

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²Department of Respiratory & Sleep Medicine, Austin Health, Heidelberg VIC Australia
³Institute for Breathing and Sleep, Heidelberg VIC Australia

**Introduction/Aim:**
In pulmonary rehabilitation (PR), cycle training is recommended at 60% peak oxygen uptake measured during cardiopulmonary exercise testing (CPET). However, access to CPET is limited and estimation of an equivalent intensity from the 6-minute walk distance (6MWD) using published equations is associated with substantial variation. This study aimed to investigate whether a submaximal cycle exercise test (SMCT) can prescribe appropriate cycle training intensity and whether initial training intensity estimated from 6MWD and SMCT is similar.

**Methods:**
Retrospective data was collected from patients who attended PR over the previous 18 months. Each patient routinely performed a 6-minute walk test at baseline and completed a SMCT during the second exercise session. In the subsequent exercise session, cycle training was prescribed at 50% of peak work (Watts) achieved on SMCT. Initial intensity was considered appropriate if the patient could complete 15 minutes as prescribed with a reported dyspnoea and/or RPE score of 3-4 on the Borg 0-10 score.

**Results:**
Sixty-four patients (35 male) with chronic lung disease (33 COPD, 13 ILD, 18 other) were included, with mean (SD) age of 70(10), 6MWD 441(87) metres and SMCT peak work of 60(23) watts. Eighty percent of patients achieved the target intensity, 12% found the initial workload too easy and 8% were unable to maintain the target intensity. There was a moderate correlation between work rate predicted from 6MWD 35(8) Watts and SMCT 30(11) Watts ($r=0.67$, $p<0.001$). Estimating cycle training intensity from 6MWD over-predicted (>5 Watts) appropriate training in 47% patients and under-predicted in 9%.

**Conclusions:**
In chronic lung disease, prescribing cycle exercise intensity at 50% of SMCT peak work achieves an appropriate training intensity that was tolerated by 80% of patients. Prescribing work rate from SMCT and 6MWD results in similar training loads, although SMCT may provide more accurate cycle training intensity.

**Grant support:** nil
Achieving the minimal important difference following exercise training in interstitial lung disease.

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²Physiotherapy Department, Austin Health, VIC Australia
³Institute for Breathing and Sleep, VIC, Australia
⁴Department of Rehabilitation, Nutrition and Sport La Trobe University, VIC, Australia
⁵Physiotherapy Department, Alfred Health, VIC, Australia

Introduction/Aim:
Exercise training delivers significant short-term improvements in functional exercise capacity, symptoms and quality of life, across the range of interstitial lung diseases (ILD) but to what extent do individuals experience a clinically significant benefit? This study aimed to establish the proportion of patients achieving the minimal important difference (MID) in 6-minute walk distance (6MWD) and in the dyspnoea and fatigue domains of chronic respiratory questionnaire (CRQ).

Methods:
Data from 142 participants with ILD [61 idiopathic pulmonary fibrosis (IPF), 22 asbestosis, 23 connective tissue disease-related ILD (CTD-ILD) and 36 with ILD of other aetiologies] randomised to either eight weeks of supervised exercise training or usual care were reviewed. We compared the percentages of patients who achieved the MID for 6MWD for ILD (29-34m), CRQ dyspnoea (2.5 points) and CRQ fatigue (2.0 points) between exercise training and control group for the entire ILD population and each subgroup (IPF, asbestosis and CTD-ILD) using Pearson chi².

Results:
Following exercise training at least a third of participants achieved improvements in 6MWD that exceeded the MID, increasing to 43% and 55% in the IPF and asbestosis subgroups respectively (see Table). Compared to the control group, a greater percentage of participants achieved improvements that exceeded the MID for CRQ dyspnoea and fatigue for the entire ILD sample, IPF and asbestosis; this was significantly greater than the control group for CRQ fatigue. Improvements that exceed the MID were limited in CTD-ILD and more likely occur in CRQ dyspnoea and fatigue than 6MWD.

Conclusion: A third to a half of participants with ILD achieve clinically meaningful improvement following exercise training, including those with IPF, the most devastating of all ILDs. Fatigue and 6MWD appear more responsive to change than dyspnoea.

Grant Support: This abstract is funded by the ATS Foundation/Pulmonary Fibrosis Foundation, National Health and Medical Research Council, Eirene Lucas Foundation and Institute of Breathing and Sleep.

<table>
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<tr>
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<td>57%</td>
<td>55%</td>
<td>40%</td>
</tr>
</tbody>
</table>

*p<0.05 compared to control group; ILD, interstitial lung disease; CTD ILD, connective tissue disease-related ILD; IPF, idiopathic pulmonary fibrosis.*
Lucy C. Sommers $^{1,2}$, Melinda Jackson $^{1,2}$, Maree Barnes $^2$, Gerard A. Kennedy $^{1,2}$

Psychological Predictors of Adherence to Continuous Positive Airway Pressure in the Treatment of Obstructive Sleep Apnoea

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2. Institute for Breathing and Sleep, Heidelberg, Victoria, Australia.

Aim
Non-adherence to Continuous Positive Airway Pressure (CPAP) therapy for the treatment of Obstructive Sleep Apnoea (OSA) remains an ongoing concern, with 5-50% of patients prescribed CPAP either rejecting the treatment or discontinuing within the first week and 12-25% of remaining patients discontinuing within three years. The aim of this study was to investigate psychological factors that best predict adherence or non-adherence to CPAP therapy in OSA patients.

Method
A three-month retrospective review of patients who had attended the Austin Health Sleep Laboratory for an overnight CPAP titration polysomnographic study was conducted. Of the 120 patients who underwent CPAP implement studies during this time, 48 were deemed eligible for inclusion (20 females and 28 males) aged between 20 and 78 years ($M = 53.56$ $SD = 15.19$). Data from eligible patients' CPAP adherence questionnaire, exploring self-efficacy, health belief subscales benefits and susceptibility, internal locus of control and mood subscales anger/hostility, vigour/activity and depression/dejection were obtained, in addition to CPAP usage data at three-months, demographic and sleep study variables. At three-months, adherence to CPAP therapy was defined by the universal classification of $\geq 4$ hours per night for $\geq 70\%$ nights.

Results
Three months post-CPAP titration, 58% of included patients were non-adherent to CPAP therapy. Stepwise discriminant function analysis revealed psychological factors, internal locus of control and the health belief model subscale perceived susceptibility, explained 18.23% of the variance in adherence to CPAP and correctly identified 82.1% of non-adherent patients.

Conclusion
Findings from the current study add further weight to the concept that psychological factors are an important consideration when investigating CPAP adherence. Specifically, findings revealed patients who believe they’re responsible for their own health are significantly more likely to take control over their treatment. In addition, patients who felt overwhelmed by the numerous treatments and illnesses they may confront in addition to their OSA, resulted in a decrease of an individuals’ motivation to adhere to treatment. Although these factors explain only a small amount of the overall variance in adherence behaviour, we were able to identify 82% of patients who were non-adherent. In a clinical situation, this would enable clinicians to target those patients at-risk of non-adherence with appropriate supportive therapies.
Curnow, S1,2, Hutchinson, A2,3,4 & Currey, J.2,4

Nurses’ clinical risk management of delirium in cardiac surgical patients.

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2. Deakin University, School of Nursing and Midwifery, Geelong, Victoria
3. Centre for Quality and Patient Safety Research - Monash Health Partnership, Clayton, Victoria
4. Deakin University, Centre for Quality and Patient Safety Research, Geelong, Victoria

Aim
The risk for patients developing delirium after cardiac surgery can be decreased by identifying patients at risk and implementing prevention interventions early. The aims of this study were to describe the initial and ongoing nursing delirium risk assessments and documented evidence-based delirium prevention strategies implemented for cardiac surgical patients with and without diagnosed delirium in the first 72 hours following admission to intensive care. The clinical utility of tools used for nurses’ clinical risk management of delirium was also evaluated.

Method
A descriptive study using a retrospective audit of patient medical records was conducted following ethics approval. The study was conducted at a major public metropolitan teaching hospital in Melbourne, Australia. Study participants were selected from all adult patients admitted to the intensive care unit post cardiac surgery over one calendar year. Stratified random sampling was used to comprise a total sample of 50 patients: 25 patients with diagnosed delirium and 25 patients without diagnosed delirium on hospital discharge.

Results
The completion of nursing delirium risk assessments was not adherent to hospital policy or evidence-based guidelines. Nursing review of hydration and food intake, and analgesic administration were the most frequent delirium prevention interventions documented by nurses. The use of the daily Confusion Assessment Method or any other validated delirium assessment or diagnostic tool was not documented by nurses. The nursing delirium risk assessment tools were found to lack clinical utility because they were not sufficiently relevant according to published literature, and thus unlikely to be highly effective in identifying patients at risk of delirium.

Conclusions
Findings suggest a deficit in nurses’ knowledge of, and adherence to, delirium risk assessment, and implementation of delirium prevention intervention strategies for postoperative cardiac patients. Considerable amendments to the existing nursing delirium risk assessment tool are required to improve clinical utility.
Aim
The accurate position of the tip of a Peripherally Inserted Central Catheter (PICC) is vital in all patients, to enable effective administration of therapy and to help avoid potential complications. The ideal position of the PICC tip is in the superior vena cava (SVC) at the cavo-atrial junction (CAJ)\(^1\). The VPS Rhythm Device (VPS) allows real time monitoring of PICC line position using magnetic tracking and ECG guidance to position the PICC tip at the CAJ. Expected outcomes from the use of VPS include PICC tip positioning at CAJ, and malposition correction during insertion leading to fewer referrals to radiology for repositioning.

Method
At Austin Health PICC lines are inserted by the nurse led PICC insertion team, part of the Apheresis Unit. All PICC insertions for a four-week period in February/March 2018 were inserted using the VPS. PICC procedure data was recorded. An end of trial clinical product evaluation (CPE), consisting of questions and free text, was completed by staff inserting and assisting the insertion of PICC lines.

Results
45 PICC lines were inserted. Seventeen patients had malpositions corrected during their procedure. Referrals to radiology for repositioning n = 3 (6.6%). CXR confirmed 26 PICC’s (58%) were at the CAJ. No nurse wanted to continue using the VPS due to low number of PICC tip positioned at CAJ, soft magnetic wire adversely affecting PICC insertion and risk of contaminating sterile procedure. Graph below shows responses to questions from CPE.

Conclusion
The VPS performed below expectation for siting PICC tip at CAJ: 58% versus 92.86%\(^2\) reported efficiency. Use of VPS did not decrease numbers of patients referred to radiology for repositioning. Despite CPE having mostly good to excellent results free text comments highlighted dissatisfaction with the performance of VPS.

References
1. Gorski L et al., 2016, The 2016 Infusion Therapy Standards of Practice, Journal of Infusion Nursing, 39, S1-S159
Barriers to timely STEMI management as reported by paramedics and Triage nurses: a cross-sectional study.

¶
1. La Trobe University, Melbourne; Australia.
2. Austin Health, Melbourne, Australia.
3. Ambulance Victoria, Australia
4. University of Melbourne, Australia.

Introduction: Frontline clinicians are pivotal to timely STEMI management, but it remains unclear what factors influence timely STEMI management. This study explores key barriers surveyed through paramedics and Triage nurses.

Methods: An online survey was offered to a cross-sectional sample of paramedics and Triage nurses in Victoria, Australia. The 79-item survey explored the potential influence of known barriers to timely STEMI management, such as differences in patient presentation, time of presentation and failure of rapid systems of care at an operational level.

Results: There were 333 respondents; 88% paramedics and 12% Triage nurses. There were no differences in experience by professional group (paramedics 12±10 years vs nurses 12±8 years; p=0.96). The most commonly reported barriers were distance to hospital facilities, mobilising rapid access services within the hospital system and lack of access to expert advice/resources. Triage nurses treated more suspected STEMI’s per month than paramedics (0.4 vs 2.5; p<0.001). Paramedics reported higher rates of misclassification of the triage process for a suspected STEMI patient compared to Triage nurses (25% vs 10%; p<0.001). Triage nurses reported higher levels of opportunity to develop ECG recognition skills (61% vs 82%; p=0.02); higher levels of access to senior staff if unsure of a STEMI diagnosis (76% vs 95%; p<0.001).

Conclusion: The results indicate that access to experts and rapid access services need improvement to increase timely STEMI management, and that profession-specific barriers need further exploration. Further analysis will identify whether there are differences by geographical location.
Are the new European Society of Cardiology (ESC) STEMI performance targets feasible? The proportion of achievement in performance targets using the new ESC STEMI guidelines compared to existing Australian guidelines, applied to a nine-year prospectively collected dataset.

1. La Trobe University, Melbourne.
2. Austin Health, Melbourne.

Introduction: Door to balloon time (DTBT) has traditionally measured performance in STEMI management. The 2017 European STEMI guidelines replaced DTBT with first medical contact (FMC); defined as either FMC to a hospital, or field FMC when a STEMI diagnosis could be confirmed prior to hospital arrival. Target reperfusion time for patients presenting to hospital was reduced from <90’ to <60’. Patients diagnosed by a field ECG were given a target reperfusion time of <90’ starting from first ‘field’ medical contact. It is unclear whether these new ESC measures are feasible targets.

Methods: We evaluated clinical/presentation characteristics and time point data from a prospectively collected STEMI database. These characteristics and the proportion of achievement for the existing Australian target reperfusion time was compared to the new European target reperfusion times.

Results: 922 STEMI presentations were included. Mean age 63 ± 13 years; 52% presented with pre-hospital notification (PHN), 20% self-presented; 28% presented by ambulance (no PHN). The Australian target of DTBT<90’ was achieved 77% and the median DTBT was 64’. The proportion of achievement by mode of presentation was: self-presentation (61%); ambulance no PHN (55%); and ambulance with PHN (95%). When European targets were applied to the same cohort overall performance targets were achieved 37% of the time, and the median FMC-reperfusion time recalculated at 87’. The proportion of target reperfusion time of 60’ being achieved for self-presenters or those arriving via ambulance (no PHN) was only 18%. The separate target reperfusion time of ≤90’ for PHN arrivals was achieved only 55%.

Conclusion: The new European targets are difficult to achieve when retrospectively applied to an existing dataset. Further examination of time specific intervals is required to identify where delay occurs along the continuum of STEMI management. Discrete target performance groups will be compared to evaluate the impact on health outcomes.
Continuous terlipressin infusion improves dietary intake and muscle strength in patients awaiting liver transplantation

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2. Department of Gastroenterology, Austin Health, Heidelberg, Vic., Australia;

Aim

Portal hypertension contributes to the pathogenesis of malnutrition and sarcopenia in cirrhosis via multiple mechanisms, including development of ascites, reduced gastric reserve, slowed intestinal transit, malabsorption and bacterial translocation. Terlipressin is a vasopressin agonist widely used to treat portal hypertensive complications. Our centre administers terlipressin via continuous outpatient infusion as a bridge to transplantation in patients with hepatorenal syndrome or refractory ascites. We describe for the first time its impact on nutritional and muscle parameters in this novel cohort.

Methods

Nutritional status (subjective global assessment), handgrip strength, dietary intake (energy and protein), frequency of paracentesis and severity of liver disease (MELD) were prospectively recorded at terlipressin commencement and follow-up (transplantation, cessation or census date).

Results

Nineteen patients were included (89% male, median age 59.6 years, median MELD 24, hepatorenal syndrome n=14, refractory ascites n=5). All patients were malnourished at baseline, 63% (n=12) had sarcopenic-range handgrip strength, and mean paracentesis frequency was 2.86±1.62 per month. Median duration of terlipressin was 51 days (IQR 29-222) with 2379 patient days of treatment. Fourteen patients (74%) were transplanted, two delisted (10%) and three (16%) continue terlipressin.

Energy and protein intake improved significantly following terlipressin, from 17.94±5.43kcal/kg to 27.70±7.48kcal/kg, and 0.74±0.28g/kg to 1.16±0.31g/kg, respectively (both p<0.001). Handgrip strength increased from 25.36±8.13kg to 28.49±7.63kg (p=0.001). Linear regression analysis demonstrated HGS increased 0.075% for every 1-day of terlipressin (p=0.005). Frequency of large-volume paracentesis reduced by 46%, to 1.57±1.51/month (p=0.001). No clinical complications were attributed to terlipressin.

Conclusion

Continuous terlipressin infusion significantly improves both nutritional and functional muscle parameters in cirrhotic patients on the liver transplant waitlist, in whom such characteristics usually demonstrate progressive decline. This confirms both the aetiological role of portal hypertension in the development of malnutrition and represents a promising new anabolic therapy.
Coffee reduces steatosis in non-alcoholic fatty liver disease

Aim
Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease worldwide. Diet and lifestyle modifications to induce weight loss remain the cornerstone of management, but are difficult to achieve and maintain. Recent data demonstrate an inverse relationship between coffee consumption and prevalence of NAFLD but no prospective studies have attempted to treat NAFLD with coffee. This pilot study aimed to determine if moderate coffee consumption in NAFLD patients is superior to traditional dietary advice in reducing hepatic steatosis and improving components of the metabolic syndrome.

Methods
Non-coffee drinking adults with NAFLD were randomized to coffee and diet-advice or diet-advice alone for 4 weeks. Participants received dietary education at baseline consistent with current evidence-based guidelines. The coffee group were prescribed 3 cups of coffee daily (EXPRESSI® capsules, Aldi, Germany). The primary study endpoint was hepatic steatosis quantitation measured using MRI spectroscopy. Anthropometry (weight, BMI, waist circumference), biochemistry (liver function, cholesterol, insulin sensitivity, glycaemic control) and hepatic steatosis (liver MRI, fibroscan) were measured at baseline and 4-week follow up.

Results
Twelve patients (5M/7F, 51.4±14.9 years) completed the trial. At baseline, subjects were abdominally obese (mean BMI 31.2±8.3 kg/m²; waist circumference 101.8±14.5 cm) with elevated liver enzymes and HOMA-IR. Fasting concentrations of glucose, cholesterol and triglycerides were normal. Compliance with coffee prescription (3/d) was high (97%). The coffee group had a 17% relative reduction in hepatic steatosis measured by MRI, compared with a 10.6% relative increase in the diet-advice only group, which trended towards significance (p=0.12). Weight loss was minimal (<0.5kg) and waist circumference remained stable over the 4-weeks and was not different between groups. There were no significant changes in insulin sensitivity, liver function or fibroscan results.

Conclusion
In non-coffee drinkers with NAFLD, the consumption of 3 cups of coffee per day reduces liver steatosis even in the absence of weight reduction. Confirmation of results in a larger study is required.

1. Austin Health. Chronic Kidney Disease CNC.

Aim - Patients with end stage kidney disease who have a planned dialysis start receive education about renal replacement therapies. However, they may still feel uncertain about their choice of dialysis when they start treatment. The SURE questionnaire is a 4 item checklist which screens for decisional conflict. SURE stands for: sure of myself; understand information; risk-benefit ratio; encouragement. (1) We used the SURE questionnaire to understand how frequent decisional conflict is when a patient starts dialysis.

Methods - The SURE questionnaire was completed by 44 planned dialysis patients within 2 months of starting dialysis. They had all received education prior to dialysis. Other data collected included; age, sex, language. In addition, the number and format of education sessions attended were recorded.

Results - A negative response to 1 or more questions indicates possible decisional conflict around their choice of dialysis treatment. (1) 9 of 44 patients (20%) answered no to one or more questions. The most common area of uncertainty surrounded the benefits and risks of treatment.

<table>
<thead>
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<tbody>
<tr>
<td>S</td>
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<tr>
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</table>

Of these 9 patients, 6 received individual education, and 3 a combination of group and individual. They received between 1 and 4 education sessions prior to starting dialysis. 1 of 9 chose to change dialysis modality, compared with 3 of 35 who initially answered yes to all 4 questions, who have since changed dialysis modality.

Conclusion - Despite education, decisional conflict and uncertainty around dialysis choice can be expected. Pre-dialysis education focuses on the pros and cons of each dialysis treatment, and its effects on various aspects of the patient’s life more than using risks and benefit terminology. The use of a treatment option grid with risks and benefits should be added to the education syllabus. It is important that education is continued during the transition to dialysis.

The Effect of Residual Kidney Function on Uraemic Solutes and Symptom Burden in Haemodialysis Patients

Jessica Kong¹, Matthew Davies² and Peter Mount¹,²,³

¹. Faculty of Medicine Dentistry and Health Sciences, University of Melbourne, Vic., Australia
². Department of Nephrology, Austin Health, Heidelberg, Vic., Australia
³. Institute for Breathing and Sleep, Austin Health, Heidelberg, Vic., Australia

Background: Residual kidney function (RKF) is associated with improved solute clearance, anaemia and phosphate control in haemodialysis (HD) patients. The Kidney Diseases Outcomes Quality Initiative (KDOQI) guidelines have suggested that dialysis dose could be reduced in patients with residual urea clearance (KRU) ≥2 ml/min/1.73m². Despite this, however, a thrice-weekly, 4-5 hours per week HD regimen is typically prescribed regardless of the RKF levels.

Aim: To determine the prevalence of RKF and the associations of RKF with fluid control, solute clearance and symptom burden in a cohort of maintenance HD patients.

Method: This prospective cohort study recruited 90 maintenance HD patients. Demographic, clinical and dialysis parameters were collected. RKF was assessed as KRU and glomerular filtration rate (GFR) by interdialytic urine collection if self-reported interdialytic urine output was >200ml. Outcomes measured were: serum potassium, phosphate, albumin, C-reactive protein (CRP), beta2-microglobulin (β2M), haemoglobin, and erythropoietin requirement and symptom burden.

Results: Of 90 included patients, 31.9% had KRU ≥1ml/min/1.73m² and 17.6% had KRU ≥2ml/min/1.73m². The mean KRU was 0.92±1.36 ml/min/1.73m², whereas the mean GFR was 1.55±2.16 ml/min/1.73m². RKF was negatively correlated with time on renal replacement therapy (p<0.0001). Higher RKF was significantly associated with lower β2M (p<0.0001). Patients with KRU ≥1ml/min/1.73m² also had significantly lower serum potassium levels compared to those with KRU <1ml/min/1.73m² (p=0.02). RKF was not associated with phosphate, haemoglobin, CRP or serum albumin. Patients with KRU ≥1ml/min/1.73m² had fewer symptoms (5±3 vs. 7±4) as assessed by the Patient Outcome Scale-Symptoms (POS-S) renal questionnaire (p=0.026).

Conclusion: A proportion of Australian HD patients have significant RKF that contributes to their total solute clearance. RKF is significantly associated with improved middle molecule clearance, potassium control and fewer symptoms, therefore, strategies to preserve RKF are warranted.
Incidence and demographics of abnormal eGFR in the Austin Health outpatient population 2012-2017

1. Austin Health and Health and Biomedical Informatics Centre, University of Melbourne
2. Department of Nephrology, Austin Health

Aim
We aimed to investigate the prevalence, incidence and demographics of outpatients with Chronic kidney disease (CKD) through eGFR pathology and electronic health record data at Austin Health, a tertiary teaching hospital in Melbourne, Australia.

It is predicted there will be a significant financial burden in Australia by 2020, but studies on the epidemiology of CKD in Australia are outdated, with studies in tertiary health systems scarce.

Methods
Outpatient clinic and pathology data originally collected in routine care was obtained from the Austin Clinical Research Data Warehouse. The study period was 2012-2017. Data linkage with inpatient records was performed on outpatients that had an abnormal eGFR.

Patients were separated into Normal (no abnormal eGFRs) and Abnormal (>=1 abnormal eGFR).

Results
Initial searches identified 248515 eGFR episodes, 57325 eligible patients, with a 2017 mean age in of 59.76 +/- 16.62 years. There were recorded. Of these, 13067 patients had an abnormal eGFR during the study period, and 11468 patients were successfully linked to an inpatient record.

Abnormal patients compared to Normal patients were older, required more eGFR and more outpatient appointments. Males were more common in the Abnormal group compared to the Normal group. Patients with worse eGFRs were hospitalised more frequently and for longer periods.

Conclusion
A significant proportion of patients with at least one abnormal eGFR were linked to an inpatient admission. Worse renal function in this group was associated with more frequent hospital admission, longer time in hospital, and required more eGFR testing. Patients with abnormal renal function are therefore significantly represented in the inpatient system.

This study demonstrates that early CKD can be detected and could provide triggers for screening algorithms to enable intervention in early cases of CKD at Austin Health.
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**Increased expression of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase isoforms in urinary exosomes in pre-eclampsia**

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3. Mercy Hospital for Women,
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**Aim:** This study aims to detect and characterise the expression and phosphorylation of isozymes of the key glycolytic regulatory protein, 6-phosphofructokinase-2-kinase/fructose-2,6-bisphosphatase (PFK-2/FBPase-2), in urinary exosomes of pre-eclamptic (PE) subjects, compared to normotensive non-pregnant (NC) and normotensive pregnant (NP) subjects. Enzymes of glycolysis have altered expression and activity in many kidney diseases. No studies have looked at these changes in pre-eclampsia, a multi-system disorder with broad physiological effects on the renal system. Urinary exosomes provide a non-invasive alternative to renal biopsy for studying these changes in kidney metabolism.

**Method:** A cross-sectional study of NC (n=19), NP (n=23) and PE (n=29) subjects was performed. Exosomes were isolated from urine samples by differential ultracentrifugation. Exosomal content was analysed by Western blot and computer densitometry for expression levels of PFK-2/FBPase-2 isozymes (PFKFB2, PFKFB3 and PFKFB4) and phosphorylation levels of PFKFB2 at residues Ser483 and Ser466 and PFKFB3 at Ser461.

**Results:** There was a 4.7–fold increase in expression of total PFKFB2 in PE compared to NP (p<0.001). There was a 2.6-fold increase in PFKFB2 phosphorylated at Ser483 in PE compared to NP (p=0.002). Expression of phosphorylated PFKFB2/PFKFB3 at Ser466/Ser461 was increased (p<0.001), present in 77.4% (95% CI=59.9-88.9%) of PE and 8.3% (95% CI=1.2-27.0%) of NP samples. PFKFB3 was more commonly expressed in PE detected in 90.3% (95% CI=74.3-97.4%) of PE and 8.3% (95% CI=1.2-27.0%) of NP samples (p<0.001). PFKFB4 had a 7.2-fold increase in expression in PE compared to NP (p<0.001). No significant differences between NP and NC groups were observed.

**Conclusion:** Regulatory proteins that increase glycolysis are upregulated in the urinary exosomes of pre-eclamptic subjects, suggesting that renal glycolysis may be increased in pre-eclampsia. Whether this is a maladaptive response, as evident in other kidney diseases, remains unknown.
Factors Influencing Caesarean Section Rate after Induction of Labour in Nulliparous Women

Introduction

Induction of labour (IOL) can result in emergency caesarean section (CS), which carries substantial maternal morbidity. We aimed to determine which methods of IOL and indication result in higher CS rates in nulliparous women.

Methods

We conducted a retrospective study examining the rate of CS in nulliparous women induced in a single tertiary-centre from 2008-2018. We included term, cephalic, singleton pregnancies. We examined the effect of cervical ripening, gestation, indication for induction, maternal age and BMI.

Results

Almost 10,000 women were included. 3296 (33.0%) women had a CS. 4414 (44.2 %) women had cervical ripening. The rate of CS increased with increasing gestation (37 weeks=24.0%, 42 weeks=48.2%,p<0.0001), BMI (18-25=28.7, >40=49.3%, p<0.0001), need for cervical ripening (ripening=37.5%, no ripening=29.5% p <0.0001) and with increasing maternal age (<30=29.2%, >35=40.3%, p<0.0001). CS rate was similar for indications including hypertensive disorders of pregnancy, diabetes, prolonged pregnancy and pre-labour rupture of membranes, but increased in inductions for macrosomia when compared to prolonged pregnancy (Odds Ratio 2.7, P<0.0001, 95% Confidence interval 2.2-3.4). The CS rate was similar for either method of cervical ripening; prostaglandin (37.1%) or mechanical methods (37.0%). These findings remained significant after adjustment for maternal age, gestation, BMI, indication for delivery and method of ripening.

Discussion

CS rate increased with maternal age, advancing gestation and increasing BMI. When cervical ripening is needed there is no difference in the rate of CS between prostin and balloon catheters. There is no increase in CS rate for any of the indications for IOL except for macrosomia. This information may help inform women and clinicians on the likelihood of CS after induction.
Nguyen-Ngo C, Lim R, Lappas M.

Polyphenols as preventatives for gestational diabetes mellitus (GDM)

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Aim
Gestational diabetes mellitus (GDM) is a transient carbohydrate intolerance during pregnancy that leads to long-term risk for metabolic and cardiovascular diseases. It is driven by peripheral insulin resistance, low-grade maternal inflammation and oxidative stress. Polyphenols, such as naringenin, nobiletin and curcumin, are the active compounds of fruits and vegetables, and possess anti-diabetic, anti-inflammatory and antioxidant properties. However, the effects of naringenin, nobiletin and curcumin on either in vitro or in vivo models of GDM have not yet been studied. Therefore, the aims of this study were to 1) examine the effects of the above polyphenols on insulin resistance, inflammation and oxidative stress associated with GDM; and 2) identify the mechanistic pathways through which they act.

Methods
An in vitro explant model was used to determine the effects of naringenin, nobiletin and curcumin on glucose uptake in skeletal muscle, and TNF-α-induced expression of pro-inflammatory mediators and antioxidants in human placenta and adipose tissue (n=6 patients/treatment). An in vivo mouse model of GDM was used to assess the effects of polyphenols on glucose metabolism, and maternal and intrauterine inflammation (n=6-7 mice/group).

Results
In vitro, all polyphenols significantly attenuated TNF-α-induced decrease in glucose uptake in skeletal muscle. All polyphenols also significantly reduced TNF-α-induced expression of pro-inflammatory cytokines and chemokines from human placenta and adipose tissue. Naringenin and curcumin significantly increased antioxidant expression in placenta and adipose tissue. The polyphenols act through a combination of the NF-κB, Akt and MAPK signalling pathways. In GDM mice, when compared to control, naringenin and nobiletin significantly reduced fasting glucose levels. Additionally, all polyphenols significantly decreased expression of pro-inflammatory cytokines and chemokines in placenta, visceral and subcutaneous adipose.

Conclusion
Naringenin, nobiletin and curcumin possess potent anti-diabetic, anti-inflammatory, and antioxidant properties in both in vitro and in vivo models of GDM.
Genetic testing technologies are advancing at a rapid pace. Although it may be logistically possible to offer testing to minors, that is, individuals under the age of 18, it may not always be appropriate or recommended. Most of the time adults give consent for themselves to undergo genetic testing. Immature minors, however, have their parents or guardians give consent for such testing. Mature minors may give consent for themselves during the process of genetic counselling. Genetic counsellors and other clinical genetics staff act as advocates for minors within this context. Some conditions may have an onset in adult years whereas other genetic conditions may have a presentation of symptoms during childhood. Genetic testing of minors is a contentious area with some conditions having conflicting recommendations. Depending on the age of the minor, they may be able to be involved in the conversation regarding the genetic testing. Staff follow guidelines such as “Pre-symptomatic and Predictive Testing for Children and Young Adults” produced by the HGSA and best practice in this area is informed by literature such as Delatycki et al. 2012 and Mand et al. 2011. An audit was conducted to review the genetic testing of minors at Austin Health.

Rational: The results of the audit will be used to help with quality assurance activities in the department. Development of guidelines for presymptomatic/predictive testing of minors will be able to occur within the context of such data.

Method: A search was performed on the department’s database of all genetic tests conducted in minors between 1st July 2009 and 30th June 2018.

Results: 319 genetic tests were conducted on minors during this 9 year period. The vast majority (249/319) where in dysmorphic children and/or in children with intellectual disability or with another presentation which warranted a genetic test in them as they were symptomatic. However 71 of the 319 tests were in minors who were asymptomatic. These conditions were mostly cancer predisposition conditions but some were not cancer genetic conditions.

Some of these conditions have medically actionable recommendations for known mutation carriers in minors such as FAP and VHL. Other conditions, by contrast, do not have any medical recommendations until adulthood such as MSH2 and BRCA. For some cases consent was given by parents where their children were not involved in the discussion or decision to test, but other cases were where the minors were 16 or 17 and gave consent for testing for themselves.

Discussion: An analysis of the data will be presented. Three broad groups were identified; infants that were not involved in the conversation regarding testing at all, young adolescents who were involved in the conversation, but where their parents gave consent and mature minors who gave consent for themselves. A pathway for dealing with the predictive testing of minors has been developed.

Limitations: These numbers do not take into account the minors who attended appointments with the aim of discussing genetic testing and who did not proceed with testing.

Conclusions: Although not frequent, genetic testing of minors is requested. Having a framework for procedures will be helpful in navigating issues related to genetic testing of minors.
AIM
Maternal antenatal depression is associated with adverse neuro-developmental outcomes in offspring, yet few studies have evaluated the impact of effective treatment. We aimed to assess the developmental progress of children, at age 2 and age 5, whose mothers had received either cognitive-behavioural therapy or routine care for depression while pregnant, in a previous randomised controlled trial (n=54).

METHOD
Twenty eight follow-ups were conducted at 2 years and 24 were conducted at 5 years. The 2-year follow-up included the Parenting Stress Index (PSI), Bayley Scales of Infant Development (BSID-III) and Child Behaviour Checklist (CBCL). The 5-year follow-up included the Wechsler Preschool and Primary Scales of Intelligence (WPPSI-III) and the CBCL.

RESULTS
Treatment during pregnancy showed some significant benefits for children’s development at age 2, but not at age 5. At 2 years, intervention effects were found with lower scores on the PSI Total score, Parent domain and Child domain (d = 1.44, 1.47, 0.96 respectively). A non-significant trend favoured intervention children on most subscales of the CBCL and the BSID-III (notably motor development: d = 0.52). Irrespective of treatment allocation, at 5-year follow-up, higher maternal depression during pregnancy was associated with lower child Verbal IQ and higher CBCL Anxiety/Depression and Internalizing scores. Higher anxiety during pregnancy was associated with lower child IQ in all domains and with higher CBCL Total problems, Anxiety/Depression, Withdrawn, Attention, Aggressive, Internalizing and Externalizing scores.

CONCLUSION
This small, controlled study confirmed the associations of maternal anxiety and depression during pregnancy with poorer cognition and behavioural problems in children – a pattern previously described in uncontrolled, longitudinal cohort studies. Whilst some benefits of treatment on child outcomes and promising trends were found, the small sample size is likely to have contributed to the lack of significant between-group differences. A larger, more powerful study funded by NHMRC is underway.
DEVELOPING A SPINAL CORD RESEARCH HUB FOR ALL SCI RESEARCH STAKEHOLDERS


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Introduction

For decades, SCI research has been thwarted by small numbers of participants in studies that do not lead to significant results. The solution is for multi-centre studies to ensure the recruitment of large numbers to achieve scientifically valid outcomes.

Changing from a local to a global focus in research requires a culture change. Part of the solution is the Spinal Research Institute’s (SRI) development of an online collaboration platform, the Spinal Cord Research Hub (SCoRH), which will support the development of research networks. SCoRH will be underpinned by administrative support available to all stakeholders. SCoRH will provide an online space dedicated to SCI research, enabling the development of networks and partnerships for researchers, consumers, clinicians and funders to work together to undertake large-scale research projects.

Methods

Since 2016 the SRI has been working on an online web-based network dedicated to SCI research.

An advisory group of experienced SCI researchers from nine countries around the world and other stakeholders advised the project group and the platform developer on functional features and governance for the online platform.

The development of mutual trust and respect amongst researchers has also been encouraged by annual travel grants and research workshops. These both working to facilitate networking and promote discussion on multi-centre research, to build actions that lead to outcomes.

Results

The SCoRH online platform is now being tested with a view to launch at ISCoS 2018. During its development the platform has been tested by an advisory group to ensure that functionality and usefulness to SCI researchers is appropriate for their purposes.

The platform is now ready for SCI researchers.

Conclusions

By encouraging a culture of collaborative SCI research, SCoRH will support the development of SCI research from a local to a global focus, ultimately improving the lives of those living with SCI.
Urine cultures: Let’s have a wee think

Aim
Urine cultures are a commonly ordered test in the hospital setting particularly in the emergency department despite a low diagnostic yield for patients with undifferentiated abdominal pain. The aim of this project was to reduce the inappropriate ordering of urine cultures across the whole hospital and reduce the volume of contaminated samples.

Methods
A multifaceted behaviour change strategy was developed which included audit and feedback to the top 10 ordering units, feedback to individual ED clinicians, guideline development, education sessions and online modules in addition to changes to the way urine cultures were ordered on the electronic ordering system. Pre- and post-urine culture volume data were collected. In addition, education around correct collection techniques was delivered to emergency department staff and patients. Patients were surveyed on the utility of this education.

Results
Prior to the implementation of the multifaceted behaviour change strategy, an average of 341 urine cultures were ordered each week across the hospital with 143 of these being ordered by the emergency department. After 5 months of strategy implementation, a statistically significant drop was observed both across the hospital and in ED with the weekly average volume of tests being 250 and 88 respectively. Contamination rates were also observed to have decreased. 50 consumers were surveyed to assess their views on the educational poster instructing how to collect a urine sample and minimise contamination. While 26% were able to recall seeing the poster, 86% felt the instructions were clear and would use the poster if required.

Conclusion
The results of this study have indicated that targeted behaviour strategies in addition to hospital wide interventions have been successful in reducing the volume of urine cultures. The reduction in urine cultures has been sustained overtime.
Gamification: A novel approach to improve hand hygiene compliance amongst healthcare workers

1. University of Melbourne
2. Quality and Patient Safety Department, Austin Health

Aim
Hand hygiene is vital in the prevention of hospital-acquired infections. Despite increasing efforts to promote hand hygiene, performance amongst healthcare workers are suboptimal, and hospital-acquired infections remain a problem. The aim of this study was to determine whether gamification is effective in increasing hand hygiene compliance amongst healthcare workers.

Method
This study was conducted in the Intensive Care Unit over 11 weeks. A competition for the best hand hygiene compliance was created between doctors, nurses and allied health workers. The winning team was rewarded with a pizza prize at the end of the study. Daily prizes which consisted of a coffee voucher and a token of encouragement were given to healthcare workers identified to have achieved excellent hand hygiene compliance. In this study, this was defined as performance of hand hygiene both before and after patient contact. A survey to elicit individual views on the influence of gamification on hand hygiene practice was also conducted at the end of the study.

Results
Overall hand hygiene compliance increased significantly over the study, from 67.2% in period 1 to 80.9% in period 4 (p<0.001). Nurses achieved the highest compliance rate in period 4 (82.0%) compared to doctors (78.4%) and allied health (75.8%), and therefore won the competition. The hand hygiene performance of both doctors (p = 0.046) and nurses (p<0.001) improved significantly. Survey responses indicated that 86.1% of healthcare workers enjoyed gamification as an alternative to standard hand hygiene promotion interventions, and 63.9% felt that gamification improved their hand hygiene performance.

Conclusions
This study suggests that gamification, in the simple form of a competition, is effective in increasing hand hygiene compliance amongst healthcare workers. Although further follow-up studies are required, our findings suggest that gamification can be used to optimise hand hygiene performance, and ultimately reduce rates of hospital-acquired infections.
Hose K, ¹ Moran J.¹

Bridging the gap between hospital and home for older cancer patients

1. Olivia Newton-John Cancer and Wellness Centre

Aim
Discharge from hospital can be a difficult time for elderly cancer patients and their carers. This project aimed to explore the gaps in transition from hospital to home for cancer patients over the age of 65 known to Palliative Care at Austin Health, and the relationship to unplanned readmissions.

Methods
This was a 2-part study:
- Audit of 30 cancer patients > 65yo referred to the inpatient palliative care consultancy team from October 1 to November 30, 2016
- Interviews with key stakeholders involved in the discharge and readmission process to explore their experiences and insights into the transition from hospital to home.

Results
During the study time period, 79 older oncology patients presented to the Emergency Dept (ED). 81% of these patients required admission to Austin Health. 90% of these patients had more than one re-admission during the study period.
The stakeholder survey reinforced the importance of effective clinical handover between hospital and community, especially aged care facilities. Patients referred to community palliative care services need to be visited within 2 weeks of discharge. Patients with brain tumours were considered a high-risk population. A suggested model of transitional support visits from hospital to home was supported by all stakeholders.

Conclusion
This study has highlighted the importance of continuity of care and the high levels of support needed in the days immediately after hospital discharge for older cancer patients and their carers. The next step is to develop a hospital-based nursing community liaison nurse role that would facilitate the transition home and ensure effective handover to the community services.

Acknowledgement
Supported by a North East Metropolitan Integrated Cancer Services grant.
Why are residential care residents being admitted to a hospital palliative care unit?

1. Olivia Newton John Cancer and Wellness Centre.

Aim
The Government expects residential aged care facilities (RACF) to provide end-of-life care (EOLC) for their residents, to enable people to die in their current home. However, there are an increasing number of RACF patients being admitted to the Palliative Care Unit (PCU) at Austin Health for EOLC. This audit investigated patients from RACF admitted to the PCU to explore the factors leading to admission and barriers for patients returning to their RACF for EOLC.

Methods
Twenty consecutive patients admitted to PCU from RACF were identified. Files were reviewed to identify reason for admission, treatment provided and facility or family factors that may have contributed to the need for hospital admission. Reasons for not being transferred back to the RACF were also examined.

Results
Most were direct admissions from Emergency following an acute event. Half of patients had no medical interventions whilst 30% received only hydration. Length of PCU admission ranged from less than 1 hour to 19 days, with the median length of stay being only 1.5 days. Uncontrolled symptoms and family dissatisfaction with facility care were identified as barriers, however 80% of cases were not suitable for transfer back to their RCF due to their imminent death.

Conclusion
Once patients have left their RACF and are admitted to hospital, they are often too sick to return. Additional resources are required in RACFs to manage emergency situations so residents can avoid a hospital admission and remain in their home for EOLC.
Trial of weekend palliative care consult nurses in a hospital without on-call registrars

1. Olivia Newton John Cancer and Wellness Centre.

Aim
The Palliative Care Service consists of an outpatient clinic, inpatient Palliative Care Unit (PCU) and Consultation Service (PCCS). There is no PCCS service on weekends, which can lead to delays in symptom management, discharge planning, and referrals to the PCU. This is the evaluation of a 4-month trial of weekend palliative care consult services.

Methods
Two senior clinical nurse consultants (CNC) worked alternate weekends providing on-site nursing for 18 hours every fortnight. The nurses were available for phone advice for an additional 30 hours over the weekend. A dedicated mobile phone was used so that there was a single point of contact. Data was collected on a simple audit form. Users were asked to complete a satisfaction survey on the value of service.

Results
There were 141 contacts with 136 patients. 75% of visits were planned reviews of existing patients, and 25% were new referrals. The most common reason for review was symptom management although 82% of all consultations involved a discussion about redirecting goals of care, with the patient, family and/or treating team. 84% of users were very satisfied and felt that it had provided a good outcome for the patient and family. 79% of respondents felt that the weekend service had improved patient flow in the hospital.

Conclusion
The introduction of weekend nursing was well received. There were perceived benefits to the patient, families and hospital flow. The majority of the work was symptom management, but there was a significant number of discussions about goals of care. This data will be used to apply for ongoing funding for a weekend PCCS service.
Can a Palliative Care Consultation Service Reduce Health Care Costs?

Aim
Hospital Palliative Care Consultation Services (PCCS) assist with symptom control, prognostication and communication. A recent Australian study has identified cost savings and improvements in end of life care with the involvement of hospital PCCS compared to without. This was a pilot study to see if the findings could be replicated at Austin Health.

Methods
Matched cases and controls from deaths occurring at Austin Health between Jan-June 2017 were established using age, gender, malignancy status, principle diagnosis (major organ system) and Charlson Comorbidity Index score. Differences in service utilisation and costs between those seen by the PCCS and those not seen were analysed.

Results
The average total cost of a terminal admission for a patient seen by the PCCS was $19,527 and for a patient not seen by the service $26,638, with an average saving of $7,111 (p=0.5234). Cost savings in the PCCS group were in pathology, radiology, radiotherapy, and reduced intensive care and theatre use.

Conclusion
This audit has suggested potential cost savings with the involvement of the palliative care service. This pilot has shown that it is possible to easily obtain the required data. A larger study has been planned.

References
Crescens Tiu\textsuperscript{1}, Zoe Loh\textsuperscript{1}, Chun Gan\textsuperscript{1}, Joanne Hakanson\textsuperscript{1}, Hui Gan\textsuperscript{1}, Thomas John\textsuperscript{1}, Eliza Hawkes\textsuperscript{1}

Effect of Reasons for Screen Failure (RFSF) on Standard of Care in Cancer Patients Screened for Clinical Trials

1. Olivia Newton-John Cancer Research Institute, Austin Health, Vic., Australia

Aim
Researchers are questioning the rationale for current rigidity of eligibility criteria in cancer clinical trials. In ineligible patients, the effect of RFSF on subsequent standard treatment (SST) is unclear. We review RFSF in a tertiary centre and their impact on SST.

Methods
From Feb 2011-Mar 2018, patients were identified from a tertiary hospital cancer trials screening log. Details of RFSF, SST and outcomes were collected. Patients were excluded if RFSF was lack of specific biomarker, absence of measurable target lesion, inadequate tissue sample, or patient choice.

Results
216 patients were eligible, with median age of 62 years (range 18-87). 82% had ECOG performance status (PS) 0-1 and 42% had ≥1 comorbidity. The most common cancers were lung (28%), melanoma, colon and pancreatic (all 11%).

RFSF were rapid disease progression (PD, 16%); PS 2-4 (12%); abnormal liver function tests (aLFT, 12%), of which 19/25 had liver metastases; brain metastases (11%); active comorbidity (11%); renal impairment (17, 8%); suspected metastases (15, 7%) and concurrent cancer (11, 5%). Other reasons (19%) included abnormal blood test, heart disease, contraindicated medications and leptomeningeal disease.

132/216 (61%) had SST. Only 8/132 (6%) had a dose reduction of SST, most commonly due to renal impairment (n=3) or active comorbidities (n=2). RFSF stabilised or improved in 87/132 (66%) on SST. Of note, aLFT improved in all patients without liver metastases, but only in 26% of those with liver metastases. Only 19% of poor PS patients improved.

Response to SST occurred in 44/132 (33%). 31/216 (14%) died ≤2 months after screening.

Conclusions
Most RFSF do not impact SST in cancer patients, however those with poor PS and aLFTs with liver metastases rarely respond to SST. Careful broadening of trial eligibility is warranted.
Lamanna A¹, Hynes M¹, Ranatunga D¹, Goodwin M¹

Adverse events following TACE – a single centre experience

1. Department of Interventional Radiology, Austin Health, Heidelberg, VIC, Australia

Aims
To evaluate the actual complication, readmission and prolonged hospital stay rates following transarterial chemoembolization (TACE) over a 1-year period at a major tertiary liver transplant hospital compared with hospital-reported data.

Materials and Methods
Ethics approved by the hospital ethics committee. A retrospective audit was performed of all TACE procedures that occurred between 1st Jan 2016 and 31st Dec 2016. Procedure reports, discharge summaries and admission notes were used to document periprocedural complications, prolonged hospital admissions (>36 hours) and readmissions to hospital (within 30 days) following TACE.

Results
107 patients (118 male, median age 60) underwent 141 TACE procedures. Routine hospital surgical mortality and morbidity meeting data reported no complications or deaths related to TACE during this period. An audit of hospital records revealed that complications occurred following 20/141 procedures (14.18%). 6/141 (4.26%) were periprocedural and 14/141 (9.93%) were postprocedural. Periprocedural complications included hypotension (3/141), hypertension (1/141), vessel dissection (2/141), groin site haematoma (1/141) and excessive pain (1/6). Prolonged admission due to pain (5/141), fever (2/141), tachycardia (2/141), dizziness (1/141) and nausea/vomiting (1/141) occurred following 7/141 procedures (4.96%). Readmission to hospital occurred following 6/141 procedures (4.26%) for encephalopathy (1/141), anorexia-nausea (2/141), pain (1/141), fever (2/141) and haematemesis/melena (1/141). No patients died within 60 days following TACE.

Conclusion
A significant number of patients experience complications following TACE. Unfortunately, the lack of active interventional radiology follow up predisposes radiology departments to being unaware of these. Prospective radiology department patient follow up may provide more accurate data whilst improving patient outcomes and experience.
Dufton, P., 1,2 Krishnasamy, M., 2,1,3 Gerdtz, M. 2.

An evidence-based, nurse-led model of care, to support cancer patients

1. Olivia Newton John Cancer and Wellness Centre, Heidelberg, Vic., Australia; 2. Department of Nursing, University of Melbourne, Parkville, Vic., Australia; 3. Victorian Comprehensive Cancer Centre, Vic., Australia

Aim
Ambulatory cancer settings have one of the highest rates of 28-day Emergency Department (ED) representation of all patient groups 1,2. The aim of this study was to identify patients at risk of making an unplanned ED presentation after receiving systemic anti-cancer therapy (SACT) in the ambulatory setting and translate findings from this research into clinical practice.

Research Design
A multiphase explanatory sequential mixed methods design was used to identify demographic, disease and social determinants that may increase patients’ risk of making an unplanned ED presentation within 28-days of receiving SACT.

Results
Patients more likely to make an unplanned ED presentation included those who were older (rpb (1) = .059, p = .002), diagnosed with colorectal (OR = 1.457, 95% CI 1.135 – 1.869), lung (OR = 2.491, 95% CI 1.963 – 3.161) or upper gastrointestinal (OR = 2.122, 95% CI 1.598 – 2.818) cancers, those born outside of Australia (OR = 1.324, 95% CI 1.135 – 1.545), and those of lower socio-economic status (OR = 1.207, 95% CI 1.024 – 1.422).

Conclusion
An appreciation of the factors linked to unplanned admission is now being used to target at risk patients in the context of a new nurse-led model of care. Patients identified at risk are proactively contacted by a specialist cancer nurse and offered additional support with the aim of reducing unplanned ED presentations.

References
Wang X, 1, Dufton P, 1,2, Mellerick A, 1

A nurse led symptom and urgent review clinic in the ambulatory cancer care setting
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Aim
Around 39% of Austin patients who receive systemic anti-cancer therapy (SACT) in the ambulatory setting make an ED presentation within 28-days. Of those patients, 30% were discharged home directly from the ED. A nurse-led Symptom and Urgent Review Clinic (SURC) was identified as an alternative model of care to meet the needs of this patient group.

Methods
Patient experience surveys were conducted pre-SURC implementation. The surveys aimed to explore the current level of information and support provided to patients and to explore the patient experience of managing side-effects of SACT. The results of the surveys aimed to identify current service gaps to inform the SURC model of care.

Results
Twenty-eight patients completed the pre-SURC implementation survey. The majority of respondents (n= 23, 82%) noted they received information about how to manage side-effects of treatment at home before they began, and that a nurse checked that they understood the information given to them. Despite being provided with this information, only 11 (39%) of respondents felt ‘confident’ in managing side-effects that may occur as a result of cancer treatment. The majority of patients identified nursing advice as useful in the practical aspects of managing side effects of treatment (n=20, 74%), but only 7 (25%) patients felt they had a dedicated nurse they could contact if they had questions or concerns. Overall, only two respondents (29%) were ‘definitely satisfied’ with the advice provided on managing side-effects of treatment.

Conclusion
The SURC provides rapid access to a dedicated oncology nurse. The results of the pre-SURC patient experience surveys supports a nurse-led model of care in the ambulatory cancer setting. The model aims to empowering patients with knowledge and support to self-manage toxicities associated with SACT, and reduce the number of unplanned ED presentations.

References
Background & Significance
Patients receiving SACT commonly experience a number of treatment related toxicities. Increasingly, these therapies are delivered in the ambulatory setting, shifting the burden of toxicity management onto patients and their carers (McKenzie & Hayes et al 2010). This is additionally problematic with unfamiliar toxicity profiles of new agents. The literature describes a number of nurse led interventions aimed at patient education, symptom assessment, coaching of self-care strategies and re-evaluation of symptoms. Austin Health was successful in receiving DHHS funding to pilot a nurse led model of care to address the needs of patients receiving cancer treatment within the ambulatory setting.

Aim
To implement a nurse led Symptom and Urgent Review Clinic (SURC) model of care to provide standardised patient education and a single point of contact for patients and their carers receiving systemic anti-cancer treatment (SACT) in the ambulatory setting. Identified benefits include improved patient understanding of toxicities associated with SACT, improved self-management capability, and a reduction in emergency department presentations.

Methods
A mixed methods evaluation including

- Patient experience - pre and post SURC implementation.
- 6 months SURC activity by number and type of contacts, tumour type, reason for presentation and outcome of each episode of care.
- Staff engagement and acceptability of the model.

Results
The model of care was implemented on January 2018. During the first 6 months of operation a total of 900 patients presented via SURC including

- 200 (22%) physical presentations. 115 patients said they would have otherwise attended ED. There have been 23 direct admissions from SURC completely bypassing ED.
- 513 (58%) telephone triages.
- 176 (20%) education sessions.

Patient and clinician satisfaction with the model of care has been very high.

Conclusion
A nurse led model of care within a SURC framework offers an effective and affordable service model that provides a clear point of contact to support patients throughout their treatment improving the patient experience and a reduction in unplanned presentations to the Emergency Department.
Predictive value of mutant TP53 overexpression for response to 5-fluorouracil based chemotherapy in microsatellite stable BRAF wild type colorectal cancers

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Aim: TP53, a key apoptosis regulator, is mutated in 50% of colorectal cancers (CRC), often resulting in P53 protein overexpression. We aimed to determine whether P53 expression can predict response to chemotherapy in CRC.

Methods: CRC cell lines treated with 5-fluorouracil (5FU) were tested for apoptosis after 72 hours. Correlation between chemosensitivity and TP53 mutation status, TP53 mRNA expression and P53 protein expression was assessed in MSS and MSI cell lines. Immunohistochemistry (IHC) for P53 on genotyped cell lines and human CRCs was used to determine a cut-point correlating with mutation status. Tissue microarrays of 285 stage 3 CRC, of which 190 had been treated with adjuvant 5FU or FOLFOX chemotherapy, were independently scored by 2 observers.

Results: High TP53 mRNA expression significantly correlated with missense mutations and lack of response to 5FU in MSS BRAF wt CRC cell lines, but not in MSI or BRAF mutant cell lines. Some highly sensitive MSS BRAF wt cell lines had nonsense or frameshift mutations in TP53 with corresponding low TP53 mRNA and low P53 protein expression. Allred IHC scores ≥6/8 optimally identified cases with a missense mutation, with high inter-observer reproducibility (Kappa 0.873 (95% CI 0.783-0.963)). High P53 expression was present in 105/190 stage 3 CRCs treated with adjuvant chemotherapy and 42/95 cases treated by surgery alone. Low P53 expression predicted a benefit in MSS BRAF wt tumours treated with adjuvant therapy (3 year relapse 36.84% vs 73.91% surgery alone; OR 0.2059 (95% CI 0.0703-0.6033, p=0.0040)), but not in P53 high MSS BRAF wt tumours (51.85% vs 50%; OR 1.0769 (95% CI 0.4430-2.6786, p=0.8733)).

Conclusion: High P53 expression identifies TP53 missense mutations and predicts lack of response to chemotherapy in MSS BRAF wt CRC. Non-expressing TP53 mutations were found within several chemosensitive cell lines, suggestive of functional differences between TP53 mutation types.
All-trans retinoic acid inhibits pancreatic cancer growth and enhances gemcitabine sensitivity by down-regulation of PAK

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Abstract

Aim: Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies worldwide due to the aggressive tumour biology and lack of effective therapeutics. ATRA has been used as an anti-stromal agent in PDAC, and its anti-tumour effect has also been reported in various kinds of cancer, including PDAC. P21-activated kinases (PAKs) play an important role in PDAC development. Inhibition of PAK has been reported to be associated with decreased tumour growth and increased gemcitabine sensitivity. The aim of this study was to determine the inhibitory effects of ATRA and its combination with gemcitabine on cell growth and migration of both wildtype and gemcitabine-resistant PDAC cell lines and the potential mechanism involved.

Methods: Both human (MiaPaCa-2) and murine (TB33117) PDAC cell lines were incubated in an increased concentration of gemcitabine to establish resistant cell lines. Cell growth, clonogenicity and migration/invasion were determined using Sulforhodamine B assay, colony formation assay and Boyden chamber assay, respectively. The expression of PAK was measured by Western blotting. Chou-Talalay method was used to evaluate the synergism of combination treatment of ATRA and gemcitabine.
**Results:** ATRA decreased cell proliferation, colony formation and migration. Treatment with ATRA down-regulated expression of PAK1, PAK2, PAK4 and α-SMA in both wildtype and gemcitabine-resistant cell lines. PAK1 knock-down sensitized MiaPaCa-2 to ATRA inhibition in cell proliferation and colony formation, but not in cell migration/invasion. Combination of ATRA and gemcitabine synergistically reduced cell growth on both wildtype and gemcitabine-resistant PDAC cell lines.

**Conclusion:** Our data provided evidence that ATRA not only reduced cell growth, but also synergistically enhance gemcitabine sensitivity in resistant PDAC cell lines via down-regulation of PAK.
Systemic and Non-tumoural Stat3 inhibition restricts gastrointestinal tumour growth in mice

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Stat3 is a transcription factor that plays major roles in physiological processes like development, immunity, and inflammation. In the context of gastric and colon cancer, Stat3 is often abnormally elevated and hyper-activated, promoting the expression of genes that prevent tumour cell death and help sustain tumour proliferation. While the role of intrinsic Stat3 signalling in tumour cells is well characterised, the effect(s) of Stat3 signalling among the infiltrating cells of the tumour microenvironment is still poorly understood. With this project we aim to elucidate the role of Stat3 in the non-tumoural compartment, and explore the therapeutic value of Stat3 inhibition for gastric and colon cancer.

We generated the shStat3 mouse that utilises short-hairpin RNAi technology allowing for conditional and reversible Stat3 reduction. To study the effects of systemic Stat3 inhibition, the shStat3 was crossed with the gp130F/F mutant mouse that spontaneously develops gastric cancer. To assess the effects of Stat3 suppression in the non-tumoural compartment alone, the shStat3 mice were subcutaneously injected with MC38 murine colon cancer cells. Tumours and other tissues of these mice were excised and analysed.

We found that shStat3-mediated systemic Stat3 suppression resulted in significant tumour reduction in gp130F/F gastric cancer mice. Similarly, isolated Stat3 reduction in the non-tumoural compartment of the shStat3 mice restricted the growth of Stat3-proficient MC38 tumour allografts. Immunophenotyping of excised tumours highlighted an increase of a monocytic Ly6C⁺Ly6G⁻ myeloid population.

Our data provides evidence for the therapeutic value of specific Stat3 targeting in gastrointestinal cancers. Interestingly, we have shown that Stat3 suppression in the non-tumoural compartment alone was enough to result in significant tumour reduction, indicating a prominent role of Stat3 in creating a pro-tumourigenic microenvironment. We have also identified a monocytic population as candidate cell type that drives this Stat3 suppression mediated anti-tumour effect.
MicroRNA-21 mediates Stat3-dependent gastric tumour development

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Background & Aim: MicroRNA-21 (miR-21) is an established tumour promoting miRNA which is overexpressed in multiple human cancers including gastric cancer. Previous studies have linked that induction of miR-21 to Stat3 activation. Herein, we further investigate the oncogenic properties of miR-21 and its contributions on Stat3-dependent gastric cancers.

Methods: Using the gp130F/F mouse model, which spontaneously develops tumours in glandular epithelium at approximately 6-7 weeks, miR-21 expression was assessed in adenomas compared to adjacent stomach tissue. The effect of miR-21 on gastric tumour progression was assessed in gp130F/F mice by which they were subjected to either vehicle or anti-miR-21. The regulation of miR-21 by Stat3 was assessed using a shSTAT3 mouse model and in human gastric cancer cell lines via stimulation with IL-6 and IL-11. Expression of PTEN and PDCD4, established miR-21 targeted tumour suppressor genes, were evaluated via IHC in stomachs of the mice treated with/without anti-miR-21. Finally, the tumour suppressive function of PTEN in gastric cancer was confirmed using an A33CreERT2;FF;PTENFl/Fl mouse model.

Results: Mir-21 expression was found to be significantly higher in adenomas of gp130F/F mice (P<0.01), and while treatment of the gp130F/F mice with the anti-miR-21 reduced adenoma growth, the number of adenomas formed did not differ. ChIP analysis of the miR-21 promoter identified several Stat3 binding sites, and stimulation of human gastric cancer cell lines with IL-6 or IL-11 significantly induced the expression of miR-21 (P<0.05). IHC analysis of stomach sections of mice treated with/without the anti-miR-21 displayed significant re-expression of PTEN and PDCD4 in the treated group. Finally, PTEN's tumour suppressive activity in gastric cancer was re-confirmed, with the A33CreERT2;FF;PTENFl/Fl mice developing larger adenomas compared to gp130F/F mice.

Conclusion: MiR-21 is a bona-fide Stat3 target gene which functions as a tumour promoter in gastric cancers by in part suppressing the tumour suppressor genes PTEN and PDCD4.
IL-11 as a therapeutic target to treat colorectal cancer

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Introduction
Colorectal cancer is a pressing health concern and there is a demand to develop novel therapeutics to treat this disease. Accumulating evidence alludes to a role for IL-11 signalling in tumor development although the mechanisms underlying IL-11 biology in colorectal cancer remain largely unknown. We postulate that IL-11 could be a mode of immunosuppression which can be targeted as a therapeutic strategy. We present data for the first time that indicates an immunological function for IL-11 in modulating T cell anti-tumour activity.

Method
To assess the therapeutic potential for targeting IL-11 signalling in colon cancer in vivo, wild type and il11r⁻/⁻ C57BL/6 mice were injected subcutaneously in the flank on Day 0 with 1 x 10⁶ MC38 colon cancer cells. Mice were euthanised on Day 18 and harvested tumours were immune profiled by FACS. To ascertain a role for IL-11 signalling in T cell activity, CD8⁺ and CD4⁺ T cells were FACs-sorted from wild type and il11r⁻/⁻ mice, and activated with PMA/ionomycin. In addition, CD8⁺ and CD4⁺ T cells from wild type mice were activated in the absence and presence of IL-11. T cell activation was subsequently assessed by qPCR analysis (granzyme B, perforin and IFNγ gene expression) and multiplex ELISA (pro-inflammatory cytokine production).

Results
MC38 growth was attenuated in il11r⁻/⁻ mice compared to wild type hosts. No differences were observed in the level of tumour-infiltrating immune cells (i.e. CD8⁻ T cells, CD4⁻ T cells, MDSCs, macrophages and B cells). Despite observing no changes in immune cell infiltrates, CD8⁺ and CD4⁺ T cells derived from tumour-bearing il11r⁻/⁻ mice appear to assume an enhanced activated phenotype indicated by higher expression of granzyme B, perforin and IFNγ. Ex vivo T cell activation assays corroborated these in vivo findings indicating (i) ablation of IL-11 signalling enhanced CD8⁺ T cell activation, and (ii) IL-11 treatment exerted immunosuppressive effects on CD8⁺ T cells.

Conclusion
Here we report that IL-11 signalling supports tumourigenesis using the MC38 colon cancer mouse model. For the first time, we have characterised a functional role for IL-11 in modulating T cell function. Overall, the findings from this study indicate IL-11R as a potential therapeutic target for the treatment of colorectal cancer.
Aadya Nagpal, 1,2, Rick Redvers, 1,2, Miriam Fuentes,1,2, Elnaz Tavancheh, 1,2, Effie Mouhtouris1,2, Delphine Denoyer1,2, Normand Pouliot 1,2.

Evaluation of Neratinib efficacy and mechanisms of resistance in a new syngeneic model of spontaneous breast cancer brain metastasis

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Background: Human epidermal growth factor receptor-2 (HER2)-targeted therapies effectively control systemic disease but resistance to treatment is common and up to 50% of patients progress to incurable brain metastases. Previous studies have shown that αvβ3 integrin receptors contribute to the progression of brain metastases and resistance to receptor tyrosine kinase inhibitors. However, therapies co-targeting these receptors have not been evaluated due to the lack of relevant preclinical models of brain-metastatic HER2 breast cancer.

Aims: The aims of this project are to i) characterise a novel syngeneic mouse model of HER2 breast cancer brain metastasis (TBCP-1) and ii) evaluate its response to HER2 and β3 integrin inhibitors alone or in combination.

Method: TBCP-1 cells were derived from a spontaneous mammary tumour in a Balb/c mouse and characterised for hormone receptors and HER2 expression by immunoblotting or by immunohistochemistry in tumours. TBCP-1 metastasis was analysed in vivo. Resistant variants (TBCP-1NR) were developed by continuous exposure to Neratinib and RNAseq used to reveal transcriptomic changes. Response to HER2 and integrin inhibitors was evaluated in in vitro proliferation inhibition assays.

Results: TBCP-1 cells, tumours or brain metastases lack hormone receptors but naturally express high levels of HER2. Accordingly, TBCP-1 cell proliferation is reduced by HER2 inhibitors, Lapatinib or Neratinib, but not by anti-oestrogens, indicating phenotypic and functional similarities to human HER2 breast cancer. Importantly, this model gives rise to a high incidence of spontaneous brain metastases from mammary tumours or experimental brain metastases following intra-cardiac inoculation. We show for the first time that Neratinib induces cell death by ferroptosis in TBCP-1 or in human SKBR3 cells but fails to induce this response in TBCP-1NR variants. Furthermore, pharmacological inhibition of αvβ3 integrin synergistically inhibits proliferation and restores sensitivity to Neratinib in resistant variants in vitro.

Conclusion: The TBCP-1 is the only model that fully recapitulates the spontaneous spread of HER2 breast cancer to brain in immune-competent hosts and provides a unique tool to identify novel therapeutics and biomarkers.
Title
Assessment of urinary bladder motion and bladder cancer location using cine Magnetic Resonance Imaging (cineMRI)

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Purpose:
To assess the intrafraction motion of the bladder and delineate the appropriate margin size for radiotherapy planning for both the full and empty bladder.

Methods and Materials:
This is a single site, single arm study of 20 patients with histologically confirmed muscle invasive transitional cell carcinoma of the bladder, planned to undergo radical cystectomy. All patients underwent cineMRI imaging of the entire pelvis using a Siemens 3-Tesla system, prior to cystectomy. Patients were positioned as for radiotherapy delivery, supine on the MRI couch stabilised with a knee rest and foot stocks. Patients first underwent a cineMRI first with a full bladder, then voided and underwent a second MRI with an empty bladder. All MRI sequences acquired over the 18 minutes of each scan, for both the full bladder and empty bladder, were contoured by a single observer using MIM Meastro. In doing so, we assessed the differences in bladder filling and subsequent volume displacement, between the empty and full bladder, during a time period consistent with that which occurs during radiotherapy delivery.

Results:
Between August 2015 and December 2017, 20 patients underwent cineMRI imaging of the entire pelvis. In assessing the directional displacement over the duration of the scan, the empty bladder showed a mean lateral displacement of 0.14cm (range 0.01 – 0.35cm), mean anterior-posterior displacement of 0.23cm (range 0.01 – 0.69cm) and mean superior-inferior displacement of 0.44cm (range 0.0 – 1.2cm). The full bladder showed a mean lateral displacement of 0.16cm (range 0.01 – 0.41cm), mean anterior-posterior displacement of 0.25cm (range 0.05- 0.54cm) and mean superior-inferior displacement of 0.40cm (range 0.03 – 1.26cm). Patients imaged with an empty bladder showed an average volume change over 18 minutes of 49.99cc representing a change of 44.9%. Patients with a full bladder showed an average volume change over 18 minutes of 69.14cc representing a change of 41.4%.

Conclusion:
Intrafractional motion secondary to bladder filling showed minimal variation between the full and empty bladder. Similar Clinical Target Volume to Planning Target Volume margins can be applied for the delivery of radiotherapy for a full and empty bladder.

References:
Aim
Autophagy is required by cells to recycle macromolecules during nutrient scarcity, and for the removal of damaged organelles and pathogens. Beclin1 is part of a complex required for the formation of the autophagosomes that encapsulate cytoplasmic material targeted for lysosomal degradation. It is also postulated to form a second complex linked to the endocytic trafficking pathway. However, the physiological importance of Beclin1 in this context has not been well elucidated. This project aims to determine if Beclin1 plays a role in both autophagy and endocytic trafficking in the maintenance of intestinal homeostasis.

Methods
Beclin1 conditional knock-out mice were crossed to transgenic mice expressing a Cre-ERT2 recombinase fusion protein under the Rosa26 locus. Deletion of Beclin1 in these adult mice was induced with a daily dose of tamoxifen for a span of three days. The impact of systemic Beclin1 deletion was then analysed histopathologically. Additionally, fibroblasts were derived from the embryos of these mice to study the effects of Beclin1 deletion in vitro.

Results
Systemic deletion of Beclin1 in adult mice results in an intestinal dilation phenotype. These Beclin1-deleted mice become moribund or die within 6-8 days post gene deletion. Histopathological analysis revealed ulcerative and proliferative enterocolitis, with disturbance to intestinal epithelium architecture. Embryonic fibroblasts derived from these mice accumulate cytoplasmic vacuoles and lose the ability to form colonies upon induction of Beclin1 deletion in vitro, with accelerated time to death. These observations seen in Beclin1-deficient mice and cells are not seen when disruption of other known autophagy regulators such as ATG5 and ATG16L1s induced [2], suggesting a role for Beclin1 beyond autophagy.

Conclusion
This data suggests that, in addition to autophagy, Beclin1 has an alternate role critical for maintaining intestinal homeostasis and gastrointestinal cell survival.
Targeting cell survival pathways in malignant mesothelioma

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Aim
Malignant pleural mesothelioma is an aggressive malignancy with limited systemic therapy options. A significant factor hindering the development of successful new treatment strategies for mesothelioma is the lack of well-defined driver mutations or common signalling pathway defects. Promising results have been reported with use of anti-PD-1 therapy, however it appears to be confined to a subgroup of patients. As a result, we recently turned to a more generic approach and tested a new class of drugs by directly targeting proteins that are critical for cell survival.

Methods
Using cell viability assays, we performed drug titration assays on five human mesothelioma cell lines using four different drugs targeting cell survival proteins, either as single agents or in combination with standard-of-care cisplatin chemotherapy. We further analysed that the responses observed are by the expected mechanism, using FACS-based methods and specific inhibitors of the pathway.

Results
Drugs targeting key survival proteins led to potent cell killing as single agents, and impressive synergetic activity when combined with each other or with chemotherapy. Cell killing was confirmed to be by the expected mechanisms.

Conclusion
We have demonstrated for the first time that agents targeting cell survival pathways are active in mesothelioma cell lines and that when used in combination are highly synergetic. We are in the process of undertaking in vivo experiments to determine efficacy and safety.
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Investigating the cellular and molecular basis of metastatic heterogeneity in triple negative breast cancer.

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Breast cancer is a highly heterogeneous disease, as revealed by molecular profiling of patient biopsies and patient-derived xenografts (PDXs). Intra-tumoral heterogeneity is believed to fuel tumour progression and drug resistance. Therefore, understanding clonal diversity is a pre-requisite for the design of new therapeutic strategies and the complete eradication of aggressive breast cancer clones.

We are using fluorescent barcoding to study inter- and intra-metastatic heterogeneity and clonal cooperation during breast cancer progression. Cancer cells from cell lines or PDXs are labelled using a library of fluorescent proteins and using 3D imaging, we are able to follow and characterize the evolution of aggressive triple negative breast cancer clones during the metastatic process. Our results indicate interesting differences between various metastatic tissues. We also use single-cell RNA sequencing to investigate the molecular bases of intra- and inter-clonal heterogeneity in metastases of different sizes and from different organs.

Current technologies to dissect tumoral heterogeneity predominantly use single-cell sequencing approaches. However, our barcoding strategy, using fluorescent barcodes, coupled with 3D imaging and single-cell transcriptomic, offers a unique opportunity to reconcile cellular phenotype and genotype within heterogeneous tumour samples.
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PLX8394, a New Generation BRAF Inhibitor, Selectively Inhibits BRAF in Colonic Adenocarcinoma Cells and Prevents Paradoxical MAPK Pathway Activation

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Aim
BRAF inhibitors are standard treatment of melanoma, but can paradoxically activate MAPK signaling pathway with dire consequences. We reported a patient with synchronous BRAF\textsuperscript{V600E} melanoma and BRAF\textsuperscript{wt}/KRAS\textsuperscript{G12D} colorectal cancer (CRC), whose CRC relapsed and progressed whilst on BRAF inhibitor dabrafenib. BRAF inhibitor PLX8394, dubbed as “paradox breakers”, is being developed (Plexxicon©). Here, we used a colorectal cancer cell line derived from the aforementioned case and a panel of cancer cell lines of varied mutational status to study on-target inhibition and paradoxical MAPK signaling of first generation BRAFi, such as vemurafenib, and PLX8394.

Method
To asse the efficacy of both inhibitors, we treated BRAF\textsuperscript{V600E}/KRAS\textsuperscript{wt} cell lines at 0.1, 0.5, and 1 µM. To asse paradoxical MAPK signaling, we treated BRAF\textsuperscript{wt}/KRAS\textsuperscript{G12D} cell lines with the same dose range of both inhibitors. We harvested cells after 6hr and performed immunoblot-densitometry of native to phosphorylated MEK1/2 and ERK1/2 ratios. To assess functional effect, we performed cell proliferation assay after 72hr with the same dose range of both inhibitors.

Results
Vemurafenib induced an increase in phosphorylated MEK1/2 and ERK1/2 in BRAF\textsuperscript{wt}/KRAS\textsuperscript{G12D} cell lines. In contrast, PLX8394 had minimal effect. Consistently, cell proliferation was enhanced with vemurafenib but not PLX8394. Treatment of BRAF\textsuperscript{V600E} cell lines with both inhibitors expectedly reduced MEK1/2 and ERK1/2 phosphorylation.

Conclusions
Paradoxical activation of MAPK signaling and proliferation of KRAS\textsuperscript{G12D} CRC cells is reduced by BRAF inhibitor PLX8394, while their capacity to inhibit mutant BRAF-driven signaling remain effective. Our findings suggest that the new paradox breakers have the potential to mitigate the risk of promoting occult RAS activated tumour progression associated with the use of first generation BRAF inhibitors.
Authors
Wasiak J, Hamilton, D, Foroudi, F, Faggion CM.

Title
Surveying retracted studies and notices within the field of radiation oncology

Abstract
Objective: The purpose of this study was to characterize retracted studies within the field of radiation oncology.

Methods: Computerized searches were performed in Ovid MEDLINE, PubMed, Ovid EMBASE and The Cochrane Library through to May 2017 looking for retracted studies using the terms ‘retraction note’, ‘retracted note’, ‘withdrawn’ and ‘radiotherapy’, ‘radiation oncology’. Additional studies were identified by hand-searching 10 discipline-specific journals. Two authors independently screened papers, and then extracted author demographics, journal characteristics and retraction-specific variables.

Results: Of the 58 studies identified, the most common reason for retraction was misconduct (43%), methodological error (21%), authorship issues (5%), unknown causes (5%) and journal (administrative) errors (3%). A total of 13 systematic reviews or protocols (22%) were withdrawn from The Cochrane Library for being out-of-date or redundant. All but one retracted study and retraction notice was available in portable document format respectively. Of the 57 retrieved papers, 79% were identified as retracted via in-text notations or watermarks. Overall median time to retraction was 44 months (interquartile range [IQR] 11 to 98). However, 42 studies (72%) were still cited after retraction notices were published.

Conclusion: A retracted study within the field of radiation oncology remains a relatively uncommon event. Although promising, our data suggest that the majority of these retracted articles continue to be cited as valid research. As such, there is still a need for clinicians to remain vigilant with their academic rigor and good clinical research practices. There is an urgent need for publication houses to foster universal publishing standards along with discipline-specific retraction guidelines.

Keywords: Retraction of Publication as Topic; Duplicate Publication as Topic; Publications ethics; Scientific Misconduct; Radiation Oncology; Radiotherapy.
Olfactory fMRI can reveal lateralized dysfunction of piriform cortex in temporal lobe epilepsy

Aim
The piriform cortex is commonly involved in focal epileptic activity [1,2]. We hypothesize that this disrupts the normal physiological function of the piriform cortex and could lead to an impaired sense of smell. We explored whether piriform dysfunction, and thus the epileptic side, could be detected using an olfactory functional MRI paradigm.

Methods
We studied 13 adults with unilateral Temporal Lobe Epilepsy with Hippocampal Sclerosis (TLE-HS; 8 right, 5 left; age range 28-66 years) versus 14 healthy age-matched controls. Olfactory testing was performed using “Sniffin' Sticks". The olfactory-task functional MRI involved 10 minutes of regular nasal breathing, with intermittent birhinal delivery of lavender odour, each for the duration of a single inhale. Whole-brain echo-planar imaging was acquired on a Siemens Skyra 3T MRI throughout (TR=3s, TE=30ms, iPAT=2, 44 interleaved slices, 3mm isotropic voxels).

Results
Sniffin' Sticks test showed a significantly lower total threshold-discrimination-identification (TDI) score in TLE-HS, due to reduced odour discrimination and identification (each p<0.05 corrected). Odour detection threshold was preserved. Group analysis of olfactory-task fMRI showed significant activation at the bilateral piriform cortex, orbitofrontal cortex, thalamus and within the salience network. In TLE-HS, piriform cortex activation was only detected on the side contralateral to the epileptic focus. Individual analysis showed significant piriform region-of-interest activation in 5 of 10 controls, and on the non-epileptic side in 3 of 10 TLE-HS patients. Overall the TDI score was positively correlated with mean piriform cortex activation (R²=0.45, p=0.001).

Conclusions
Patients with TLE-HS have a subtle deficit in their sense of smell. An olfactory-task fMRI paradigm can detect absent/reduced piriform activation on the epileptic side in some patients. Correlation between olfactory testing and reduced piriform activation suggests that epilepsy-related piriform dysfunction contributes to the observed behavioural deficit.

References
A Retrospective Study of Patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): Identifying Ultrasonographic Features for Diagnosis and Prognosis

Objective
To determine if parameters found on neuromuscular ultrasound (NMUS) correlate with diagnosis and clinical features in patients with CIDP.

Background
CIDP often requires continued treatment over years to control the disease, with treatment decisions often made on a global impression of benefit or failure rather than more formalized measures. High frequency ultrasound of peripheral nerves has the potential to provide information about nerve function and structure, and response to treatment. These parameters can be obtained non-invasively, relatively quickly, and with minimal patient discomfort, and thus are good candidates for repeatable testing. Recent studies have confirmed that NMUS is beneficial in diagnosis of CIDP, but further research is needed to determine any role in prognosis, and whether serial assessment of CIDP patients is of benefit.

Methods
We conducted a retrospective chart review to identify patients with CIDP studied with ultrasound at Wake Forest Baptist Medical Center from January 2000 to August 2017. We extracted a standardized dataset of clinical (duration of disease, current clinical state, and treatment history), electrodiagnostic and ultrasound findings (in particular nerve size as measured by cross-sectional area (CSA)) from various upper and lower limb nerves. 148 patients coded with a diagnosis of CIDP (ICD-10 G61.8 and ICD-9 357.81) who attended the WFBMC diagnostic neurology laboratory were identified and the charts reviewed.

Results
Of the 148 patients, 50 adult patients had been studied with ultrasound at least once. After chart review it was determined that 21 of these patients had definite CIDP, 22 an alternate diagnosis, and 7 patients had possible CIDP but had insufficient follow up to confirm. Abnormalities on ultrasound (in particular focal nerve enlargement) were common in our CIDP cohort, with 20 of 21 subjects having at least one abnormal finding. We analyzed our data in line with previously published diagnostic scores and protocols, and differences between CIDP and not CIDP patients were clearly evident, despite the often-incomplete data acquisition in this real-world retrospective cohort (sensitivity and specificity will be presented). The findings in different clinical subtypes and distribution patterns will also be presented and discussed.

Conclusions
In this real-world study of ultrasound in patients with possible CIDP, there are clear differences in ultrasound parameters between those who have CIDP compared with those who have an alternate neuropathy.
CODE STROKE ALERT – Development of a new open-source platform to streamline acute stroke care

Background

Effective, time-critical intervention is crucial to mitigate stroke mortality and morbidity but is often hampered by systemic pre- or in-hospital delays. In the era of rapid reperfusion therapy for ischaemic stroke, there is urgent need to improve multi-disciplinary communication to synchronise and coordinate rapid clinical, imaging assessment, and therapeutic decision making across the entire stroke journey from initial emergency medical service (EMS) assessment to in-hospital assessment and treatment.

Purpose

To develop an open source multi-platform application that provides a purpose-built, efficient, user-friendly communication system that links pre-hospital emergency services, stroke and neuro-interventional teams, aiming to reduce the time from first medical contact to cerebral reperfusion time.

Method/Results

The Health Insurance Portability and Accountability Act (HIPAA) compliant, open-source platform can be accessed by EMS and hospital staff involved in acute stroke care. When a new stroke alert is lodged by EMS, the application will prompt calculation of relevant clinical scores that aid decision making. Depending on the patient’s clinical status, an appropriate hospital is recommended and will be pre-notified of impending stroke patient arrival. Empowered by geotagging, an estimated time of arrival is broadcast to all relevant team members, ensuring effective communication between teams.

Conclusion

Code Stroke Alert streamlines communication and coordination of stroke care, possibly negating any room for errors. This facilitates and accelerates the logistical processes required to achieve reperfusion, potentially improving patient outcome.

The platform will be available free to health networks globally to expedite treatment and improve quality and safety of stroke care. The open-source nature of the software may promote future development of plug-ins and add-ons based on individual institutional needs, e.g. for Hospital Information System (HIS) or Picture Archive Communication System (PACS) integration. In addition, data logs are created, with an auditable trail of all relevant quality improvement metrics with a view to overall system quality improvement.
Medial temporal lobe atrophy in ischaemic stroke patients is modulated by presence of the apolipoprotein E (APOE) epsilon-4 (ε4) allele

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Aim
The APOE ε4 allele is a known risk factor for the development of cognitive impairment and dementia. Carriers have been reported as having lower hippocampal volume than non-carriers in Alzheimer’s disease, mild cognitive impairment, and in healthy cohorts¹. However, this is not well investigated in stroke. Here, we compared volumes in the medial temporal lobe in ischaemic stroke survivors, with and without the ε4 allele, three (t1) and twelve (t2) months after stroke.

Methods
21 non-carriers and 21 carriers of APOE ε4 – matched for neurological impairment and for lesion size and location – were sampled from the Cognition And Neocortical Volume After Stroke (CANVAS)² study. We used a linear mixed-effect model to compare hippocampal, entorhinal, and parahippocampal volumes estimated in FreeSurfer5.3; adjusting for age, sex, years of education, and total intracranial volume.

Results
Left hippocampal ($p_{t1}^{\text{t1}}=0.038$, $p_{t2}^{\text{t2}}=0.04$) and entorhinal ($p_{t1}^{\text{t1}}=0.044$, $p_{t2}^{\text{t2}}=0.038$) volumes were significantly lower in ε4-carriers at both timepoints. Right entorhinal ($p_{t1}^{\text{t1}}=p_{t2}^{\text{t2}}=0.002$) and parahippocampal ($p_{t1}^{\text{t1}}=0.018$, $p_{t2}^{\text{t2}}=0.02$) volumes were also significantly lower in ε4-carriers; but no significant difference in right hippocampal volume ($p_{t1}^{\text{t1}}=p_{t2}^{\text{t2}}=0.055$). Group-time interaction was significant in left parahippocampal cortex ($p=0.019$): ε4 non-carriers showed a significant volume increase ($p=0.018$) between timepoints.

Conclusion
Our findings suggest that carriers of APOE-ε4 allele will experience greater atrophy in the medial temporal lobe twelve months after their stroke. This may represent an increased risk for developing dementia.

References
Epilepsy of Infancy with Migrating Focal Seizures: a genetically heterogeneous developmental and epileptic encephalopathy

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**Aim**

Epilepsy of infancy with migrating focal seizures (EIMFS) is a rare devastating infantile developmental and epileptic encephalopathy (DEE), marked by seizure migration between hemispheres, seizure onset before 6 months, and developmental plateau or regression. Here, we report a large international case series of 120 patients and identify novel genes associated with EIMFS.

**Methods**

Patients were recruited to our Epilepsy Genetics Research Program or collaborating groups. The phenotypic and genotypic spectrum of EIMFS was analyzed.

**Results**

120 patients (114 families) were recruited. 79/120 (66%) had pathogenic variants (46 previously reported): 61 cases with dominant mutations, 18 with recessive causes. Six novel genes for EIMFS (Dominant: \textit{PIGA}, \textit{GABRB1}, \textit{GABRA1}, \textit{CDKL5}, Recessive: \textit{ITPA}, \textit{KARS}) were identified. Mutations in \textit{KCNT1} were the most frequent cause (31/79, 39%), followed by \textit{SCN2A} (10/79, 13%). Mosaicism was observed in two probands (\textit{SCN2A}, \textit{GABRB3}) and in three unaffected mothers of probands with \textit{KCNT1} mutations. Median age of seizure onset was 1 month, with onset in the \textit{SCN2A} group on day two of life, compared with 4 weeks for \textit{KCNT1} cases. Profound to severe developmental impairment was usual; 3 patients with less severe impairment had \textit{SCN2A} mutations and 2 had \textit{KCNQ2} mutations. A range of co-morbidities is seen including movement disorders, spasticity and scoliosis. EIMFS has a high mortality of 35% at a mean age of 3 years 5 months.

**Conclusion**

EIMFS is a highly genetically heterogeneous disease, following dominant or recessive inheritance. We increase the number of genes associated with EIMFS to 26. 66% of EIMFS cases are genetically solved. \textit{KCNT1} remains the most frequently cause. The new genes associated with EIMFS are seen in small numbers of patients. It will take larger numbers of patients with each gene to dissect whether the comorbidities associated with EIMFS are gene-dependent or relate to this devastating epilepsy syndrome.
Utility of Whole Exome Sequencing in Complex Neurologic and Neurodegenerative Disorders

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Aim

Complex neurologic and neurodegenerative disorders are often associated with diagnostic uncertainty and delay; this adds to stress and negative impacts on patients, families and the healthcare system. This study aims to investigate the utility of whole exome sequencing on diagnosis rate as well as wider impacts on clinical management, psychosocial and health economics outcomes.

Methods

We aim to recruit 168 Victorian patients with a range of complex neurologic disorders with onset less than 60 years (ataxia, dystonia, spastic paraplegia, Parkinson’s disease, motor neurone disease, dementia and complex/multisystem disease) via genetics clinics, where they will also receive genetic counselling and follow up. Patients will undergo whole exome sequencing with targeted analysis of specific genes for each condition. The primary outcome is the diagnostic rate in the entire cohort. Secondary outcomes are diagnostic rates in individual conditions, impacts of results (e.g. changes in management, psychological and social impacts for patients and families), and cost-effectiveness analyses.

Results

222 patients were referred between September 2017-August 2018 and recruitment is ongoing. 157 patients were eligible, 123 have been seen at genetics clinics and recruited. As of August 2018, results are available for 35 patients: 10 (29%) had a pathogenic or likely pathogenic variant, 14 (40%) had a variant of unknown significance, and 11 (31%) had a negative result. Diagnostic rates were highest in spastic paraplegia (3/6, 50%), followed by ataxia (2/5, 40%), Parkinson’s disease (1/3, 33%), and complex/multisystem (3/10, 30%).

Conclusion

The success of recruitment reflects great interest and demand for genetic testing in complex neurologic disorders. Our preliminary findings are very encouraging, demonstrating an almost 30% diagnostic rate which is consistent with emerging literature. Ongoing recruitment and analysis of genomic, clinical management, psychosocial and health economic data will establish the place of this revolutionary technology.
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Factors associated with stroke survivors’ return to work in A Very Early Rehabilitation Trial (AVERT)

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Aim
Worldwide, the proportion of strokes occurring in the working age is increasing(1). As a result, returning to work is growing in importance as a rehabilitation and economic outcome. This study aimed to describe the characteristics of young working age stroke survivors in AVERT, and examine factors associated with return to work by 12 months.

Methods
Data was collected as part of A Very Early Rehabilitation Trial (AVERT) at 56 acute stroke units across Australia, New Zealand, the United Kingdom, Singapore and Malaysia from 2006-2015. AVERT was a randomised control trial studying the effects of very early mobilisation after stroke. AVERT participants were included in this study if they were aged less than 65, were working at the time of stroke, and had complete 12 month return to work data. The primary outcome was return to paid work at 12 months post stroke. Univariable and multivariable logistic regression analysis was conducted to determine the association of various factors on return to work.

Results
Of the 2104 patients in AVERT, 376 (17.9%) met the inclusion criteria. By 12 months, 221 (58.8%) participants had returned to work at a median of 38 hours per week. There was no significant difference in 12-month return to work rates between Australasia, the United Kingdom and Asia. When controlling for multiple factors with multivariable analysis, younger age (OR 0.94, 95% CI 0.91-0.98), lower stroke severity (NIHSS; 0.92, 0.86-0.99), full-time work prior to stroke (2.33, 1.24-4.40), and lower 3-month disability (mRS) demonstrated a positive association with a return to work by 12 months.

Conclusion
This study found that younger age, lower acute stroke severity, lower 3-month disability and prior full-time work are important factors associated with return to work. This study uniquely examines a large international and longitudinal cohort. Future research is required to determine effective interventions.

References