POSTER SESSIONS

Poster Opening
Education Precinct
L4 Austin Tower
Tues 4 Oct 17.00–18.00

Poster Exhibition
Education Precinct
L4 Austin Tower
Mon 3 Oct to Fri 7 Oct

Poster Author Sessions
Rooms 4.4 & 4.5
Education Precinct
L4 Austin Tower
Tue 4 Oct 14:30–15:30
Thu 6 Oct 14:30–15:30

OCTOBER

M	T	W	Th	F
			TH	
3	4	5	6	7
10	11	12	13	14
17	18	19	20	21
24	25	26	27	28
31				

austin.org.au/ResearchFest
hub/ResearchFestOct

CUTTING EDGE RESEARCH

Consumer Engagement Awards
Education lecture theatre
L4 Austin Tower
Tue 4 Oct 14:00–15:00

3D Med Symposium
Education lecture theatre
L4 Austin Tower
Thu 5 Oct 14:00–18:00

Quality projects Nursing Forum
Education lecture theatre
L4 Austin Tower
Thu 6 Oct 14:00–15:00

RJ Pierce Symposium
Education lecture theatre
L4 Austin Tower
Fri 14 Oct 11:00–13:00

Research Week Oral presentations
John Lindell lecture theatre
L4 Austin Tower
Tue 18 Oct 10:00–12:00

AMRF Young Investigator Symposium
John Lindell lecture theatre
L4 Austin Tower
Tue 18 Oct 12:30–13:30

Research Week Oral Presentations; Sustainability; health and the environment
Education lecture theatre
L4 Austin Tower
Wed 19 Oct 14:00–16:00

Research Week Oral Presentations
Education lecture theatre
L4 Austin Tower
Wed 26 Oct 10:00–12:00

Dunlop Medical Research Foundation Symposium
John Lindell lecture theatre
L4 Austin Tower
Wed 26 Oct 12:15–13:30

RESEARCH° FEST

OCTOBER 2016

Austin LifeSciences

RESEARCH LECTURES

Physiotherapy Research Event
Education lecture theatre
L4 Austin Tower
Tue 4 Oct 16:00–17:00

Research Week Debate
John Lindell lecture theatre
L4 Austin Tower
Thu 13 Oct 12:30–13:30

Research Week Plenary Session Professor Tim Flannery
John Lindell lecture theatre
L4 Austin Tower
Wed 19 Oct 12:30–13:30

ResearchFest Oct 2016 Poster Session Tuesday 4 October 2.30 - 3.30 Education Precinct level 4 Austin Tower

		Consumer Engagement Awards
Tues001	Leanne Rees	Victorian Spinal Cord Service (VSCS) Discharge Review Clinic (DRC) – Review
Tues002	Nicole Hosking/ Julie Preston	We can individualise consumer care and reduce anxiety by using the resources of a large public hospital
Tues003	Adam Blake / Jane Negus	Reducing Restrictive Interventions (RRI)
Tues004	Mr Pat O'Leary / Dr Joanne Sais	Peer Support at Austin Child and Adolescent Mental Health
Tues005	Emma Burns	Patients as Teachers
Tues006	Phuong Phan / Jo Bombos	Reviewing the Health Independence Program (HIP) Central Phone Number Voice Message and Options
Tues007	Emma Burns	A New Social Aphasia Support Group: Transition of the Austin Aphasia Integration Program into the Community
Tues008	Rob LoPresti	Patient Centred Care Education
Tues009	Bernadette Vandenberg	Plain English Coaching
Tues010	Mel Kotze	Partnering with patients to contribute to student feedback
Tues011	Katina Aspridis	The Cottage Garden Project
Tues012	Mark McDonald	After Hours Spinal Gym
Tues013	Robyn Purcell	Bringing simulation to life
Tues014	Caitlyn Green	Improving access to care for Austin Health Home Enteral Nutrition (HEN) patients
Tues015	Jannette Blennerhassett	People's preferences for ongoing exercise programs
Tues016	Francis Lagan	Cognitive Dementia and Memory Service (CDAMS) Information Session
Tues017	Nonie Rickard	Model of Care (Nursing)

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		Physiotherapy
Tu01	Vera Ciavarella	This abstract is not included at the request of the author
Tu02	Bridget Hill	Evaluation of internal construct validity and unidimensionality of the Brachial Assessment Tool (BrAT), a patient-reported outcome measure for Brachial Plexus Injury
Tu03	Sharon Kramer	Stroke survivors use more energy while walking early after stroke compared to age and gender matched controls
Tu04	Sharon Kramer	Validity of the SenseWear armband to measure energy expenditure during walking early after stroke
Tu05	Joleen Rose	Commencing early rehabilitation in critical care. What influences clinical decision-making?
Tu06	Liam Johnson	Quantitative measurement of cardiovascular fitness longitudinally after stroke
Tu07	Jannette Blennerhassett	This abstract is not included at the request of the author
Tu08	Jannette Blennerhassett	This abstract is not included at the request of the author
Tu09	Cathy Said	This abstract is not included at the request of the author
		Occupational Therapy, Nutirition, Speech Pathology and Pharmacy
Tu10	Liana Cahill	This abstract is not included at the request of the author
Tu11	Tamara Tse	The Activity Card Sort - Australia: Validation and reliability in an Australian stroke cohort
Tu12	Tamara Tse	Longitudinal changes in activity participation after mild stroke.
Tu13	Catherine Cooper	Tele-rehabilitation: Extending the ""reach"" of hand therapy in tetraplegia
Tu14	Lauren Le Fevre	This abstract is not included at the request of the author
Tu15	Kate Hamilton	The addition of high amylase resistant starch to reduce stool output in people with short bowel syndrome.
Tu16	Emma Burns	Austin Aphasia Integration Program for People with Chronic Aphasia Following Stroke
Tu17	Hailey Meaklim	A topical vasoconstrictor and the upper airway of patients with quadriplegia and obstructive sleep apnoea: An MRI study
Tu18	Rizwan Jaipurwala	Compromised bone structure and density in end stage renal disease

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Tu19	Jane Booth	Adverse Drug Reaction reporting - one tertiary institution's systematic approach, getting below the tip of the iceberg
Tu20	Yixin Tan	Can hospital pharmacists improve the accuracy of medication information in medical discharge summaries?
		Oncology and Haematology
Tu21	Hema Vaithianathan	Radiation Dose to the Vaginal Vault during Brachytherapy - Early experience and an Audit
Tu22	Mariah Alorro	Exploring the Signal transducer and activator of transcription-3 (STAT3) as a therapeutic target
Tu23	Lucy Fox	The Incidence and Natural History of Dasatinib Complications in Chronic Myeloid Leukaemia
Tu24	Laura Jenkins	Combination treatment using MAPK and HDACi to enhance differentiation as a novel therapeutic strategy for colorectal cancer
Tu25	Jennifer Huynh	This abstract is not included at the request of the author
Tu26	Jose Diego Tagaro	Adapting our Approach to Image Verification: Clinical Implementation of ExacTrac in a 3D-Image Rich Department
Tu27	Puey Ling Chia	Attitudes of patients and physicians to repeat biopsies for lung cancer
Tu28	Andrew Carey	This abstract is not included at the request of the author
		Surgery
Tu29	Anthony Yao	A case series of Orbital Tuberculosis: Perspectives from Victoria, Australia
Tu30	Linh Nguyen	This abstract is not included at the request of the author
Tu31	Stefanos Kanatsios	Survival outcomes following definitive surgical resection of stage IV melanoma
Tu32	Brian Ngo	Factors affecting the timeliness of haematuria assessment
Tu33	Brian Ngo	Factors affecting the timeliness and adequacy of haematuria assessment
Tu34	Chien-Tse (Tony) Kao	3D Printed Abdominal Aortic Aneurysm Model for Patient Education
Tu35	Todd Manning	Retroperitoneal Lymph Node Dissection: an analysis of a contemporary Australian cohort in an experienced institution.
Tu36	Myles Davaris	This abstract is not included at the request of the author
Tu37	Jasamine Coles-Black	3D Printing in Surgery: Developing a Universal Workflow

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Tu38	Marlon Perera	This abstract is not included at the request of the author
Tu39	Damian Ianno	Colonoscopic localization accuracy for colorectal resections in the laparoscopic era
Tu40	Madeleine Tancock	The role of the Renin-Angiotensin System on tumour recurrence and the immune system following resection of colorectal liver metastases
Tu41	Su Kah Goh	Donor-specific cell-free DNA as a non-invasive marker of organ rejection after liver transplantation: a pilot study.
Tu42	Laura Machan	Apnoeic oxygenation vs. low tidal volume ventilation in anaesthetised cardiac patients: a prospective, single centre, randomised trial
Tu43	Todd Manning	Laparoscopic Lens Fogging: Updated solutions for a common, but misunderstood problem.
		Psychiatry and Psychology
Tu44	Cameron Dawson	Parental Perceptions of Informed Consent in a Public Child and Adolescent Mental Health Service
Tu45	Alaric Indranada	The Pre-ictal Rise of Autonomic Parameters in Psychogenic Non-epileptic Seizures
Tu46	Sarah Hall	This abstract is not included at the request of the author
		Neurosciences
Tu47	Anthony Yao	Bilateral Facial Nerve Palsies Secondary to Chronic Inflammatory Demyelinating Polyneuropathy Associated with Anti-TNF-α use: Case Presentation and Literature Review
Tu48	Luke Baker	Botox Therapy in Simple partial seizures - Evaluated with FDG PET
Tu49	Brenda Grabsch	Quality of care over-time: new evidence from the Australian Stroke Clinical Registry
Tu50	Michael Hildebrand	This abstract is not included at the request of the author
Tu51	Gareth R Jones	Comparison of early dynamic Amyloid and Tau-PET scans to 18F-FDG-PET images
Tu52	Tia Cummins	In vivo assessment of markers of Alzheimer's disease pathology in Vietnam war veterans with Traumatic Brain Injury & Post-Traumatic Stress Disorder
Tu53	Nazuk Yusup	Anterior versus posterior stroke: No difference in cognitive impairment
Tu54	Sheila Patel	This abstract is not included at the request of the author
Tu55	Laura Bird	This abstract is not included at the request of the author

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Tu56	Emilio Werden	Cognition is associated with hippocampal volume and cortical thickness early after ischaemic stroke
Tu57	Toby Cumming	The Stroke Exercise Preference Inventory (SEPI): Development of a new tool
Tu58	Susannah Bellows	Phenotypic Analysis of 303 Multiplex Families with Common Epilepsies
Tu59	Karen Borschmann	Growing collaborative partnerships to enhance stroke recovery research
Tu60	Paul Yates	Antihypertensive Treatment and Longitudinal Aβ Measures: Results from the AIBL Study of Ageing
Tu61	Paul Yates	Cerebrovascular disease, Alzheimer's disease biomarkers and Longitudinal Cognitive Decline
Tu62	Aaron Warren	This abstract is not included at the request of the author
Tu63	Peter Goodin	Characteristics and differences of somatomsensory impairment post-stroke based on lesioned hemisphere.
Tu64	Leeanne Carey	SENSe: Individual characteristics that predict favorable outcomes for sensory rehabilitation after stroke
Tu65	Amy Schneider	Severe infantile-onset epileptic encephalopathy caused by mutations in autophagy gene WDR45
Tu66	David Nadebaum	This abstract is not included at the request of the author

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		Infectious Diseases
Tu67	Kyra Chua	Cefepime susceptibility: an assessment of the performance of VITEK2 versus agar dilution
Tu68	Andrew Stewardson	This abstract is not included at the request of the author
Tu69	Natasha Holmes	This abstract is not included at the request of the author
Tu70	Natasha Holmes	This abstract is not included at the request of the author
Tu71	Jason Kwong	PAM-2: a novel carbapenemase identified in Pseudomonas alcaligenes through bacterial whole-genome sequencing
Tu72	Jason Trubiano	The Impact of an Antimicrobial Stewardship Lead Antibiotic Allergy Testing Program on Prescribing
Tu73	Andrew Mahony	This abstract is not included at the request of the author
Tu74	Ruth Colley	An audit of melatonin prescribing for delirium treatment and prevention at a large tertiary care hospital
		Gastroenterology
Tu75	Raany Rahme	This abstract is not included at the request of the author
Tu76	Catherine Brock	This abstract is not included at the request of the author
Tu77	Laurence Jacuzzi	This abstract is not included at the request of the author
Tu78	Moritz Eissmann	This abstract is not included at the request of the author
Tu79	Indu Rajapaksha	A small molecule diminazene aceturate inhibits acute and chronic hepatobiliary fibrosis in mice
Tu80A	Chandana Herath	ACE2-AAV gene therapy ameliorates severe biliary fibrosis in mice
Tu80B	Indu Rajapaksha	ACE2-AAV gene therapy ameliorates liver fibrosis in diabetic mice with non-alcoholic fatty liver disease

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		Endocrinology and Metabolism
Tu81	Lauren Winter	Neutrophil-lymphocyte ratio is increased in diabetic kidney disease with albuminuria
Tu82	Ling Yeong CHIA	Androgen action via the Androgen Receptor in the brain positively regulates muscle mass by actions in fast-twitch muscle fibres
Tu83	John Mariadason	This abstract is not included at the request of the author
Tu84	Cara Tanner	Short and mid-term renal function in patients with type 1 and type 2 diabetes during and after pregnancy
Tu85	Sabashini Ramchand	Oestradiol depletion in premenopausal women with non-metastatic breast cancer is associated with severely deteriorated cortical and trabecular microstructure
Tu86	Felicity Pyrlis	Improving the transition of care of inpatients with type 2 diabetes
Tu87	Jas-mine Seah	Tumour Necrosis Factor-alpha Receptor 1 and 2 are Reduced in patients with Type 1 Diabetes and Hyperfiltration
	Mark NG TANG FUI	This abstract is not included at the request of the author
	Mark NG TANG FUI	This abstract is not included at the request of the author
Tu88	Sandra Iuliano	Improved nutritional status in female aged-care residents with 12 months of dairy supplementation: A cluster randomised trial
		Critical care and Emergency Medicine
Tu89	Glenn Eastwood	Conservative oxygen therapy in cardiac surgery: A prospective before and after observational study
Tu90	Matthew Chan	Near-Infrared Spectroscopy In Adult Cardiac Surgery Patients: A Systematic Review And Meta-Analysis
Tu91	David Taylor	Iatrogenic Acute Decompensated Heart Failure
Tu92	David Taylor	Alternative Therapies used by adult Emergency Department patients
Tu93	David Taylor	Outpatient asthma management of Emergency Department patients
Tu94	David Taylor	Accuracy of information sources used to determine the medication history in the ED
Tu95	David Taylor	Intravenous midazolam-droperidol (combination), droperidol (only) or olanzapine (only) for the acutely agitated patient: A multi-centred, randomised, double-blind, triple-dummy, clinical trial

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Tu96	Sok Shin Yap	Taboo or not taboo: Advance Care Planning in the Chinese-Australian community
		Cardiology
Tu97	Lorelle Martin	Does mode of presentation to hospital in ST-segment elevation myocardial infarction (STEMI) impact on total ischaemic time and health outcomes?
Tu98	Kylie Clarkson	Activated clotting time (ACT) guided transradial (TR) band removal post coronary angiography: a pilot study.
Tu99	Ahmed Al-Kaisey	Clinical Characteristics and Predictors of Readmissions in Heart Failure Patients Admitted Under General Medicine
Tu100	Samia Toukhsati	This abstract is not included at the request of the author
Tu101	Francis Ha	The 6 minute walk test improves exercise confidence in chronic heart failure patients
Tu102	Jay Ramchand	The short-term effect of right ventricular mid-septal pacing on right ventricular function
Tu103	Nicholas Jones	This abstract is not included at the request of the author
Tu104	Nicholas Jones	This abstract is not included at the request of the author
Tu105	James Theuerle, et al	Is Percutaneous Coronary Intervention to Complex Lesions Associated with Worse Long-
Tu106	James Theuerle, et al	This abstract is not included at the request of the author
Tu107	Kimberley Chan	Prescribing of mandated medicines in HF-rEF
Tu108A	Matias Yudi	This abstract is not included at the request of the author
Tu108B	Matias Yudi	This abstract is not included at the request of the author
Tu108C	Matias Yudi	This abstract is not included at the request of the author
Tu109A	Matias Yudi	This abstract is not included at the request of the author
Tu109B	Matias Yudi	This abstract is not included at the request of the author
Tu110	Daniel Gayed	Should All Patients Presenting with STEMI Be Screened for Familial Hypercholesterolaemia?
Tu111	Daniel Gayed	Is a Family History of Premature Coronary Artery Disease Associated with Higher Long-term Mortality in Patients with Stable CAD?

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		Nursing
Th01	Polly Dufton	Unscheduled emergency department presentations by cancer patients
Th02	Kate Schimmelbusch	Post operative hypotension MER calls reduce as a result of a multidisciplinary education.
Th03	Andrea Driscoll	Nurse-led titration of angiotensin converting enzyme inhibitors and beta-adrenergic blocking agents for patients with heart failure with reduced ejection fraction: a meta-analysis
Th04	Andrea Driscoll	In-patient heart failure nurse practitioner service significantly increases mandated medications and reduces re-hospitalisation rates.
Th05	Julie Preston	Nurse led medical orientation program improves patient outcomes
Th06	Robyn Purcell	Learner evaluation of a tertiary hospital inter-professional simulation faculty education development program
Th07	Julia de Marchi	An evaluation of a smart phone application for post graduate nurses in Intensive Care Specialty Training
Th08	Robyn Peel	Creating a Culture of Research in Nursing at HRH - Phase One Early Graduate Year (EGY) Nurse Quality Projects
Th09	Ann Rust	Mission impossible? Ceasing routine commencement of oxygen therapy in a recovery unit.
Th10	Joey Ting	Exploring nurse's ability to correctly stage pressure Injuries
Th11	Fran Pearce, Liz Watt, David Edvardsson	Is the patient experiences of caring and person-centredness associated with perceived nursing care quality?
Th12	Tom Kupfer	Employing statistical process control charts as evidence for improving linac isocentre quality control and frequency optimisation
		Surgery
Th13	Matthew Pappas	This abstract is not included at the request of the author
Th14	Marlon Perera	Sensitivity, specificity and predictors of positive 68Ga-PSMA PET in advanced prostate cancer: a systematic review and meta-analysis

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Th15	Chih-Chiang (Jason) Hu	Renal tubular sodium transporter expression and phosphorylation is altered in pre-eclampsia
Th16	Damian Ianno	Physiologic fluid optimisation algorithm improves outcomes in patients undergoing pancreaticoduodenectomy: a prospective multicentre randomized controlled trial
Th17	Jonathan Banting	Goal-Directed Fluid Therapy is Associated with Improved Outcomes in Patients Undergoing Pancreaticoduodenectomy
Th18	Dominique Grant	This abstract is not included at the request of the author
		Respiratory and Sleep Medicine
Th19	Robert O'Donoghue	This abstract is not included at the request of the author
Th20	Yet H Khor	This abstract is not included at the request of the author
Th21	Yet H Khor	This abstract is not included at the request of the author
Th22	Yet H Khor	This abstract is not included at the request of the author
Th23	David Berlowitz	A randomized controlled trial of auto-titrating continuous positive airway pressure treatment for obstructive sleep apnoea after acute quadriplegia (COSAQ).
Th24	Tom Churchward	The Impact of Tele-Monitoring CPAP on Adherence in a Clinical Setting: A Pilot Study.
Th25	Tom Churchward	Combined Full EEG with Polysomnography in a clinical setting: a review.
	Jennifer Cori	Arousal induced hypocapnia does not reduce genioglossus muscle activity on return to sleep in obstructive sleep apnea.
	Jennifer Cori	Upper airway dilator muscle after-discharge occurs following arousal from sleep but is reduced by hypocapnia.
Th26	Pasquale Alvaro	The direction of the relationship between symptoms of insomnia, depression and anxiety in adolescents
Th27	Marnie Graco	Continuous Positive Airway Pressure (CPAP) for management of Obstructive Sleep Apnoea (OSA) following acute, traumatic tetraplegia: adherence rates and factors influencing adherence.
Th28	Jack Ross	Use of the Montgomery Cannula as an interim step in high risk tracheostomy decannulation.
Th29	Julie Tolson	A CPAP intervention program to improve treatment adherence and selfefficacy in patients with Obstructive Sleep Apnoea

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		Psychiatry and Psychology
Th30	Joshua Rosen	Getting informed about consent: Clinicians' perspectives on informed consent in a public child and adolescent mental health service
Th31	Jessie Rucker	This abstract is not included at the request of the author
Th32	Eleanor Pilioussis	PTSD and Dissociation
Th33	Carolina Restrepo	This abstract is not included at the request of the author
Th34	Carolina Restrepo	This abstract is not included at the request of the author
		Infectious Diseases and Pharmacy
Th35	Sharmila Khumra	Drug Induced Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis -The Experience of a Tertiary Referral Centre
Th36	Sharmila Khumra	A comparative analysis between antibiotic allergy labels and non-antibiotic allergy labels in liver transplant recipients
Th37	Leona Taylor	Phenotypic identification of multiple B-lactamases in extensively resistant Enterobacteriaceae
Th38	Anne McGrath	Comparison of medication prescription safety and quality using an electronic medication management system to paper-based prescribing systems nationally.
Th39	Simone Taylor	So what are we waiting for? Outpatient clinic patient perceptions and expectations of outpatient pharmacy services.
Th40	Emily O'Halloran	Review of the prescribing of oxycodone on discharge from a metropolitan hospital.
Th41	Simone Taylor	Successful implementation of an electronic Controlled Drug Register in a major public hospital pharmacy department.
Th42	Simone Taylor	Listening to the voice of the patient to inform outpatient pharmacy dispensary service quality improvements.
Th43	Frances Hurren	The Carbapenem Inactivation Method (CIM) for the detection of OXA enzymes in Gram-Negative Bacteria.

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		Oncology and Haematology
Th44	Li Yen Ng	What is the significance of a positive central venous catheter blood culture without a concordantly positive peripheral blood culture? - a prospective study in uninfected Haematology patients
Th46	Eka Moseshvili	This abstract is not included at the request of the author
Th47	Eka Moseshvili	This abstract is not included at the request of the author
Th48	Ingrid Burvenich	This abstract is not included at the request of the author
Th49	Riley Morrow	This abstract is not included at the request of the author
Th50	Pathum Thilakasiri	This abstract is not included at the request of the author
Th51	Daniel Batey	This abstract is not included at the request of the author
Th52	Jennifer Mooi	This abstract is not included at the request of the author
Th53	Tom Witkowski	TCR beta sequencing to determine clonal T-cell populations in melanoma patients undergoing immunotherapy
Th54	Jessica Duarte	Protein Microarrays for the Immunological Profiling of Melanoma
Th55	Dylan King	Implications of Fc-engineering to a humanised anti-Ley antibody on receptor binding and cellular effector function
Th56	Ian Luk	The EHF transcription factor is downregulated in poorly differentiated colorectal cancers and inhibits cell migration
Th57	Alex Owen	Targeting Jak Kinases to treat Colon Cancer
Th58	Austen Lavis	Combination therapy to overcome acquired resistance to FGFR3 targeted therapeutics in metastatic urothelial cancer
Th59	Ortis Estacio	This abstract is not included at the request of the author
Th60	Melissa Garwood	Safety and efficacy of high-dose methotrexate as central nervous system prophylaxis in diffuse large B-cell lymphoma
Th61	Thomas Mikeska	Accredited MGMT Methylation Analysis for use in Molecular Diagnostics
Th62	Katherine Woods	Inflammation mediates profound changes to the immunopeptidome of melanoma.
Th63	Camilla Reehorst	The in vivo effect of Ets homologous factor (EHF) on intestinal homeostasis
Th64	Zoe Loh	Routine Blood Investigations Have Limited Utility in the Follow-up of Aggressive Lymphomas

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Th65	Anh Le	Investigating Epithelial-Mesenchymal Plasticity in Circulating Tumour Cells from Breast Cancer Xenograft Models
Th66	Anh Le	This abstract is not included at the request of the author
Th67	Arielle van Mourik	Cerebral toxoplasmosis in a patient with prolonged CD4 lymphopenia post autograft
Th68	Rachel Edmonds	Treatment of Solitary Adrenal Metastases using Stereotactic Ablative Body Radiotherapy: a Case Study
Th69	Bibhusal Thapa	Correlation of PD-L1 expression with immune cell infiltrates, genome-wide copy number aberrations and survival in mesothelioma.
Th70	Peter Wookey	The switch between the pre-apoptotic cell stress response and apoptosis seen through new rose-tinted glasses
Th71	Peter Wookey	Recalcitrant tumours require powerful medicine: a comparison of the potency of immunotoxins and an antibody:drug conjugate to kill glioma stem cells.
Th72	Janson Tse	This abstract is not included at the request of the author
		Obstetrics and Gynaecology
Th73	Elizabeth Lockie	This abstract is not included at the request of the author
Th74	Stella Liong	Phytophenols improves inflammation and insulin resistance associated with gestational diabetes mellitus.
Th75	Hannah Bergin	Prevention of mother-to-child transmission of hepatitis B virus: Successful implementation of new management guidelines for hepatitis B virus positive women in a hospital with a specialized clinical service
Th76	Roxanne Haste	New medical therapeutics for ectopic pregnancy
Th77	Amy Gratton	Steroid sulfatase mRNA is upregulated in the placenta and maternal whole blood of preterm preeclamptic women
Th78	Natalie Hannan	New generation antiplatelet therapies to prevent preeclampsia
Th79	Alan Gemmill	Randomised Trial of Antenatal Depression Treatment - Impact on Early Child Developmental Outcomes
Th80	Louis Chhor	This abstract is not included at the request of the author
Th81	Kate Desneves	Energy requirements and body composition in acute spinal cord injury

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		Neurosciences
Th82	Georgie Hollingsworth	Novel SCN1A phenotype: Early Profound Developmental Epileptic Encephalopathy with Movement Disorder with hotspot mutation
Th83	Natalia Egorova	Cognitive control network connectivity in mild post-stroke depression
Th84	Dr. Kathleen Bagot	Strokes, TIAs, mimics: a comparison of Emergency Department and discharge diagnosis coding
Th85	Dr. Kathleen Bagot	Sustaining the use of a new stroke telemedicine service: barriers and facilitators identified after implementation
Th86	Chris Shirbin	This abstract is not included at the request of the author
		Medical Imaging
Th87	Lucy Milligan	Diagnostic Adequacy of Non-targeted liver biopsies in Radiology-a retrospective audit
Th88	Sarah Jesudason	Chromobacterium Violaceum Bacteraemia - A Case Report.
Th89	Jessica Welch	Does Metformin contribute to poor quality FDG-PET brain images?
Th90	Wesley Ng	Implementation of modulated low dose CT for PET/CT scans to reduce radiation dose to patient
Th91	Mangor Pedersen	Adjusted Local Connectivity (ALC) for subject-level fMRI analysis in focal epilepsy
Th92	Vincent Doré	Regional association between cortical volumes and imaging tau pathology using 18F-AV1451 and 18F-THK5351
Th93	Vincent Doré	Effects of MAPT over brain grey matter atrophy in the AIBL cohort.
Th94A	Andrew Scott	Engineering Anti-Lewis-Y Hu3S193 Antibodies with Improved Therapeutic Ratio for Radioimmunotherapy of Epithelial Cancers
Th94B	Andrew Scott	Synthesis of fluorine-18 agents for PET imaging of hypoxic tissue in tumours
Th95A	Andrew Scott	Investigation of novel Oncrasin-1 analogues for use in imaging kRAS mutant cancers
Th95B	Andrew Scott	Development of a Molecular Imaging Probe for Imaging Tissue Transglutaminase 2
Th96	Sylvia Gong	Kinetic Analysis of [C11]Choline PET Uptakes in the Prostates of Patients Undergoing Neoadjuvant Docetaxel Chemotherapy

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Th97	Sylvia Gong	Information-based Implementation of Radiation Management and Assessment of Radiation Protection in Molecular Imaging and Therapy
Th98	John Sachinidis	High yield radiolabeling of DOTA-TATE and PSMA with 68Ga using the new MultiSyn radiosynthesizer
Th99	Uwe Ackermann	Uptake and metabolism of 16β-[18F]fluoro-5α-dihydrotestosterone in castration resistant prostate cancer
Th100A	Gordon Chan	Minimising radiation exposure of PET radiopharmacists following implementation of Tema µDDS-A automatic dose dispensing system and optimising work practices
Th100B	Gordon Chan	Observed interference effects of reagent water in critical HPLC analysis
Th100C	Gordon Chan	A versatile GMP compliant semi-automated system for filling open or closed vials and syringes
Th101A	Gordon Chan	Quality Control Method Validation for 68Ga-DOTA-TATE
Th101B	Gordon Chan	Quality control validation of 16β-[18F]fluoro-5α-dihydrotestosterone produced with the FlexLab radiosynthesiser
Th102C	Gordon Chan	A practical evaluation of effectiveness of commonly used syringe shields for PET dose dispensing
		General
Th103	Piyapong Khumrin	The Implementation of Clinical Decision Support Systems to Support Medical Students Diagnostic Reasoning Skills
Th104	Daniel Saitta	"That's a bit surprising" students' interactions with and reactions to personalized feedback reports for multiple-choice tests.
Th105	Paul Yates	Aged Care Nurse Practitioner-Led Outreach Model Reduces Hospital Representation For Frail Community-Dwelling Elderly
Th106	Henry Zeimer	This abstract is not included at the request of the author
Th107	Giulia Valente	Genomic sequencing for Austin Health patients through the Melbourne Genomics Health Alliance
Th108	Pieter Neef	This abstract is not included at the request of the author
Th109	King Cheung	This abstract is not included at the request of the author
Th110	Stephen Casey	This abstract is not included at the request of the author
Th111	Justin Ng	This abstract is not included at the request of the author

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Endocrinology and Metabolism

Th112	Patricia Russell	Androgens act via the Androgen Receptor (AR) in progenitor cells residing within the bone marrow to reduce fat mass in male mice.
Th113	Sandra Lin	Contributing factors to increased mortality in men undergoing long-term androgen deprivation therapy.
Th114	Alistair Tinson	Lack of improvement in fat mass following cessation of androgen deprivation therapy: A 4 year case-control study
Th115	Ali Ghasem-Zadeh	Sexual and racial dimorphism in bone microarchitecture requires adjustment of the region of interest for skeleton dimensions
Th116	X F Wang	This abstract is not included at the request of the author
Th117	X F Wang	This abstract is not included at the request of the author
Th118	Karen Borschmann	The influence of physical activity on volumetric bone density at the tibia two years after stroke
Th119	Jeremy Lew	This abstract is not included at the request of the author
Th120	Adrian Michalopoulos	This abstract is not included at the request of the author
Th121	Jas-mine Seah	Functional MRI changes in Type 1 Diabetes with and without Renal Hyperfiltration
Th122	Chandana Herath	ACE2-AAV gene therapy improves plasma glucose and pancreatic islet function in diabetic mice with NAFLD
Th123	Michele Bardin	Changes in insulin requirement and glycaemic control during the third trimester in women with type 1 diabetes on insulin pump therapy.
Th124	Anthony Verberne	This abstract is not included at the request of the author
Th125	Sarah Price	Pilot Study: The impact of substantial pre-conception weight loss in obese women and on glucose control at 26-28 weeks gestation
Th126	Meilun Ly	Impact of substantial weight loss on thyroid function in obese women planning pregnancy
Th127	Salvatore Mangiafico	This abstract is not included at the request of the author
Th128	Dorothy Liu	The effect of habitual dietary salt intake on endothelial microparticle levels in Type Two Diabetes Mellitus

Evaluation of internal construct validity and unidimensionality of the Brachial Assessment Tool (BrAT), a patient-reported outcome measure for Brachial Plexus Injury

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Background
People with Brachial Plexus Injury (BPI) form a very heterogeneous group, with a wide spectrum of ability. While a number of patient-reported outcome measures have been used to assess outcome following adult traumatic BPI, none has been developed or psychometrically evaluated for this population.
Aim
To evaluate the internal construct validity and dimensionality of a new patient-reported outcome measure for people with traumatic BPI based on the ICF definition of activity.
Methods
Adults with confirmed traumatic BPI completed a 51 item 5-response questionnaire. Responses were analyzed in 4 phases: missing responses, item correlations, Exploratory Factor Analysis and Rasch analysis to evaluate the properties of fit to the Rasch model, threshold response, local dependency, dimensionality, Differential Item Functioning and targeting to the sample.
Results
106 adults (age range 18-82) were recruited from five outpatient clinics across Australia. Six items of the 51items were deleted for missing responses and items rescored to 4 responses. Ten items were deleted for high inter-item correlations >0.81. The remaining 35 items, while demonstrating fit to the Rasch model, showed evidence of local dependency and multidimensionality. Items were divided into three subscales. Following removal of four items all three subscales demonstrated fit to the model with no local dependency, minimal disordered thresholds, no unidimensionality with no DIF for age, time post injury or self-selected dominance. The subscales were combined into 3-testlets and achieved overall fit to the model, no misfit and unidimensionality allowing calculation of a summary score.
Conclusion
This preliminary analysis of the BrAT supports the internal construct validity of the BrAT a unidimensional targeted 4-response patient-reported outcome measure designed to solely assess activity following traumatic BPI regardless of level of injury, age at recruitment, premorbid limb dominance and time post injury.

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Title:

Stroke survivors use more energy while walking early after stroke compared to age and gender matched controls

Authors/affiliations

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Background and rationale

Several stroke guidelines recommend that rehabilitation should start early after stroke and that cardiorespiratory fitness (CRF) training should be part of stroke rehabilitation. The evidence for CRF training is mainly based on studies including chronic stroke patients and it is unclear what the optimum dose of training is. It has been shown that the energy cost (EC) of walking is higher in chronic stroke patients compared to a healthy population. There are few studies that measured the EC of walking early post-stroke. Our aim was to determine the difference in EC of walking between stroke survivors < 2 weeks post-stroke and age and gender matched healthy controls.

Methods

We recruited 13 stroke survivors <2 weeks post-stroke at an acute stroke ward and 10 age and gender matched healthy controls. Participants performed 2 bouts of 6-minute overground walking at a comfortable walking speed, including a 30-minute rest-period. EC was assessed by measuring oxygen uptake in ml/kg/m over 6-minutes and steady-state (final 3 minutes of each bout) walking, using a mobile metabolic cart and breath-by-breath analysis. Differences between groups were analysed using the t-test.

Results

We included 13 stroke survivors and 10 age and gender matched controls in our analysis. Average age of stroke survivors was 75 ±13 and 73±13 years for healthy controls. The average number of days post-stroke was 4±3. Stroke survivors showed higher EC of walking during 6 minutes (0.10 95% CI 0.18 to 0.02 ml/kg/m) and steady state (0.10 95% CI 0.18 to 0.02 ml/kg/m) compared to healthy controls.

Conclusion

We showed that stroke survivors require more energy while walking compared to healthy controls. Our findings should be taken into account when setting exercise intensity goals early post-stroke and it may help to inform the development of more specific exercise prescription guidelines for stroke survivors.

Title: Stroke survivors use more energy while walking early after stroke compared to age and gender matched controls

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Background and rationale
The energy cost (EC) of walking in chronic stroke is higher compared to healthy controls; it is unclear if this is the case in acute stroke. A metabolic cart is a widely excepted reliable method to determine EC by measuring volume of oxygen uptake, but is a highly specialised, expensive method. The SenseWear Armband (SWA) is a wireless, tri-axial accelerometer worn on the upper arm that can be used to monitor EC. But there is a lack of studies that validate the accuracy of the SWA to estimate EC post-stroke.

Methods
We recruited 16 participants from an acute stroke ward. Two SWAs were used to measure EC, one worn on each (affected and non-affected) arm. The SWA records movement heat flux, galvanic skin response, skin and near body temperature. The Oxycon Mobile (OM) metabolic measurement system was used to measure oxygen uptake continuously. The participants performed 2 six-minute walk tests with a 30 minute rest-period in between. For the purpose of this abstract we will report on the level of agreement between the tools in measuring energy costs during the last three minutes of a six minute walk test, i.e. steady-state walking.

Results
We were able to include data of 13 participants in the analyses (9 males, mean age 75±13, mean days post-stroke 4±3). The level of agreement was poor (< 0.70) (Kottner et al. 2011) between OM and SWA on the affected arm (ICC=0.56) and non-affected arm (ICC=0.05). However, when inspecting the correlations graphically, we found that SWA on the non-affected arm systematically underestimated EC, which was not the case for the affected arm.

Conclusion
The SWA armband seems to systematically underestimate the EC of walking early after stroke. The SWA should not be used on the affected arm of acute stroke participants to measure EC.

A/Prof Sue Berney[1,2], Miss Joleen Rose[1], Prof Linda Denehy[2], Dr Catherine Granger[2,3], A/Prof George Ntoumenopolous[4], Ms Elise Crothers[5], Dr Elizabeth Skinner[2,6,7]

Commencing early rehabilitation in critical care. What influences clinical decision-making?

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Aim
Early out of bed rehabilitation for patients who are critically ill is increasingly being advocated as standard practice despite national and international data reporting it is not common. It is unclear what factors influence clinical decision making and how they relate to each other in determining if rehabilitation is provided. The aims of this study are to describe the clinical decision making of ICU practitioners around the provision of out of bed rehabilitation; determine the influential factors; report safety and describe the relationship between clinical decision making and clinical practice.

Method
ICU practitioners (Intensive Care Specialist, Nurse and Physiotherapist) at four Australian metropolitan hospitals who were responsible for the care of patients were asked to nominate a) if a patient was ready to commence out of bed rehabilitation and b) to rank any factors that influenced their decision.

Results
There were a total of 1416 decisions made by the intensive care practitioners; this represented 472 individual patient decisions. Classification and regression tree (CART) analysis revealed only the presence of an artificial airway followed by sedation state were the only discriminative variables in the decision to provide out of bed rehabilitation. Sedation was most frequently rated variable by clinicians. Although the CART predicted rehabilitation would occur on 149 occasions it actually occurred on 122 occasions and only 57 occasions (38.3%) when the team predicted. Clinical deterioration requiring an escalation of care occurred on 3 occasions. Only 47% of patients presented with intensive care acquired weakness (ICUAW) when all clinicians agreed rehabilitation should occur.

Conclusion
The results indicate that the presence of an airway was the most important reason patients didn't receive rehabilitation in ICU. In the critically ill, clinicians asses risk rather than potential benefit in the provision of rehabilitation and despite consensus, clinical practice did not represent clinical decision making.

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Quantitative measurement of cardiovascular fitness longitudinally after stroke

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Aim
Exercise after stroke can mediate cardiovascular risk and reduce disability,[1] but the cardiovascular fitness of stroke survivors early after stroke, and how it changes over time, is unknown. This pilot project aimed to establish the cardiovascular fitness levels of stroke survivors longitudinally after stroke using a supervised, submaximal, incremental exercise test.

Methods
Individuals with a diagnosis of ischemic stroke or TIA within the previous 14 days were recruited from the acute stroke ward of the Austin Hospital. Participants were excluded if they demonstrated evidence of heart problems, or major medical or neurological comorbidities. Peak volume of oxygen consumption (VO_{2peak} in ml/kg/min), a measure of cardiovascular fitness, was assessed within 14 days, and at 1 and 3 months after stroke via a submaximal, incremental exercise test.

Results
Sixteen participants have been recruited (5 female; mean age 69±13 years; mean days post-stroke 7±3.6; median modified Rankin score 0), and all but one was able to complete the initial exercise test. The participants demonstrate low cardiovascular fitness early after stroke (14.6±3.2 ml/kg/min), and only marginal improvements were found in the 7 participants that have completed testing at 3 months post-stroke (14.1±4.2 v 14.7±4.7 ml/kg/min; 4.4% increase). Given a loss of independence is likely if VO_{2max} levels fall below 18 ml/kg/min in men and 15 ml/kg/min in women,[2] our results suggest that stroke survivors with little to no disability are borderline dependent as a result of their poor fitness.

Conclusion
This is the first study to quantify the cardiovascular fitness levels of stroke survivors early post-stroke and monitor the change in fitness over time. We have demonstrated that stroke survivors can feasibly complete a submaximal, incremental exercise test, and that stroke survivors have low cardiovascular fitness. Our findings can be used to inform the development of early post-stroke exercise training guidelines.

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The Activity Card Sort – Australia: Validation and reliability in an Australian stroke cohort

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Background and rationale

Participation is a broad concept and difficulties operationalizing it have been reported(Dijkers, 2010). In a review of participation measures used in clinical stroke studies, the Activity Card Sort (ACS) was identified as the tool that covered the most domains of the ICF Activities and Participation and met the most psychometric properties(Tse, Douglas, Lentin, & Carey, 2013). The aim of this study was to evaluate the validity and reliability of the ACS-Aus in an Australian stroke cohort.

Methods

Stroke survivors recruited through the START-PrePARE program of research (n=100) were assessed using the Activity Card Sort – Australia, the Stoke Impact Scale and the modified Rankin Scale at 3 and 12 months post-stroke.

Results

The internal consistency for the ACS-Aus total retained activity participation score was excellent (α = 0.91 at 3 months, α = 0.89 at 12 months) and moderate to excellent for the sub-categories (α ranged from 0.67 to 0.85 at 3 months and 0.72 to 0.84 at 12 months). The ACS-Aus demonstrated moderate to good concurrent validity with correlations with the SIS-Participation score (rho = 0.61 $p < 0.001$ at 3 months, rho = 0.47 $p < 0.001$ at 12 months), moderate to good convergent validity with correlations with the Modified Rankin Score (rho = 0.52 $p < 0.001$ at 3 months, rho = 0.46 $p < 0.001$ at 12 months).

Conclusion

The ACS-Aus is a valid and reliable measure of activity participation after stroke. Future studies are needed to examine further the psychometric properties for people with different diagnoses.

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Longitudinal changes in activity participation after mild stroke.

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Background and rationale

Since the endorsement of the World Health Organization(WHO) International Classification of Functioning, Disability and Health (ICF) in 2001, participation has become a term used by health professionals and is considered a critical outcome of successful rehabilitation. Yet few longitudinal studies of participation exist. Therefore, the research question for this study was "does activity participation improve over time in the first year of recovery after stroke?"

Methods

Stroke survivors recruited through the STroke imAging pRevention and Treatment (START) - Extending the time for Thrombolysis in Emergency Neurological Deficits and START_Prediction and Prevention to Achieve Optimal Recovery Endpoints were assessed using the Activity Card Sort – Australia (ACS-Aus) at 3 and 12 months post-stroke. The scores used in this study were pre-stroke and current activity participation at 3 month and 12 month, with sub-categories of high- and low-demand leisure, social/educational and household activities.

Results

The mean age of the study participants 69 years (range 27 to 90 years) and the majority had National Institutes of Health Stroke Scale scores below five consistent with mild neurological stroke severity. Significant improvements in current activity participation from 3 months to 12 months was observed (t - 4.5 95% CI -4.2 to -1.7, $p < 0.01$). All sub-categories of the ACS improved over time with greatest improvement in low-demand leisure activities. The average number of activities the participants engaged in pre-stroke, at 3 months and 12 months post stroke showed a decrease at 3 months that improved by 12 months but did not return to pre-stroke numbers.

Conclusion

This study is the first longitudinal study using the ACS, a comprehensive and psychometrically sound measure of participation, in stroke survivors with mild stroke severity in the first year of recovery after stroke.

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Tele-rehabilitation: Extending the "reach" of hand therapy in tetraplegia

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Aim

Reconstructive hand surgery for tetraplegia is very specialized and only offered at a few centres worldwide including Austin Health. Spinal Cord Injury (SCI) patients must often travel interstate or long distances to and for assessment, surgery and treatment. Centre based therapy, whilst the accepted gold standard, is not always practical for this client group meaning specialist follow up treatment is suboptimal or impossible.¶

The aim of this study was to assess the reliability and efficacy of tele-rehabilitation for the delivery of specialist therapy sessions following reconstructive hand surgery in tetraplegia, including tendon and nerve transfer procedures.

Methods

Twenty eight participants including people with SCI, family members, carers and therapists were recruited across 3 states of Australia. A minimum of three post-op treatment sessions via telehealth was provided, followed by a qualitative survey. Therapy sessions conducted on line and in the clinic were observed to compare treatment techniques utilized in each setting.

Results

Some unsurprising technical difficulties arose with internet connections related to phone and tablet use but frequency and impact of this was less than anticipated. System usability ratings were generally excellent. Overall differences in treatment themes between tele-rehabilitation and centre based rehabilitation were minimal with the same critical therapy issues routinely addressed. More impairment based assessment was utilized in the clinic setting. Participants found tele-rehabilitation simple to use and it was widely accepted.

Conclusion

Tele-rehabilitation is uniquely placed to support SCI out-reach services given large geographic catchment areas and ongoing and extensive co-morbidities. This study demonstrates one example of the value of Tele-rehabilitation for this patient group and to improve the outcomes and quality of care after reconstructive hand surgery. Tele-rehabilitation is now standard practice for remote patients at our clinic.

THE ADDITION OF HIGH AMYLASE RESISTANT STARCH TO REDUCE STOOL OUTPUT IN PEOPLE WITH SHORT BOWEL SYNDROME.

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Aims: This study aimed to determine if the addition of 50g/day of High Amylase Resistant Starch (HARS) can reduce diarrhoea in people with Short Bowel Syndrome (SBS). SBS is defined as having insufficient bowel to absorb the necessary nutrition and hydration to maintain weight / sustain growth. Malabsorptive diarrhoea and the resultant dehydration can be difficult to manage despite dietary manipulations. Evidence has shown that supplementing the diet with HARS can reduce diarrhoea from a number of causes including gastroenteritis and cholera. It is hypothesised that the addition of HARS will decrease total stool output via increased water reabsorption in the colon.

Methods: Participants with SBS with colon in continuity who were eating and drinking were recruited from the intestinal rehabilitation clinic at Austin Health. The study was a 2 week crossover trial. Each participant completed the control (usual diet) followed by the intervention (addition of 50g HARS to usual diet) for 1 week each. Total daily stool weight and number of bowel actions per day were compared between groups using paired t-tests.

Results: Eight adults (58% male, mean age 55.7 years) were recruited. 5 participants completed the trial. Length of remaining small bowel ranged from 20 – 120cm. Total daily stool weight was reduced 1049±519g/d vs 804±585g/d (p=0.023) when consuming HARS. Number of bowel actions per day was not significantly (p=0.6) different.

Conclusion: This small pilot study gives validity to the hypothesis that the addition of 50g HARS into the diet of people with SBS with colon in continuity can help reduce total daily stool output. HARS is a soluble tasteless powder which can be easily and cheaply incorporated into the diet and may have the potential to decrease reliance on intravenous nutrition or hydration.

This study was funded by a grant received from the Austin Medical Research Foundation.

Emma Burns, Lauren Kovesy, Phuong Phan

Austin Aphasia Integration Program for People with Chronic Aphasia Following Stroke

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Background and Aim

One-third of all survivors of stroke live the remainder of their lives with aphasia. Without appropriate tailored intervention the high rates of psychosocial distress, reduced social participation and quality of life in aphasia lead to reliance on outpatient services, and greatly increase carer burden. This study investigated the efficacy of the Austin Aphasia Integration Program (AAIP) to improve, mood, functional communication, and community integration for people with chronic aphasia post stroke and perceived burden of relevant carers.

Methods

12 participants with chronic aphasia were recruited to a speech pathologist-led multidisciplinary group program. The program commenced with an eight week intensive group comprised of group activities, conversation, technology, music, art and leisure/community integration followed by a four week transition and integration program. Quantitative measures taken pre- and post-program included Goal Attainment Scale (GAS), Community Integration Measure (CIM), Assessment of Living with Aphasia (ALA) and Bakas Caregiver Outcomes Scale (BCOS).

Results

Upon completion of the program all 12 participants had commenced establishing their own social aphasia support group, were linked in with community services, and had been discharged from the Health Independence Program. Positive improvement was seen on the scaling for 24 of the 28 goals measured with the GAS: 18/28 (64%) were achieved, 6/28 (21%) were partially achieved, and 4/28 (14%) were not achieved. There were positive trends for all other outcomes measured (pre-average score, post-average score): ALA (2.19, 2.43), CIM (11.95, 15.75) and BCOS (37, 65.33). These results suggest an increase in mood, functional communication, and community integration for people with chronic aphasia, and a decrease in burden for their carers.

Conclusion

A pilot 12-week AAIP improved multiple aspects of function and community integration for people with chronic aphasia following stroke and their carers. Delivery of a multidisciplinary group program provided a forum for peer support and facilitated transition and integration into the community.

A topical vasoconstrictor and the upper airway of patients with quadriplegia and obstructive sleep apnoea: An MRI study

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Introduction:
Obstructive sleep apnoea (OSA) is extremely prevalent among people with quadriplegia, but the reasons for this increased prevalence rate are not well established. It has been suggested that OSA in quadriplegia may in part be attributable to unopposed upper airway parasympathetic activity causing mucosal vascular engorgement. This study investigated the effect of a topical vasoconstrictor, phenylephrine, on the upper airway of people with OSA and quadriplegia using 3-Tesla (3T) magnetic resonance (MR) imaging.

Method: 33 participants from Melbourne were recruited: 6 people with quadriplegia and OSA (SCI-OSA), 15 able-bodied participants with OSA (AB-OSA), and 12 able-bodied participants without OSA (AB-CTRL). Participants underwent a 3T-MR scan of their upper airway before being administered an atomised dose of phenylephrine to their nose and throat, and then having a repeat MR scan five minutes later. Volumetric analysis of the upper airway was performed on both pre- and post-phenylephrine scans.

Results: One-way (univariate) ANOVA was used to compare the change in upper airway volumes from pre- to post-phenylephrine across groups and indicated a marginally significant increase in velopharyngeal volume across groups post-phenylephrine (Mean change ± SE; SCI-OSA: 0.3±0.3 vs. AB-OSA: 0.9±0.2vs. AB-CTRL: 0.1±0.2cm^3; ANOVA p = .050). However, post-hoc LSD tests indicated the

difference was only significantly observed for the AB-OSA group (ANOVA, post-hoc LSD $p < .001$). No other upper airway structures showed significant changes before and after phenylephrine administration.

Conclusion:
Vasoconstriction of the upper airway using phenylephrine produces enlargement of the velopharynx across groups, however it was only significantly increased for the AB-OSA group. Due to the reduced acceptance of conventional treatment options it is extremely important that we continue to investigate the causes of OSA in quadriplegia and to develop novel treatments that may be able to improve sleep quality and ultimately, quality of life, for people living with quadriplegia.

Compromised bone structure and density in end stage renal disease

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Abstract

Background:
End-Stage renal failure (ESRF) is associated with reduced cortical bone density, increased fracture risk and higher mortality rates following hip fractures. We aimed to quantify bone structure and density at the distal radius and tibia, in patients receiving dialysis and those with a renal transplant. We hypothesise that renal transplant recipients will have less reduced cortical density than those receiving dialysis, but both will demonstrate deficits, relative to healthy age and sex matched controls.

Methods:
We performed high resolution peripheral quantitative computed tomography (HRpQCT, Scanco Medical X-treme CT 1, Switzerland) scans at the distal radius and tibia on 38 males (mean age 61 ± 11 years) and 31 females (mean age 59 ± 14 years) with ESRF being treated at the Austin Hospital, and 138 (76 males and 62 females) healthy age and sex matched controls recruited from the community. In patients with ESRF, 50 had a renal graft and 19 were receiving dialysis.

Results:
Relative to age and sex matched controls, cortical density at the radius was 9% lower ($p=0.039$) in female dialysis patients and 13% lower ($p<0.001$) in female transplant patients. Similarly, cortical density at the radius was 15% lower ($p=0.001$) in male dialysis patients and 10% lower ($p<0.001$) in male transplant patients. There were no significant differences in radial cross-sectional area or bone size in dialysis and transplant patients compared to controls. Cortical thickness was 27-36% lower, total bone mineral density 18-27% lower and cortical area 27-37% lower in dialysis and transplant patients compared to controls (all $p<0.05$). Similar deficits compared to controls were observed at the tibia. No significant differences were observed in cortical area, density and thickness between dialysis and renal transplant patients.

Discussion:
Reduced cortical density, thickness and area, contribute to increased risk of non-vertebral fractures in CKD-MBD subjects. The magnitude of the deficits in cortical bone is similar in dialysis and post- transplant patients, therefore fracture risk prediction and prevention is equally important in both groups.

Keywords:
CKD (chronic kidney disease) / CKD-MBD (chronic kidney disease-mineral bone disorder) / ESRF (end stage renal failure) / BMD (bone mineral density) / DXA (dual energy x-ray absorptiometry) / HRpQCT (high resolution peripheral quantitative computed tomography) / eGFR (estimated glomerular filtration rate)

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Adverse Drug Reaction reporting – one tertiary institution's systematic approach, getting below the tip of the iceberg

¶

1. Adverse Drug Reaction Committee, Austin Health

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Background

Under-reporting of adverse drug reactions (ADRs) via voluntary systems is a universal challenge of pharmacovigilance (1). We describe the ADR reporting program at our 980 bed health service and how practice has evolved in recent years.

Method

The health service has a long-standing local ADR reporting process. Since 2012, several innovations have been introduced. Clinical staff can flag suspected ADRs for follow-up at any stage during the patient journey using a simplified intranet-based form. Information technology systems within our hospital, including electronic medical records, greatly facilitate case follow-up. Primary functions of the ADR process are undertaken by Medicines Information Pharmacists. In addition, a multidisciplinary committee meets fortnightly, during which specialist pharmacists and medical staff (Clinical Pharmacology and Infectious Diseases) provide input. Each ADR case is reviewed; follow-up activities can include reporting to the TGA, an alert in the electronic medical record, sending the patient a wallet-sized alert card, communication to the patient's general practitioner (GP) and referral for formal allergy testing.

Results

The ADR committee database documents cases dating back to 1994. The introduction of electronic reporting in 2013 has seen a sustained increase in the number of reports received. In 2015, 299 ADR reports were formally documented within our institution; 241 (81%) of these were reported to the TGA (by Pharmacy, Radiology, Clinical Trials, or the manufacturer). Of the 58 cases not reported to the TGA, 46 described adverse events deemed not due to a medicine. The remaining cases were lost to follow-up or did not impact on the future care of the patient.

Conclusion

Our institution takes a proactive approach to ADR reporting. The process includes patient and GP notification, regulator reporting and documentation within the electronic medical record. Future directions could include benchmarking, collection of indigenous status data, a proactive focus on high-risk groups and institution-level pharmacovigilance activities.

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Can hospital pharmacists improve the accuracy of medication information in medical discharge summaries?

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Background: Inaccurate or incomplete medication information in medical discharge summaries (DSs) is well documented. Strategies to improve the quality of medication information in DSs have had mixed success. Evidence for pharmacist involvement in preparing DSs is scarce. The use of electronic medication management systems linked to an electronic DS creates opportunities for pharmacists to contribute.

Aim: To evaluate the impact of a quality improvement strategy encompassing an expanded pharmacist role, on the accuracy of medication information in electronic DSs.

Method: A quality improvement strategy was developed following a baseline audit of medication information in DSs and stakeholder consultation. It included:

1. Doctor-pharmacist partnerships in documenting and verifying medication information in DSs;
2. DS template modifications to facilitate documentation of medication changes and rationale for changes.

The strategy was evaluated using retrospective audits of DSs from randomly selected patients discharged between April-June 2014 (pre-intervention) and April-June 2015 (post-intervention). Medication information in DSs was compared with pharmacist-reviewed and reconciled discharge prescriptions, which were considered the most accurate discharge medication lists. Medication changes (new, ceased, and dose-adjusted medications) were identified by comparing patients' pre-admission medication histories with their discharge prescriptions. Medication changes were classified as clinically significant or insignificant based on the likelihood of adverse events if the change was not communicated in the DS.

Results: Ninety-three (pre) and 96 (post) DSs were audited. The proportion of DSs containing a correct discharge medication list increased from 33 to 63% ($p<0.0001$). Clinically significant medication changes stated in DSs increased from 50 to 81% ($p<0.0001$). Documentation of rationale for medication changes increased from 46 to 64% ($p<0.0001$).

Conclusion: The quality improvement strategy led to improved accuracy of medication information in DSs. The findings from this study support pharmacist involvement in the documentation of medication information in DSs.

Hema Vaithianathan, Nikki Shelton, Maryann Marr, Carminia Lapuz, Lim Adeline

Radiation Dose to the Vaginal Vault during Brachytherapy – Early experience and an Audit

Olivia Newton John Cancer and Wellness Centre, Heidelberg, Vic., Australia

Aim

Thickness and anatomy of the vaginal cuff can differ in individuals resulting in underdosage of the high-risk area with library plan. Hence, this study was undertaken to assess dose to clinical target volume (CTV) and to organs at risk (OAR) with library plans.

Methods

The dosimetric parameters of 10 intermediate/high risk endometrial carcinoma patients treated using CT/MRI multichannel vaginal cylinder with adjuvant vault brachytherapy in 2015 were analyzed. CT scan prior to their first fraction was done to delineate OAR and CTV. Standard library plans generated with applicator model option in Oncentra Brachytherapy planning software (version 4.5.1, M/s Elekta Ltd) were used for clinical treatments. Variations between the standard 5mm margin around the applicator and the actual CTV for each patient were assessed. D2cc, the minimum dose to the most irradiated volume of 2cc of the OAR (rectum, bladder, bowel, sigmoid) was obtained for all OARs. Target coverage was measured using D95, the minimum dose delivered to 95% of the target volume. Dose was to the surface of the applicator calculated using AAPM TG-43 formalism.

Results

RO-CTV and 5mmexp volumes varied from 8.6-29.3cc and 21.9-28.5cc respectively. D95 for 5mmexp ranged from 60-65.5% while for RO-CTV, it was 31-70%. The median dose to 5mmexp & RO-CTV was 75% of prescription dose (except for one patient RO-CTV received median dose of 65% only due to “dog-ear” configuration due to post-operative remnants of the vaginal fornices). D2cc (as percentage of prescription dose) ranged from 33-60% for bladder, 42-66% for rectum, 16-51% for sigmoid and 12-69% for bowel respectively.

Conclusion

RO-CTV and 5mmexp volumes and D95 are comparable, indicating the standard 5mm expansion is acceptable for routine treatment eliminating the need for CTV contouring. Caution must be exercised for choosing the adequate depth for dose prescription to minimise the chances of local recurrences.

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Conclusion

RO-CTV and 5mmexp volumes and D95 are comparable, indicating the standard 5mm expansion is acceptable for routine treatment eliminating the need for CTV contouring. Caution must be exercised for choosing the adequate depth for dose prescription to minimise the chances of local recurrences.

Exploring the Signal transducer and activator of transcription-3 (STAT3) as a therapeutic target

Mariah Grace Cabais Alorro[1,2], Matthias Ernst[1,2] and Frederic Masson[1,2]

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Background: The aberrant activation of STAT3, a transcription factor that regulates the expression of genes involved in cell proliferation, cell survival, angiogenesis and invasion, has been identified as a driver of tumour-promoting inflammation and immunity in a variety of cancers. Consequently, STAT3 is a promising target for cancer therapy.

Aim: To genetically study the effect of specific STAT3 inhibition, we exploited a novel mouse strain, in which a short hairpin (sh) RNA directed against Stat3, alongside the GFP reporter gene, can be reversibly induced by administration of Doxycycline. As a proof of principle, the resulting shStat3 mice were crossed with our clinically-validated mouse model of gastric cancer, the $gp130^{F/F}$ mice, which develop gastric tumours in response to excessive STAT3 activation [Ernst et al., J Clin Invest 2008].

Methods: $Gp130^{F/F}$ **;***CAG-rtTA3;shSTAT3* compound mice were treated with doxycycline and various organs including stomach (normal antrum and antrum tumour), liver, colon and spleen were collected. Flow cytometric analysis was used to map shSTAT3 expression, based on GFP reporter expression. In parallel, tissue samples were subjected to quantitative RT-PCR (qRT-PCR) and Western-blot to monitor the expression of STAT3 at the RNA and protein level, respectively. Finally we used immunochemistry (IHC) and flow cytometric analysis to determine the consequence of STAT3 reduction within the gastric tumour microenvironment.

Results: Flow cytometric analysis indicated broad expression as well as reversibility of the shSTAT3. STAT3 silencing was confirmed both at the protein and RNA level, while re-establishment of normal STAT3 expression was only partially effective one week upon doxycycline withdrawal. Importantly, STAT3 reduction resulted in a significant decrease in tumour burden paralleled by a down-regulation of STAT3 target genes such as Socs3, Vegfa or Gadd45g. Interestingly, gene expression analysis of the tumour tissue also revealed an increase in Cd274 (encoding PD-L1) expression. Further analysis showed that PD-L1 expression was increased predominantly in the tumour-infiltrating macrophages.

Conclusion: Our data provided compelling evidence of the benefits of therapeutically targeting STAT3 in a STAT3-driven gastric cancer model, while also offering some insight to the possible biological effects of STAT3 inhibition in the tumour microenvironment, such as the up-regulation of PD-L1 expression in tumour infiltrating macrophages. This latter observation suggests that therapeutic strategies aiming at targeting STAT3 expression could possibly be more effective in combination with checkpoint immune blockade or macrophage depletion.

Fox L[1], Putt F[1], Yeung D[2], Carne L[2], Cleary R[3], Cummins K[4], Fleming S[4], Costello B[4], Forsyth C[5], Dixon M[5], Tatarczuch M[6], Motorna O[7], Gambrill M[8], Ashraf A[8], McQuillan A[9], Schwarer A[10], Devos J[11], Harrup R[12], Zwe Z[12], Holmes A[13], Ratnasingam S[14], Chan K[15], Hsu B[16], Bury K[17], Grigg A[1]

The Incidence and Natural History of Dasatinib Complications in the Treatment of Chronic Myeloid Leukaemia

[1]Austin Hospital, Melbourne, [2]Royal Adelaide Hospital, [3]Princess Alexandra, Brisbane, [4]Alfred Hospital, Melbourne, [5]Gosford Hospital, Gosford, [6]Peter MacCallum Cancer Centre, [7]Monash Medical Centre, Melbourne, [8]Calvary Mater Hospital, Newcastle, [9]Hollywood Medical Centre, Perth, [10]Box Hill/Epworth, Melbourne, [11]Concord Hospital, Sydney, [12]Royal Hobart Hospital, [13]Canberra Hospital, [14]Royal Melbourne Hospital, [15]St Vincent's Hospital, Melbourne, [16]Royal Prince Alfred, Sydney, [17]Townsville Hospital, Australia

Aim

Dasatinib (DAS) has shown superiority over imatinib in achieving cytogenetic and molecular responses in chronic phase chronic myeloid leukaemia (CML-CP) but with a different toxicity profile. We reviewed the incidence of DAS side-effects (s/e) in a survey of Australian patients (pts) with a focus on risk factors, the response of the toxicity to changes in therapy and the effect on the underlying CML.

Methods

Retrospective study of all pts who received DAS for CML-CP at 17 Australian institutions. Each pt's history was tracked to identify any complications potentially attributable to DAS, and the treatment and outcome of these complications in response to alterations in DAS dose.

Results

Side effects were reported in 116/221 (52%) pts receiving DAS. The most common s/e was pleural effusion (PE), observed in 53 (24%) pts. Age and dose were significant risk factors for PE (p-values <0.01 and 0.047 respectively), gender (p=0.54) and line of therapy (p=0.22) were not. In pts who continued DAS post PE, there was a very high risk of PE recurrence in the absence of dose modification and a substantial risk despite dose reduction. 16/18 (89%) pts who ceased DAS due to PE while on 100mg had a stable/improved molecular response (MR) at 6 months, 10 of whom were routinely changed to an alternative tyrosine kinase inhibitor (TKI) within 5 weeks of DAS cessation. 8/8 pts who remained off all TKI therapy following PE maintained MR4.5 at 6 months. 15/17(88%) pts who continued DAS following PE had a stable/improved MR at 6 months following first PE. Other s/e included Gr 3-4 haemorrhage in 8 pts (4%). Ten (5%) pts had elevated pulmonary artery pressures meeting criteria for pulmonary hypertension (PHTN) and notably 8 had either concurrent PE or developed PE within 6 months.

Conclusion

PE was the most common s/e observed, with age and dose being risk factors. Recurrence was very high in the absence of dose reduction, was still substantial despite dose reduction and resulted in 38% of these pts eventually stopping DAS. Importantly, in the setting of PE, dose reduction or switching to another TKI did not compromise molecular response. Our results suggest that with DAS dosing appropriate for age, supported by adjustment according to levels, severe s/e requiring permanent DAS cessation are likely to be rare.

Combination treatment using MAPK and HDACi to enhance differentiation as a novel therapeutic strategy for colorectal cancer

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Aim/Background:

The 5 year survival rate for patients with metastatic colorectal cancer remains below 15%, necessitating an urgent need to develop novel therapeutic approaches for this disease. Differentiation therapy has proven to be successful in the treatment of acute promyelocytic leukemia however, whether this will also be efficacious in colorectal cancer is unknown. We and others have previously shown that MAPK pathway inhibitors (MAPKi) or Histone deacetylase inhibitors (HDACi) can induce markers of differentiation in colorectal cancer cells. The aim of this study is to determine the effect of combination therapy with these agents on differentiation and apoptosis and elucidate the mechanistic basis by which they induce differentiation.

Methods:

QRT-PCR, western blotting and immunohistochemistry were used to determine changes in levels of differentiation markers and drivers following treatment of colon cancer cells with HDACi and MAPKi. Knockdown experiments were performed using siRNAs. Apoptosis was measured by PI staining and FACS analysis.

Results:

Combination treatment of poorly differentiated colorectal cancer cell lines HT29 and T84 with Trametinib (MAPKi) and Panobinostat (HDACi) significantly enhanced mRNA and protein expression of the differentiation markers, cadherin 17 and keratin 20. Mechanistically, both agents induced expression of the Cdx2 transcritpion factor, a well-established driver of colonic cell differentiation. Knockdown of Cdx2 attenuated the induction of differentiation by the combination, indicating a central role for this transcription in drug induced differentiation. Furthermore, the combination synergistically enhanced apoptosis in HT29 and T84 cells, suggesting the promotion of a terminal differentiation program.

Conclusion:

This study demonstrates the differentiating capacity of combination treatment of colorectal cancer cells with HDACi and MAPKi, and identifies a central role for the Cdx2 transcription factor in driving this process. Furthermore, this drug combination synergistically enhanced apoptosis. Collectively, this study identifies a novel drug combination with therapeutic potential for colorectal cancer.

Title: Adapting our Approach to Image Verification: Clinical Implementation of ExacTrac in a 3D-Image Rich Department

Author/Co-Authors: Jose Tagaro, Karen Daly, Nicci Oliver, Benjamin Harris

Discipline: Radiation Therapy

Presentation Type: Presentation

Keywords: ExacTrac, IGRT, iGUIDE, HexaPod

Introduction:

Cone-beam CT (CBCT) is used for treatment positioning verification for radical cases. The introduction of ExacTrac poses considerable challenges for a department that typically bases clinical decisions on 3D images showing both soft tissue and bony anatomy. Hence a hybrid imaging workflow, combining CBCT and ExacTrac, was established to gain experience and confidence in a new imaging system.

Objectives/Aims:

To implement and integrate ExacTrac within current departmental protocols for accurate patient positioning and image verification. and to determine the accuracy and validity of ExacTrac positional corrections through comparison against CBCT verification images.

Description/Methodology:

An Exactrac-CBCT hybrid imaging workflow was designed so that shifts were executed by Exactrac, and positioning verification images taken using both imaging systems prior to treatment. The verification images, and residual shifts, were then compared to determine the agreement between the two systems. To date, four cranial cases have been treated with this hybrid protocol.

Results:

Of the four cranial cases treated on the hybrid imaging workflow thus far, initial analysis shows agreement within 1 mm and 1 degree for the majority of treatments. Larger deviations were attributable to inexperience. This has led to further improvements in the imaging workflow.

Conclusion:

Implementation of the hybrid imaging workflow has been successful, allowing the performance of the new Exactrac imaging system to be benchmarked against the department's clinical standard CBCT. Initial treatments have shown that Exactrac and CBCT imaging systems can agree to within 1 mm and 1 degree. Further utilisation is required to determine suitability for other treatment sites and Exactrac-only imaging workflows.

Attitudes of patients and physicians to repeat biopsies for lung cancer

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Background:

As targetable resistance mutations and other molecular drivers are discovered in lung cancer, increasingly repeat biopsies are suggested both in the clinical and research context. However patient and clinician attitudes towards repeat invasive procedures may be discordant. We conducted a prospective patient and physician survey to investigate patient's and physician's attitudes towards repeat biopsies in lung cancer.

Methods:

Under an ethics approved protocol, patients attending the lung oncology clinic at a large academic centre in Melbourne were invited to complete a questionnaire assessing their attitudes on repeat biopsies. Physicians and surgeons who treat lung cancer patients were invited to complete an online questionnaire through the Australasian Lung Trials Group (ALTG).

Results:

89 respondents completed their respective questionnaires. There were 50 patients [Male: Female ratio 1:1, median age 68 years, metastatic (61.2%): locally advanced/adjuvant (38.8%)] and 39 physicians.

The most important factor in a patient's decision to undergo repeat biopsy was their oncologist's recommendation (56.8%). The approximate percentage of risk for complication that physicians would be able to accept for repeat biopsies was between 10-20% (48.7%) and the majority (92.3%) of physicians would support re-biopsy to investigate for further potential therapeutic biomarkers. Whilst 52.63% of physicians were happy to recommend research-only biopsies (which did not have direct impact on management), only 50% of patients were agreeable to it. However, the majority of patients would agree to a repeat biopsy in order to participate in a clinical trial (62.8%) or on progression of disease to check on the resistance mechanism (68.2%). Most respondents felt that a wait time of up to 14 days for molecular analysis is acceptable.

Conclusions:

The decision by lung cancer patients to undergo rebiopsy was strongly influenced by their oncologists' recommendations. Most would agree to a repeat biopsy in order to participate in a clinical trial or on progression of disease to check on the resistance mechanism. However, only 50% of patients and clinicians were interested in repeat biopsies solely for research purposes.

Yao A [1], Aboltins C [2], McNab AA [3], Denholm J [4], Khong JJ [1, 3]

A case series of Orbital Tuberculosis: Perspectives from Victoria, Australia

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2. St Vincent's Hospital, Fitzroy, Vic., Australia
3. The Royal Victorian Eye and Ear Hospital, East Melbourne, Vic., Australia
4. The Peter Doherty Institute for Infection and Immunity, Melbourne, Vic., Australia

Aim:
Orbital tuberculosis is a rare extrapulmonary manifestation of tuberculosis and its clinical implications pose unique challenges to ophthalmologists. The aim of this study is to identify common aspects of orbital tuberculosis in Victoria, Australia, in order to help guide local doctors in their identification and management of this disease in clinical practice.

Methods:
We present a retrospective case series of orbital tuberculosis as identified by members of the Australian and New Zealand Society of Ophthalmic Plastic Surgeons (ANZSOPS), as well as systematic review for further cases by the Victorian Tuberculosis Program

Results:
Cases of orbital tuberculosis presenting with orbital mass lesion without bony involvement and chronic dacryoadenitis were described, with comparison of demographic data, risk profile, clinical features, treatment and outcome.

Conclusion:
Orbital tuberculosis remains an important differential diagnosis of orbital mass lesions. The clinical presentation of this disease is heterogeneous, with the potential for destructive complications to both bone and soft tissue. The medical risk factors, clinical presentation, radiographic and microbiological features, as well as medical treatment and prognosis are here discussed.

Survival outcomes following curative surgical resection of stage IV melanoma

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2. Olivia Newton John Cancer and Wellness Centre, Heidelberg, Vic., Australia
3. University of Melbourne, Parkville, Vic., Australia

Supervisors: David Gyorki, Jonathan Cebon

Introduction:

The aim of this study was to retrospectively analyse survival rates of patients who underwent complete surgical resection rendering patients disease free of stage IV melanoma. Treatment of metastatic melanoma has historically been associated with poor survival outcomes. However, prior studies have highlighted that surgical resection demonstrates promising results. In an era where new biological and immunotherapies have shown improved survival, selection of surgical candidates has never been so important in providing the best possible patient care. Therefore, determining parameters that impact survival is necessary.

Methods:

Patients who underwent surgical resection of metastatic melanoma were extracted from the Melanoma Melbourne Project and Austin Hospital Melanoma databases. Eligible patients underwent complete surgical resection and had available follow up information. Data was imported into IBM SPSS 2.0 and analysed. Survival estimates were derived from Kaplan-Meier, Log-Rank and Breslow tests.

Results:

281 patients were identified. 186 patients did not meet eligibility criteria. The remaining study population (n = 95) consisted of 60 males and 35 females. Median age at time of surgery was 57 years and median overall survival (OS) from resection was 49 months (95% CI, 31-67 months). Overall survival at 1, 2 and 5 years was 92, 87 and 50% respectively. 72 patients (75%) had visceral disease at time of surgery, highlighting no difference in overall survival when compared to non-visceral resections (P = 0.08). Predictors of survival included the ability to achieve clear margins. 89 individuals with complete resections experienced longer survival compared to patients with melanoma present on histological specimen margins (median OS 53 vs. 20 months, P = 0.026). Additionally, a preoperative Neutrophil to Lymphocyte Ratio less than 5 was associated with improved outcomes (median OS 65 vs. 15 months, P = 0.006).

Conclusion:

This study's results are consistent with other research, demonstrating favourable long-term outcomes associated with resection of metastatic melanoma. Additionally, disease location had no impact on survival as long as clear margins were achieved. Furthermore, preoperative Neutrophil to Lymphocyte Ratios may now play a role when choosing surgical candidates for stage IV melanoma.

Ngo B[1], Papa N[2], Sengupta S[1, 2]

Factors affecting the timeliness of haematuria assessment

1. The University of Melbourne, Parkville, Victoria, Australia
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Aim
Haematuria is the most common presenting symptom in bladder cancer, occurring in over 80% of cases. However, most instances are due to benign causes or are idiopathic, hence primary care physicians may be reluctant to over-investigate their patients, potentially leading to delayed haematuria evaluation. The aim of our study was to determine the factors that impact on timely haematuria assessment.

Methods
Using electronic medical records, we undertook a retrospective cohort study assessing adult patients referred to the Department of Urology at Austin Health. Cystoscopic procedures occurring between January 1 2015 and December 31 2015 were identified. Those with a known history of bladder, urinary tract or renal cancer, and cystoscopy for indications other than haematuria were excluded. Data on patient demographics, smoking status, anticoagulation status, degree of haematuria and investigation results were collected. The primary outcomes were time from urology referral to urology consultation and time from urology consultation to cystoscopy.

Results
Over the study period, 308 cases (228 males, 80 females) meeting study criteria were identified. In consideration of general practitioner-initiated urology referrals, multivariable regression analysis identified that increasing socioeconomic status was associated with quicker review by urology ($p=0.019$) and anticoagulated patients saw a urologist 27 days sooner than those not on anticoagulation ($p=0.011$). Unsurprisingly, patients with predictors of bladder cancer, such as macroscopic haematuria ($p=0.002$) and suspicious findings on imaging ($p<0.001$) were seen more promptly by urology as well. A suspicious finding on imaging was also associated with a quicker assessment with cystoscopy ($p<0.001$).

Conclusion
Socioeconomically disadvantaged patients wait longer to see a urologist after referral, while anticoagulated patients and those with predictors of bladder cancer are seen more expediently. Suspicious findings on imaging is also a predictor of prompt cystoscopic evaluation.

Ngo B[1], Sengupta S[1, 2], Perera M[1, 2]

Factors affecting the timeliness and adequacy of haematuria assessment

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Aim
Patients with bladder cancer typically present with haematuria, which is the strongest predictor of underlying disease. Despite this, many patients experience sub-optimal haematuria evaluation. The aim of our study was to review the literature to identify factors affecting haematuria assessment.

Methods
We performed a systematic search of publications indexed in MEDLINE, EMBASE and PUBMED in March 2016, using the keywords *hematuria, urinary bladder neoplasm(s) and bladder tumor*. Studies evaluating the timing and adequacy of haematuria assessment in the context of bladder cancer were included. Exclusion criteria included age <18 years, animal studies and non-English articles.

Results
A total of seventeen articles were included in our study. Three studies found female patients waited longer to see a urologist. A further three articles identified that women experienced greater delays for cystoscopy and subsequent bladder cancer diagnosis. In addition, seven studies found that female patients were less likely to be referred to urology, or undergo imaging or cystoscopy. Women also had more pre-referral consultations (three studies) and were more likely to be managed for urinary tract infection (four studies). One study identified that smokers, despite their increased risk of bladder cancer, were less likely to receive cystoscopy or imaging for haematuria evaluation. Macroscopic haematuria was found to be a predictor of a prompter and more thorough work-up.

Conclusions
Factors including gender, smoking status and type of haematuria were found to influence haematuria assessment. Further research on the impact of other factors is required, in the hope of informing clinicians and effecting positive change in the approach to haematuria.

Kao C-T[2], Kucchal T[3], Chuen J[1]

3D Printed Abdominal Aortic Aneurysm Model for Patient Education

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3. *Department of General Surgery, Austin Health, Heidelberg, VIC, Australia*

Aim Studies have shown that participants undergoing abdominal aortic aneurysm (AAA) repair do not always appreciate the scope of their condition with misconceptions regarding the natural history of AAA and the risks of surgery prior to making a decision (1, 2). The aim of this study is to assess the impact of using a 3D printed AAA model to improve patients' understanding of their condition.

Methods A 3D printed AAA model was created based on a representative CT angiogram. A randomised controlled trial was conducted on participants currently known or referred to the Austin Hospital Vascular Surgery Department. Only participants with a known diagnosis of AAA were identified and recruited from the outpatient clinic and Vascular Laboratory. All participants were randomised to attend one of two education sessions, control group (verbal information alone) and intervention group (verbal information and the use of 3D printed model). Baseline knowledge was established upon completion of a questionnaire and any improvement in knowledge was assessed with an identical questionnaire after the education session. Patient satisfaction with the mode of education was also assessed by a ten-point scale survey.

Results 50 participants were enrolled in the study of which 35 had received prior education regarding AAA's and 15 had received no prior knowledge. 30 participants registered English as their first language, 16 registered English as their second language and 4 required an interpreter. 24 participants were randomised into the control group and 26 participants to the interventional group. Using 3D models was shown to be an effective method of patient education. Nevertheless, this study failed to demonstrate that 3D models were a superior method of education compared to conventional education.

Conclusion This pilot study demonstrates that a 3D printed anatomical model is a feasible adjunct to patient education regarding their pathology. 3D printing may play an important future role in patient education and deserves further exploration.

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Retroperitoneal Lymph Node Dissection: an analysis of a contemporary Australian cohort in an experienced institution.

T. G Manning, M Perera, N Papa, S McGrath, J Ischia, S Sengupta, N Lawrentschuk

Introduction & Objectives:
Retroperitoneal Lymph Node Dissection (RPLND) is a specialised procedure done in few centres. Generally, specialised oncology fellowships are required to acquire the requisite skills to perform this surgery, with higher volume centres reflecting better patient outcomes[1]. The main indication is following chemotherapy in germ cell tumours. However, increasingly there is a role in Renal cell carcinoma, Urothelial cancer and even with other organ malignancies[2]. We aimed to review our contemporary short and longer term outcomes in a tertiary Australian Centre.

Method:
Medical records assessed retrospectively helped formulate a database which was then utilized to review short and longer term outcomes of this procedure from January 2010 until July 2016 at Austin Health.
Three different Urologists performed the procedures all of which had completed fellowships in uro-oncology.
Statistical analysis was then undertaken and comparisons were made to outcomes in current literature.

Results:
A total of 30 patients were included in the analysis. The vast majority of patients underwent RPLND for germ cell tumours following chemotherapy, RPLND was also performed for renal cell carcinoma. The median operative time was 379 minutes; the median intraoperative blood loss was 1300ml. One patient returned to theatre.
Median length of stay was limited to 8 days, with intensive care involvement to just 14 hours.

Short term complications were acceptable with only 3 patients requiring readmission for an average length of 5 days. Long-term oncological outcome was better than expected. All patients in our cohort survived. One patient had an identified recurrence.

Conclusions:
RPLND may be done safely where fellowship-trained surgeons participate in a program with multidisciplinary help in the pre, peri and post operative patient course. Good short term and longer term oncological outcomes and surgical results can be achieved which are competitive with international standards.

References:
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2 **Hu, Brian et al.** Lymphadenectomy for testicular, upper tract urothelial and urethral cancers. *Current Opinion in Urology 2015; 25(2): 129-135*

3D Printing in Surgery: Developing a Universal Workflow

3D Med Lab, Department of Vascular Surgery

JASAMINE COLES-BLACK, Mr Jason Chuen

Aim:
The applications of 3D printing in surgery are promising; however, a major barrier is the lack of technical expertise amongst surgeons. We present a low cost, easily reproducible medical imaging to 3D printed model workflow using open source software that can be 3D printed with inexpensive, commercially available desktop 3D printers.

Methodology:
3D Slicer (version 4.5; Harvard, US, 2015) was used to create anatomical models that could be 3D printed on a AUD$5000 Makerbot Replicator 2X 3D Printer. CT/MRI datasets were automatically segmented using the "Threshold" function. When required, the "Dilate" and “Subtract Scalar Volume” functions were used to generate hollow models. The "Volume Clip" extension was utilised to isolate regions of interest that were irregular in volume. The models produced were shown to experienced surgeons, who rated the clinical utility of the models in their respective fields.

Results:
The 3D printed models were well received, with immediate requests for more models. The physical models were felt to be a valuable addition to standard imaging modalities, especially in complex cases. The resultant models have been rated highly by experts for their potential in preoperative planning, patient education, and trainee education.

Conclusion:
There are clear applications for 3D printing in surgery, with positive feedback from the assessed cohort of experienced surgeons that the anatomical models would be useful in challenging cases. Our workflow methodology has been applied across specialties such as vascular surgery, urology, cardiothoracic surgery, orthopaedic surgery, anaesthetics, radiation oncology and clinical education.

Ianno D [1], Yap R [1], Burgess A [1]

Colonoscopic localization accuracy for colorectal resections in the laparoscopic era

1. Department of Surgery, Austin Health, Heidelberg, Victoria, Australia;

Aim:
Colonic resection is increasingly performed laparoscopically, where intraoperative tumor localization is difficult. Incorrect localization can have adverse surgical results. This has not been studied in laparoscopic resection. This study aimed to evaluate colonoscopic localization accuracy, contributing factors, and subsequent surgery.

Methods:
Retrospective review of patients who underwent colonic resection after colonoscopy between 2008 and 2013 at a single institution, with subsequent univariate and multivariate analysis.

Results:
Of 221 lesions identified, 79.0% were correctly localized. Nine (4.0%) incorrectly localized cases required changes in surgery. Two factors were significant on multivariate analysis: gastroenterology training and incomplete colonoscopy were associated with incorrect localization.

Conclusion:
Colonoscopy is reasonably accurate at localizing lesions. Methods such as tattooing should be used, but error is still possible. Communication between endoscopists and surgeons is vital to minimize the risk of incorrect localization. Emphasis is needed during colonoscopic training of awareness and protocolization of colonoscopic position and methods to improve localization.

Tancock M, [1], Nguyen L, [1], Fifis T, [1] ,Gomez E[1], Christophi C[1]

The role of the Renin-Angiotensin System on tumour recurrence and the immune system following resection of colorectal liver metastases

1.The University of Melbourne, Department of Surgery, Austin Health

Background and Aims
Over 50% of colorectal cancer (CRC) patients develop liver metastases. Surgical resection is the only potentially curative treatment for these patients, but 40-80% of them develop disease recurrence. Liver regeneration, following metastatic resection, induces upregulation of growth factors/ cytokines that impact on any micrometastases present leading to tumour recurrence. Immune cells including macrophages are a major part of the tumour microenvironment adopting different phenotypes, depending on local stimuli thus influencing tumour progression. Inhibition of the Renin Angiotensin System (RAS) was shown to inhibit tumour growth. This study aims to determine how the macrophages are effected by Captopril (RAS inhibitor) treatment in the context of tumour recurrence in the regenerating liver.

Methods
1. Changes in macrophage receptors and secreted factors are investigated in murine CRC liver metastases, following 70% liver resection and RAS inhibition. Mice were treated with Captopril (250mg/kg) or with saline. Livers were harvested on days 16 and 21 after surgery and archived as formalin fixed paraffin embedded (FFPE). Double immunohistochemistry was performed for F4/80 (macrophage marker) and activation markers (MHC II, iNOS, Arginase, IL-10, VEGF, Tie2) to determine macrophage activation state.
2. Macrophage cell lines (J774 and P388D1) and a mouse CRC cell line (MoCR) were cultured with Captopril. Cytokines/growth factors released in response to treatment were evaluated with ELISA. The effects of culture conditioned media were also directly tested (macrophages on to tumour and vice versa) to determine changes in the cross talk between these cells, effected by the treatment.

Results
These studies are ongoing. Captopril altered the expression of key cytokines/ growth factors following resection and decreased pro-inflammatory cytokine secretion by macrophages. Captopril altered the phenotype of macrophages compared to control and modulated the *in vitro* tumour kinetics.

Conclusion
Captopril treatment during liver resection and *in vitro* alters macrophages towards an anti-inflammatory phenotype.

Su Kah Goh[1,2], Hongdo Do[2], Vijayaragavan Muralidharan[1], Christopher Christophi[1] & Alexander Dobrovic[2]

Donor-specific cell-free DNA as a non-invasive marker of organ rejection after liver transplantation: a pilot study.

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[2] *Translational Genomics and Epigenomics Laboratory, Olivia Newton-John Cancer Research Institute*

Aim:
Up to 20% of patients will develop an episode of rejection in the first year after liver transplantation. Conventional means to diagnose organ rejection are either inaccurate or highly invasive. Hence, better biomarkers for the non-invasive diagnosis of organ rejection are needed. Recent studies have proposed the use of donor-specific circulating cell-free DNA (dscfDNA) as a non-invasive marker of organ rejection. Unlike current methodologies adopted to evaluate dscfDNA, we have developed a rapid digital PCR methodology to accurately measure dscfDNA levels.

Methods:
Eight patients who underwent liver transplantation were prospectively recruited. Genotyping of a set of deletion/insertion polymorphisms was performed to identify donor-specific alleles. Droplet digital PCR was then utilized for the serial quantification of dscfDNA in the circulation of the recipient. DscfDNA levels were measured in pre-transplant and post-transplant bloods for each recipient at days 3, 7, 14, 28 and 42.

Results:
DscfDNA levels were reflective of organ health. In six recipients who underwent uneventful transplantation, levels of dscfDNA markedly reduced at day 3 and rapidly plateaued to a very low level from day 7 onwards. We also found that dscfDNA levels were independent of cholestasis in a separate recipient. On the other hand, dscfDNA levels were markedly elevated in a patient who developed an episode of organ rejection.

Conclusion:
In this pilot study, we demonstrated the robustness of our methodology for the detection and quantification of dscfDNA. Our methodology was readily-performed and results were attainable in 5.5 hours. Larger validation studies are required to confirm the diagnostic performance and clinical utility of dscfDNA, especially in the setting of other common post-transplant complications.

Machan L[1], Churilov L[1,2], Hu R[3], Peyton P[1,3], Tan C[3], Pillai P[3], Ellard L[3], Harley I[3], Hayward P[1,4], Matalanis G[1,4], Roubos N[4], Seevanayagam S[4], Story D[1,3], Weinberg L[1,3].

Apnoeic oxygenation vs. low tidal volume ventilation in anaesthetised cardiac patients: a prospective, single centre, randomised trial

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Aim: Apnoeic oxygenation (i.e. suspension of lung ventilation) and low tidal volume (TV) ventilation are common techniques that allow suitable surgical exposure for the dissection of the left internal mammary artery (LIMA) during coronary artery bypass grafting (CABG) surgery. The physiologic effects of these techniques in this setting are unknown.

Methods: We performed a prospective randomised trial in 24 adult participants undergoing elective CABG surgery. Half received apnoeic oxygenation (Apnoeic group) and the other half received low TV ventilation (2.5 mL/kg ideal body weight) (Low TV group) for 15 minutes during harvesting of the LIMA. The primary endpoint was the absolute change in the partial pressure of arterial carbon dioxide ($PaCO_2$). Secondary endpoints included changes in arterial pH, pulmonary artery pressures (PAP), cardiac index, pulmonary artery acceleration time, and ease of surgical access.

Results: The mean (SD) increase in $PaCO_2$ from baseline to 15 minutes was 31.8 mmHg (7.6) in the Apnoeic group and 17.6 mmHg (8.2) in the Low TV group (effect size: 14.2 mmHg, $p<0.001$). Similarly at 15 minutes, the mean (SD) decrease in pH was -0.15 (0.03) in the Apnoeic group and -0.09 (0.03) (SD) in the Low TV group (effect size: 0.06, $p<0.001$). There were no statistically significant changes in any other variables. The interaction between the treatments over time (i.e. difference in slopes between the treatments) was statistically significant for $PaCO_2$ ($p<0.001$), pH ($p<0.001$), systolic PAP ($p=0.002$), diastolic PAP ($p=0.023$), and mean PAP ($p=0.034$). Both techniques provided adequate ease of surgical access, however apnoeic oxygenation was predominantly preferred.

Conclusion: Apnoeic oxygenation caused a greater degree of hypercarbia and respiratory acidaemia compared to low TV ventilation during harvesting of the LIMA. Neither technique had deleterious effects on PAP or cardiac function. Both techniques provided adequate ease of surgical access. To date, this is the first clinical trial to evaluate the physiological effects of these ventilation techniques in this setting. These findings may assist anaesthetists and cardiac surgeons individualise the best ventilation strategy for patients during surgical harvesting of the LIMA.

Abstract

Introduction

Laparoscopic lens fogging (LLF) hampers vision and impedes operative efficiency. Attempts to reduce LLF have led to the development of various anti-fogging fluids and warming devices. Limited literature exists directly comparing these techniques. We constructed a model peritoneum to simulate LLF and to compare the efficacy of various anti-fogging techniques.

Materials and Methods

Intraperitoneal space was simulated using a suction bag suspended within an 80L container of water. LLF was induced by varying the temperature and humidity within the model peritoneum. Various anti-fogging techniques were assessed including: scope warmers, FRED™, Resoclear™, chlorhexidine, betadine and immersion in heated saline. These products were trialled with and without the use of a disposable scope warmer. Vision scores were evaluated by the same investigator for all tests and rated according to a predetermined scale. Fogging was assessed for each product or technique 30 times and a mean vision rating was recorded.

Results

All products tested imparted some benefit, but FRED™ performed better than all other techniques. Betadine and Resoclear™ performed no better than the use of a scope warmer alone. Immersion in saline prior to insertion resulted in decreased vision ratings. The robotic scope did not result in LLF within the model.

Conclusions

In standard laparoscopes, the most superior preventative measure was FRED™ utilised on a pre-warmed scope. Despite improvements in LLF with other products FRED™ was better than all other techniques. The robotic laparoscope performed superiorly regarding LLF compared to standard laparoscope.

Cameron Dawson[1], Joshua Rosen[1], Dr. Hanna Cheng[2]

Parental Perceptions of Informed Consent in a Public Child and Adolescent Mental Health Unit

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2. Child and Adolescent Mental Health Service, Austin Health, Heidelberg, Vic., Australia

Aim
Informed consent forms a critical basis for effective health care professional-patient relationships. In paediatric mental health parents and clinicians explore concepts such as competent mature minors, Gillick competence and the dyad of paternalism and child autonomy. This study aims to evaluate parents' current experiences of informed consent in a public child and adolescent mental health service (CAMHS) in order to improve clinicians' awareness of parental consent experiences and engagement.

Methods
In this qualitative descriptive study parents attending outpatient appointments in a CAMHS from March – June 2016, who agreed to participate, were asked to describe their experiences and perceptions of consent during their interactions with staff. 20 parents from 2 different outpatient teams at a Victorian CAMHS completed semi-structured interviews. Interviews were transcribed and analysed using qualitative content analysis.

Results
Emergent results from interview analyses group into three main themes: chaos, satisfaction and values. Parents discussed their emotions and distress, logistical difficulties, desperation when engaging with services and found recalling their consent processes difficult. Despite this they were very satisfied with their consent experiences (mean 8.68, range 6.5-10 on 10-point Likert scale) and mostly felt they had been adequately informed. Parents had varying beliefs on paternalism, their child's autonomy and desiring formalized or informal consent processes.

Conclusion
By identifying subjective perceptions and values of parental stakeholders this study has explored attitudes and barriers to parental engagement with informed consent in a child and adolescent mental health setting. This has implications as to raising awareness for how CAMHS clinicians may optimize parental engagement with information and consent processes. Future research should validate and quantify this study's findings.

Indranada AM[1], Mullen SA[2], Kanaan RAA[3]

The Pre-Ictal Rise of Autonomic Parameters in Psychogenic Non-Epileptic Seizures

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Introduction: Psychogenic non-epileptic seizures (PNES) are defined as seizure-like attacks without evidence of electrographic ictal discharges. Pre-ictal somatic symptoms consistent with hyperventilation have been reported to occur in some patients with PNES, and some have reported a rising sense of unease that is ended by their seizure. Therefore, this study aims to describe autonomic variables shortly before non-epileptic seizure onset, in order to characterise pre-ictal arousal dynamics and provide quantitative evidence of any mounting anxiety.

Methods: Sixty-nine patients with previously recorded non-epileptic seizures on video EEG (vEEG) with associated ECG recordings were analysed for heart rate (HR) and respiratory rate (RR) at baseline, and at five minutes, four minutes, three minutes, two minutes, and one minute before seizure onset. HR was further recorded at onset and at the halfway point of the seizure. RR was measured by direct observation of the patient via vEEG, while HR was recorded by 3-beat measurement of heart rate variability (HRV) from the start of the indicated period.

Results: HR showed a significant increase from baseline to 5 minutes before seizure onset ($P = 0.036$), as well as a significantly increasing trend from baseline to seizure onset ($P < 0.001$, repeated measures ANOVA). Onset HR increased significantly compared to all other time measurements. RR showed a significant increase from baseline compared to 4 minutes, 2 minutes, and 1 minute before seizure onset, however there was no significantly rising trend from baseline to 1 minute ($P = 0.149$, repeated measures ANOVA).

Conclusions: Heightened autonomic arousal preceding the seizures is consistent with pre-ictal anxiety, which can be present as early as 5 minutes before seizure onset. This suggests the seizures may be a response to anxiety. Additional samples and analysis of epileptic patients as a control comparator are needed to confirm these findings.

Yao A [1], Chan H [1], MacDonell R [1], Shuey N [2], Khong JJ [1,2]

Bilateral Facial Nerve Palsies Secondary to Chronic Inflammatory Demyelinating Polyneuropathy Associated with Anti-TNF-α use: Case Presentation and Literature Review

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Aim:
The aim of this study is to discuss a case of drug-induced chronic inflammatory demyelinating polyneuropathy (CIDP) requiring strategies for corneal protection, and review the literature regarding ophthalmic implications of CIDP and its inciting agents.

Methods:
We report the case of a 37-year-old man who developed bilateral lower motor neuron facial nerve palsies after commencing treatment with adalimumab for severe Crohn's disease.

Results:
He developed facial weakness with acute inability of eye closure, with 8-10mm lagophthalmos and punctate epithelial erosions on examination which required treatment with lubricating drops, in association with mild upper and lower limb weakness and diffuse hyporeflexia. CSF was significant for elevated protein with no cells, and nerve conduction studies demonstrated prolonged F wave latencies with evidence of conduction blocks. This presentation was thought consistent with an immune-mediated demyelinating neuropathy associated with treatment with tumour necrosis factor (TNF)-alpha blocker, and the patient was commenced on prednisolone and intravenous immunoglobulin with gradual recovery over 12 months.

Conclusion:
Anti-TNF alpha agents are now employed to treat a large variety of inflammatory conditions including empirical treatment for thyroid-associated orbitopathy. CIDP is a known side effect of this medication class. The phenomenon of CIDP is here reviewed with focus on drug-induced CIDP as well as CIDP with ophthalmic complications.

Luke Baker [1], Sam Berlangieri [1], Kunthi Pathmaraj [1], Andrew Scott [1], Caroline Stark [2],

Botox Therapy in Simple partial seizures – Evaluated with FDG PET

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Aim/Background

A 78yo patient presented to the PET department for evaluation of Epilepsy partialis continua following a normal MRI study. Seizures presented as recurrent twitching/jerking of the right shoulder and neck, with no obvious trigger evident. Numerous medications were unsuccessful in relieving her symptoms, and botox therapy was being considered. An FDG-PET brain scan was requested in an attempt to identify the seizure focus, prior to commencing treatment.

Methods

^{18}F-FDG PET images (ictal & interictal) were acquired pre and post Botox therapy, using the standard epilepsy FDG PET brain protocol, consisting of IV administration of 220MBq of ^{18}F-FDG and a 30 minute uptake period, followed by a 15 minute static scan time. Patient's blood glucose level was within normal limits, at mmol/L

Findings and Conclusion

Ictal - FDG PET images showed a focal hypermetabolism in the left dorsal front cortex. This was correlated to a 3mm lesion with T2 signal at this location in the motor cortex the MRI image (reported as normal). These PET images were acquired prior to the patient starting Botox therapy.

Thereafter, Botox was injected into targeted muscle groups affected by the seizures, with a total of 150 units per treatment; the patient experienced a 95% resolution in seizure activity.

10 Days later a repeat FDG PET scan was performed.

A reduction in metabolic activity was noted in the left frontal motor cortex, previously noted in the FDG PET and MRI, and correlated with the patient's symptomatic improvement, after commencing Botox therapy.

An additional follow up FDG PET performed 16months showed absence of focal and regional cortical metabolic abnormality, confirming response to Botox treatment.

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Dewey HM[1], Cadilhac DA[2,3], Kilkenny MF[2,3], Kim J[2,3], Andrew NE[2], Hill K[4], Grabsch B[2], Grimley R[5], Lannin NA[6,7], Levi C[8], Faux S[9], Middleton S[10], Anderson CS[11], Donnan GA[2]

Quality of care over-time: new evidence from the Australian Stroke Clinical Registry

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9. Faculty of Medicine, The University of NSW, Sydney and St Vincent's Hospital, Darlinghurst, NSW, Australia
10. Nursing Research Institute, St Vincent's Health Australia (Sydney) and Australian Catholic University, NSW, Australia
11. The George Institute for Global Health, The University of Sydney, Sydney, NSW, Australia

Aim
Variations in quality of care exist for patients with stroke. Since 2009, the Australian Stroke Clinical Registry (AuSCR) has been providing clinical quality indicator data for participating hospitals to use to drive quality improvement. We investigated whether there was evidence of improvement in quality of care over time in hospitals using AuSCR.

Methods
A historical controlled design, matched by hospital, was used such that only hospitals that contributed data from 2012-2014 were included (n=25). AuSCR data for 4 national and 8 Queensland stroke care indicators for consecutive patients admitted to contributing hospitals were analysed. Comparisons were made using descriptive statistics and random effects logistic regression. Each indicator was the dependent variable and models were adjusted for audit year, hospital and known confounders.

Results
15508 episodes of care were analysed (39% 2014; mean age 73 years; 54% male). In 2012 compared to 2014, the crude proportion of patients admitted to a stroke unit (77% vs 78%, p=0.13) or receiving intravenous thrombolysis (12% vs 11%, p=0.23) was similar. In contrast, improvements in patients discharged with a care plan (45% vs 55%, p<0.001) or with antihypertensive medications (62% vs 74%, p<0.001) were observed. In adjusted analyses, evidence of improved access to stroke units (aOR: 1.31 95% CI 1.18, 1.47), provision of discharge care plans (aOR: 1.95 95% CI 1.69, 2.25) and prescription of antihypertensive medications at discharge (aOR: 2.01 95% CI 1.81, 2.23) was observed. In Queensland hospitals, improvements in the provision of aspirin within 48 hours (aOR: 1.34 95%CI 1.11, 1.63) and discharge on antithrombotic medications (aOR: 6.20 95% CI 4.93, 7.80) were also found.

Conclusion
Use of a clinical quality registry in Australia for monitoring acute stroke care has provided evidence of improvements in the quality of care at participating hospitals. Support for AuSCR should be a priority.

Comparison of early dynamic Amyloid and Tau-PET scans to ^{18}F-FDG-PET images

Background

Several studies have shown the utility of the early phase uptake of Aβ PET tracers to provide perfusion-like information. The goal of this study was to compare the perfusion-like distribution supplied by early phase of Aβ PET tracers ^{11}C-PiB (PiB) and ^{18}F-Florbetaben (FBB), as well as the tau tracer ^{18}F-AV1451 (AV1451), to ^{18}F-FDG (FDG) PET images.

Methods

Ninety-five subjects underwent either PiB, FBB, or AV1451 PET imaging which included an early (0-5 minutes post-injection) dynamic acquisition. All subjects also underwent an FDG study acquired at 30 min post injection. Images were spatially normalized in SPM8, and voxelwise comparison of the SUV images were performed between the different tracers and FDG. Furthermore, following the SPM comparisons, the early-phase images of the different tracers were visually compared to their respective FDG by an experienced reader to assess if they provided similar information.

Results

When a 2-group T-Test was performed using SPM8 to detect areas where either PiB, FBB, or AV1451 showed a significantly greater tracer uptake than FDG, significantly higher tracer uptake was only found in the cerebellum, pons and midbrain. Visual inspection of the images revealed that both the early phase images from the Amyloid and Tau tracers provided similar cortical uptake patterns as FDG.

Conclusions

The pattern of early phase tracer uptake of Amyloid and Tau PET tracers was similar to FDG images. The higher uptake in the cerebellum and midbrain should be taken into account in the visual interpretation of the early-phase images. Our results suggest that early phase imaging can provide additional cortical perfusion-like information, and can be used in cases where FDG is not available.

In vivo assessment of markers of Alzheimer's disease pathology in Vietnam war veterans with **Traumatic Brain Injury** & **Post-Traumatic Stress Disorder**

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Background: Epidemiological research indicates that amongst veterans, both Traumatic Brain Injury and Post-Traumatic Stress Disorder are associated with a 2-4-fold increase in risk of dementia; however, mechanisms contributing to this relationship are poorly understood. The aim of this study was to investigate if Vietnam war veterans without mild cognitive impairment or dementia, but with TBI and PTSD show evidence of Alzheimer's disease pathological markers, as assessed by amyloid, tau and glucose metabolism using PET.

Method: 82 male participants -41 veterans with chronic PTSD (aged 68.12 ±2.43 years), 18 with a TBI (aged 68.19 ±2.44 years) and 22 controls (aged 69.63 ±5.29 years)- underwent FDG, tau (^{18}F-AV1451) and amyloid PET (^{18}F-Florbetaben). The Standardized Uptake Value Ratio (SUVR) was calculated using the cerebellar cortex as reference region for all tracers.

Results: The TBI cohort demonstrated significantly higher ^{18}F-AV1451 retention than the control group in the temporo-parietal region (1.23 ± 0.10 vs 1.17 ± 0.08, p=0.044) and frontal cortex (1.18 ± 0.10 vs 1.11 ± 0.09, p=0.044). In addition, ^{18}F-FDG retention in the frontal cortex was significantly lower in the PTSD group when compared to the controls (1.03 ±0.06 vs. 1.07 ±0.07 p=0.014). There was no significant difference in A□ burden between the groups.

Conclusions: These preliminary findings suggest that TBI is associated with later life tau deposition, whilst chronic PTSD is associated with hypometabolism later in life. More studies to confirm these results are warranted. (233)

Anterior versus posterior stroke: No difference in cognitive impairment

ABSTRACT

Aim: To compare the incidence and nature of cognitive impairment three months post-stroke in subtypes of ischemic stroke patients, classified according to Oxfordshire criteria.

Methods: Participants were assessed three months post-stroke as part of CANVAS, a study which examines changes in brain volume and cognition after stroke. The cognitive test battery comprised measures of executive function, language, memory, attention, processing speed and visuospatial ability. Impairments were defined as domain z-scores more than 1.5 standard deviations below normative values. Stroke location was divided into anterior circulation infarction (ACI), either total (TACI) or partial (PACI), posterior circulation infarction (POCI), and lacunar infarction (LACI), based on Oxfordshire criteria. All participants underwent high resolution 3D MPRAGE MRI. Infarct size was quantified via manual tracing of FLAIR images.

Results: 126 patients were assessed, including 61 ACIs, 43 POCIs, and 15 LACIs. Seven patients with anterior and posterior circulation infarcts were excluded from the analyses. The groups did not differ with respect to age, sex, NIHSS or education level. Incidence of cognitive impairment was 57.5% in the anterior group, 51.5% in the posterior group, and 44.4% in the lacunar group (p=0.777). Incidence of impairment was 29% for the executive function domain, 8% for language, 12% for memory, 9% for attention, 1% for processing speed and 15% for visuospatial function. There was no language impairment in the lacunar group. Mean infarct volumes were significantly different in the anterior (11.8±38mm^3) and lacunar

(0.4±0.3mm^3) groups (p=0.004), and in the posterior (9.6±16.9mm^3) and lacunar groups (p=0.009). Despite these differences in infarct volume between groups, associations between stroke subtype and frequency of impairment in each cognitive domain were not significant ($p > 0.05$ for all domains).

Conclusions: Executive function was most commonly impaired on testing in all groups three months after stroke. Cognitive profiles were not different in patients with anterior and posterior circulation strokes.

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Cognition is associated with hippocampal volume and cortical thickness early after ischaemic stroke

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Aim

The aim of the study was to examine cognition early after ischaemic stroke and its association with structural MRI markers of brain aging. This is important because cognitive impairment[1] and dementia[2] are common after stroke, and hippocampal atrophy and cortical thinning are associated with dementia[3].

Methods

Cognition And Neocortical Volume After Stroke (CANVAS) is an ongoing longitudinal study. Ischaemic stroke patients without dementia are assessed within six weeks of stroke and compared to healthy age-matched controls. All participants complete a high-resolution 3T MPRAGE MRI to evaluate brain volume (total, hippocampal, white matter hyperintensity [WMH]) and cortical thickness. Cognitive tasks include the Hopkins Verbal Learning Test-Revised (HVLT-R) to measure short- and long-term memory, and the Detection, Identification, and One-Back subtests of the computerised CogState battery to measure processing speed, attention, and working memory, respectively.

Results

We recruited seventy-nine ischaemic stroke patients (age=69 ± 13 years; 59 men; education=12.8 ± 3.9 years; NIHSS=3.5 ± 3.1; days post-stroke=25.4 ± 9.3) and 40 healthy controls (age = 69.7 ± 6 years; 25 men; education = 15.4 ± 4.5 years). Stroke patients performed worse than controls in all cognitive domains, after adjusting for age and education ($p<0.05$), and additionally, for mood ($p<0.05$). In stroke patients, greater cortical thickness was associated with better long-term memory ($p=0.03$) and attention ($p=0.001$), and faster processing speed ($p=0.002$). Larger hippocampal volume was associated with better short- and long-term memory, and faster processing speed ($p<0.05$).

Conclusion

Cognition is affected early after ischaemic stroke and associated with hippocampal volumes and cortical thickness. The tracking of hippocampal atrophy and cortical thinning over time after stroke may provide valuable information about long-term cognitive decline and risk of dementia.

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The Stroke Exercise Preference Inventory (SEPI): Development of a new tool

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Aim
Physical inactivity is highly prevalent after stroke, increasing the risk of poor health outcomes. Individual tailoring, which can improve adherence to exercise interventions, is often overlooked after stroke. In other medical populations (e.g., cancer, cardiac), there are tools available to identify individual exercise preferences, but none exist for stroke.

Methods
The pool of items to be considered for inclusion in the SEPI was derived from an extensive literature review and an expert panel discussion. Once items were finalised, we recruited community-dwelling stroke survivors and asked them to respond to each SEPI item (e.g., 'I like to exercise at home') on a scale from 0% (don't agree at all) to 100% (totally agree). These data were used in an exploratory factor analysis to identify factor structure and to refine the SEPI to a core item set. In addition, regressions determined associations between exercise preferences and disability, fatigue, depression and anxiety.

Results
A group of 134 stroke survivors (mean age = 64.0, SD = 13.3) completed the 35-item SEPI. Seven distinct factors were identified: 'supervision-support', 'confidence-challenge', 'health-wellbeing', 'similar others', 'exercise context', 'home-alone' and 'music-TV'. Item reduction resulted in a core set of 13 items, and a factor analysis of the SEPI-13 yielded the same 7-factor structure as the 35-item version. Associations were found between personal characteristics and several SEPI factors; for example, participants with anxiety were more likely to express a preference for exercising with similar others (p=0.01) than those without anxiety.

Conclusion
The SEPI-13 is a brief instrument that can be used to assess individual exercise preferences in stroke survivors. We hope it will be employed by health professionals to inform the development of tailored exercise programmes, not just to boost adherence but also to increase enjoyment of physical activity.

Bellows, S. T[1], Berkovic, S.F[1], Cops, E.J[1], Burgess, R[1], Garry, S.I[1], Epi4K Consortium[1,2,3,4,5,6]

Phenotypic Analysis of 303 Multiplex Families with Common Epilepsies

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Aim
To determine if specific epilepsy syndromic features aggregate within families and establish if these constitute distinct "familial syndromes," which likely differ in their genetics.

Methods
Families (n=303) with three or more individuals with unprovoked seizures were analysed across multiple centres. Affected individuals were phenotyped and classified according to a specific electro-clinical syndrome. Families were categorised based on broad syndromic groupings of affected family members: genetic generalised epilepsy (GGE), non-acquired focal epilepsy (NAFE), genetic epilepsy with febrile seizures plus (GEFS+), or mixed GGE and NAFE epilepsy, and, where possible, specific familial epilepsy syndromes.

Results
There were 1120 individuals with unprovoked seizures phenotyped in 303 families; 117 families had GGE. Absence epilepsies predominantly aggregated independently of other GGE syndromes (e.g., Juvenile Myoclonic Epilepsy). Severe GGE syndromes such as epilepsy with myoclonic-atonic seizures and eyelid myoclonia with absences generally occurred in families with early childhood-onset absence epilepsies. Familial NAFE was identified in 62 families; 23 with temporal lobe epilepsy, and 3 with frontal lobe epilepsy. Two unrecognised familial focal syndrome patterns emerged. Fifteen families had posterior quadrant epilepsies including 7 with occipito-temporal localization, 7 with temporo-parietal foci. Four families displayed familial focal epilepsy of childhood with multiple affected siblings suggesting recessive inheritance. Twenty-two families were categorised as GEFS+. 102 families had mixed epilepsy phenotypes; 38 had both generalised and focal epilepsy features within the same individual, and 38 had first or second degree relatives affected with GGE and NAFE.

Conclusion
Two key findings emerged. First, whilst generalized and focal epilepsies commonly segregate separately, families and individuals were frequently observed with both major forms. Secondly, specific patterns of syndromic aggregation were seen, including newly recognized forms of familial focal epilepsy. Whole exome sequencing is now underway and the clinical analysis will inform bioinformatic interpretation.

Growing collaborative partnerships to enhance stroke recovery research

Karen Borschmann & Julie Bernhardt on behalf of the collaborators

Background

Collaborative partnership models enhance innovation, reduce waste and develop new directions for research to improve the global burden of stroke. While strong partnerships exist in acute stroke, recovery and rehabilitation is a complex multidisciplinary area, and is in an earlier phase of collaboration. Here we describe recent collaborations formed with the aim of enhancing the development and conduct of stroke recovery research to improve health outcomes.

Method

Using a framework for partnerships described by Patel et al (2012), these collaborations are described by context, support, tasks, interaction processes, teams, individual and overarching factors. Anecdotal quotes were elicited from individuals within the partnerships to identify personal motivators for collaborating. Qualitative descriptions will be presented.

Results

Four major collaborations are illustrated: NHMRC Centre of Research Excellence Stroke Rehabilitation and Brain Recovery (CRE), Stroke Recovery and Rehabilitation Roundtable (SRRR), Activity to Improve Outcomes after Stroke (ACTIOnS) and Australian Stroke Research Network (ASRN). Although the mission, structure and funding of collaborations differ, all partnerships emerged from individuals' shared visions of improving outcomes for stroke survivors.

Motivators for collaboration included personal satisfaction and enjoyment of working with others with different skill sets, learning opportunities, an expectation of greater impact from collaborative rather than individual efforts and heightened professional reputation. Tangible benefits include increased track record and professional networks, opportunities for career advancement, less research waste through shared resources and data, and outputs that support individuals' other interests.

Conclusion

Effective collaborations can be developed by individuals from diverse disciplines who clearly articulate a shared vision, and develop an action plan under supportive leadership. The newest partnership, ASRN, aims to improve communication and increase opportunities for collaborative research across Australia. Many individuals collaborate pro bono, therefore recognition of their motivators may enhance the development and delivery of collaborative efforts.

Reference

Patel et al (2012) Applied Ergonomics 43: 1-26

Antihypertensive Treatment and Longitudinal Aβ Measures: Results from the AIBL Study of Ageing

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Introduction

Midlife hypertension is associated with a significantly higher risk of both AD-dementia and dementia due to cerebrovascular disease, and antihypertensive treatment is associated with better cognitive outcomes in clinical trials. Hypertension has been associated with cross-sectional Aβ PET imaging measures, however whether antihypertensive treatment influences the longitudinal accumulation of Aβ is not known. We used Aβ PET imaging to determine whether treatment of hypertension influenced accumulation of Aβ over six years' follow-up.

Methods

140 cognitively-normal participants from the AIBL Study with ^{11}C-PiB PET imaging at 18-monthly intervals over six years. Only participants with three or more PET assessments were included in analysis. Linear mixed models regression was performed for Aβ SUVR (dependent variable) and Baseline Hypertension Status, Antihypertensive Treatment, Time (and their two- and three-way interactions), as well as age, gender, education, APOE ε4, cholesterol, glucose, smoking and BMI.

Results

Age, APOE ε4, Gender, Time, and APOE ε4 x Time were all associated with longitudinal measures of Aβ burden. There was also a significant three-way interaction (Hypertensive x Antihypertensive Treatment x Time, $p = 0.02$), such that participants with untreated high blood pressure at baseline had greatest increases in A β over time. Findings remained significant after adjustment for BMI, cholesterol, glucose and smoking.

Conclusion

In hypertensive cognitively-normal controls, use of antihypertensive medication was associated with less Aβ accumulation over time compared with their untreated peers. Although observational only, this study provides some *in vivo* biomarker evidence supporting that lifestyle risk factor modification may mitigate the pathology of AD.

Cerebrovascular disease, Alzheimer's disease biomarkers and Longitudinal Cognitive Decline

Background

Cerebrovascular disease (CVD) is commonly seen to co-exist with Alzheimer's disease. Recent studies suggest that the two pathologies may mediate distinct, additive insults on cognitive performance. We examined the contribution of subclinical CVD (sCVD) and Aβ burden at baseline to risk for incident dementia over six years.

Methods

219 non-demented participants from the AIBL Study (169 normal cognition, 50 mild cognitive impairment) with 3-Tesla MRI and ^{11}C-PiB PET at baseline and clinical assessments over 18-monthly intervals over six years. Persons with a history of clinical stroke were excluded from AIBL. Participants were classified as Aβ+ if PiB Neocortical SUVR $\geq$1.5 and sCVD+ if MRI evidence of stroke or significant sCVD. Incident cognitive decline and dementia were determined from clinical panel consensus following neuropsychological test performance at each timepoint.

Cox proportional hazard regression was performed including Aβ and sCVD, age, *APOE* ε4 status, gender and education as covariates, and cognitive decline, or dementia, as outcome variables.

Results

25% of participants were classified as having cognitive decline and 16% progressed to dementia. While both sCVD and Aβ were associated with incident dementia in univariate analyses, the interaction between sCVD and Aβ was not. Only the association with Aβ remained significant after adjustment for all covariates (Hazard ratio [for decline] 3.8, $p < 0.001$; [for dementia] HR = 7.4, $p < 0.001$). In participants with normal cognition at baseline, risk for incident dementia at six years was only significant in those with Aβ and sCVD at baseline (HR = 25.9, $p = 0.004$).

Conclusion.

In this non-demented cohort, Aβ more strongly predicts incident cognitive decline and dementia than subclinical CVD. Subclinical CVD lowered the threshold for incident dementia in those with Aβ, although sCVD alone was not sufficient to predict future dementia. These data have implications for clinical trials in preclinical and prodromal AD.

Title of abstract:

Characteristics and differences of somatomsensory impairment post-stroke based on lesioned hemisphere.

Authors:

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Abstract:

Impairment in sensation post-stroke are common with estimates between 49 to 80%, however our understanding of the neural networks impacted and associations of severity of sensation impairment are lacking. In this study we examined tactile dysfunction using the Tactile Discrimination Test (TDT) and functional connectivity at rest between right handed healthy controls (n=18) and two right handed stroke subgroups – those with lesioning in the left hemisphere (n=17) and those with right hemisphere damage (n=19). Connectivity from four regions (left / right S1 / S2) were correlated for all groups to all brain voxels. Preliminary analysis showed spatially similar lesioning between the two stroke subgroups, severe tactile dysfunction in the contra-lesional hand and mild dysfunction in ipsi-lesional hand. Functional imaging results showed a range of differences between the three groups, including expected intra and inter-hemispheric connectivity in contra-lesional regions and marked changes in connectivity patterns between left and right lesioned groups relative to healthy controls. Correlations between TDT scores and connectivity were found. These results suggest the importance of lesion hemisphere when assessing change in function connectivity somatosensory linked networks and the potential usefulness of resting state analysis in assessing impact on tactile dysfunction.

Leeanne Carey,[1,2,3] Thomas Matyas,[1,2,3] Johanne Walker,[1,2,4] Richard Macdonell.[5]

SENSe: Individual characteristics that predict favorable outcomes for sensory rehabilitation after stroke

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Aim
Ability to benefit from rehabilitation may be influenced by individual patient characteristics. Our aim was to quantify the impact of individual patient characteristics on ability to benefit from a novel somatosensory discrimination training program. We hypothesised that hemisphere of lesion and initial severity of sensory loss would be associated with outcome success, but that prior duration of stroke and age would not.

Methods
Fifty stroke survivors with impaired sensation received sensory training within the SENSe randomised control trial (1). The primary outcome was change in a composite index of somatosensory discrimination capacity across measures of texture discrimination, wrist position sense and tactile object recognition. Impact of individual patient characteristics was investigated using regression analyses.

Results
Both immediate and delayed intervention groups showed improvement for the primary outcome. Improvements were clinically significant and maintained at 6-week and 6-month follow ups. We did not find any significant effect of hemisphere of lesion nor initial severity of sensory deficit on ability to benefit from sensory rehabilitation either immediately post-training or at follow up. We did find a significant age effect for the immediate intervention group such that older individuals benefitted greater when exposed to the extended period of intervention. Patients who are treated earlier after stroke show an earlier improvement but the gap is closed by the final follow up, such that all showed improvement whatever the interval since stroke

Conclusion
Stroke survivors improve following sensory discrimination training, irrespective of hemisphere of lesion and initial stroke severity. Older individuals may benefit from a longer period of training and earlier intervention post-stroke is associated with a greater rate of improvement early. The potential to benefit despite individual differences is highlighted.

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Amy Schneider[1], Gemma L. Carvill[2], Aijie Liu[3], Simone Mandelstam[4,5],Matthew Zemel[2], Mark Mackay[5], Stephen Malone[6], Michaela Waak[6], Yue-Hua Zhang[3], Heather C. Mefford[2], Ingrid E. Scheffer[1,4,5,7]

Severe infantile-onset epileptic encephalopathy caused by mutations in autophagy gene *WDR45*

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Objectives: To describe the phenotypic spectrum of epileptic encephalopathies (EEs) associated with mutations of *WDR45.*

Methods: Cases were ascertained by: targeted resequencing of *WDR45* coding region in 579 patients with EE, or commercial/research whole exome sequencing (WES). Segregation testing was performed for each case to determine if the variant was inherited or *de novo*.

Results: We identified 6 girls with truncating *de novo* mutations of *WDR45*. They presented with a spectrum of EE including infantile spasms (1), infantile spasms evolving to Lennox-Gastaut syndrome (LGS) (1), LGS (1), epilepsy with myoclonic-atonic seizures (1), EE unclassified and a girl with non-refractory epilepsy. Mean age of seizure onset was 12 months (range 7-17). Seizure type at onset included epileptic spasms (2), febrile tonic-clonic seizures (2), tonic seizures (1) and myoclonic seizures (1). All patients developed additional seizure types including focal impaired awareness seizures (5), myoclonic (3), absence (3), tonic (1), atonic and myoclonic-atonic (1) and bilateral tonic-clonic seizures. Non-convulsive status epilepticus occurred in 2 patients. Four had abnormal early development while 2 were normal. Regression associated with seizure onset occurred in 5. Four had profound developmental impairment, and two had moderate intellectual disability.

Conclusions: The X chromosome gene *WDR45* is associated with a spectrum of EE typically affecting girls. In addition to the Beta-Propeller Associated Neurodegeneration (BPAN) variant of Neurodegeneration with Brain Iron Accumulation (NBIA), we show that *de novo* mutations are associated with a range of EE with profound developmental consequences.

Cefepime susceptibility: an assessment of the performance of VITEK2 versus agar dilution

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[#]*K.L. and F.H. contributed equally to this work.*

Aim: Recent studies have shown significant error rates for cefepime susceptibility in *Enterobacteriaceae*, when determined by VITEK2 (bioMerieux), an automated susceptibility testing platform in use at Austin Microbiology. This study was conducted to determine the accuracy of cefepime susceptibility testing using VITEK2 when compared to the reference agar dilution method (ADM) in *Enterobacter* spp.

Methods: Non-duplicate *Enterobacter* isolates recovered between January to November 2015 were included if they demonstrated intermediate susceptibility or resistance to a ceftazidime (CAZ) or ceftriaxone (CRO) on initial testing using VITEK2. For comparison, ten highly susceptible isolates that had CAZ and CRO VITEK2 MICs of ≤1μg/mL were included for comparison. Cefepime susceptibility was determined using parallel testing by VITEK2 and ADM, according to CLSI guidelines. Interpretation of results as susceptible (S, MIC ≤2 μg/mL), susceptible dose dependent (SDD, MIC 4-8μg/mL) and resistant (R, MIC ≥16μg/mL) were performed according to the CLSI M100-S25 guidelines. Minor, major and very major discrepancies and category agreement were assessed according to the FDA definitions.

Results: Using ADM, the cefepime MIC ranged between ≤0.032 to 32μg/mL (MIC_{50} 1μg/mL, MIC_{90} 8μg/mL). Using VITEK2, the cefepime MIC ranged between ≤1 to 32μg/mL (MIC_{50} ≤1μg/mL, MIC_{90} 2μg/mL). 38/47 (80.9%) of more resistant *Enterobacter* spp. had category agreement. 10/10 (100%) of highly susceptible isolates were concordant. Overall, category agreement was 84.2% (48/57). All of the discrepancies were minor. All nine of these, apart from one, were instances where the isolate was more resistant by the reference ADM. All isolates with discrepant results had cefepime VITEK2 MIC ≥2 μg/mL.

Conclusions: VITEK2 demonstrated a high minor discrepancy rate and poor category agreement with ADM. In patients who are being treated with cefepime for *Enterobacter* infections with isolates that have a VITEK2 cefepime MIC ⩾2μg/mL, an alternative method of susceptibility testing should be used.

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PAM-2: a novel carbapenemase identified in *Pseudomonas alcaligenes* through bacterial whole-genome sequencing

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Aim

Whole-genome sequencing (WGS) is a powerful technology that is revolutionising clinical medicine. In clinical microbiology and infectious diseases, WGS of microbial pathogens provides detailed data on each organism allowing characterisation and comparison of each isolate at the highest resolution. Here, we describe a novel metallo-beta-lactamase – an enzyme capable of conferring resistance to carbapenem antibiotics (a "carbapenemase"), and one of the most urgent antimicrobial resistance threats worldwide – identified through WGS.

Methods

Gram-negative bacteria isolated at Austin Health resistant to meropenem and other carbapenems were screened for potential carbapenemase production using a Blue-Carba test, a colourimetric test that detects the hydrolysis of carbapenems by carbapenemase enzymes. Test-positive isolates were referred to the Microbiological Diagnostic Unit Public Health Laboratory for molecular characterisation using multiplex PCR and WGS.

Results

After screening meropenem-resistant isolates, one isolate was found to have a negative PCR for carbapenemases, despite being repeatedly positive by Blue-Carba. However, through WGS, a gene encoding a class B3 metallo-beta-lactamase with 76% amino acid similarity to a beta-lactamase found in *Pseudomonas otitidis*, and 65% similarity to the L1 metallo-beta-lactamase found in *Stenotrophomonas maltophilia* was identified in the assembled genome sequence. A GenBank search found an almost identical beta-lactamase, PAM-1, capable of conferring resistance to carbapenems in *Pseudomonas* spp., though it differed by three amino acid substitutions. No flanking mobile genetic elements were identified, suggesting that the carbapenemase, subsequently named PAM-2, was likely intrinsic to *P. alcaligenes*. Our isolate was phylogenetically distant from other *P. alcaligenes* genomes in GenBank based on core-SNP and pan-genome analyses.

Conclusion

PAM-2 is a novel metallo-beta-lactamase allele identified in a *Pseudomonas alcaligenes* isolate through WGS. Our findings demonstrate the power of WGS surveillance to understand the genetic mechanisms and spread of antimicrobial resistance in bacterial pathogens.

The Impact of an Antimicrobial Stewardship Lead Antibiotic Allergy Testing Program on Prescribing

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Aim

Antibiotic allergy “labels” (AAL) are highly prevalent in the hospital setting and impact antibiotic prescribing and patient outcomes. We report on a multicenter antimicrobial stewardship (AMS) lead antibiotic allergy-testing (AAT) program.

Methods

A prospective multicenter study was undertaken at Austin Health and Peter MacCallum Cancer Centre from 1st May 2015 to 30th June 2016, evaluating an AMS lead AAT program. Baseline demographic, AAL history, AAT results and antibiotic usage for the 12-months prior to and 90-days post AAT were recorded. Antibiotic prescriptions were defined as appropriate (score 1 or 2) or inappropriate (score 3 or 4) as per the previously published National Antimicrobial Prescribing Survey definition. A patient was ‘de-labeled’ if ≥ 1 AAL was removed. A narrow penicillin course was defined as penicillin V/G, flucloxacillin/dicloxacillin or amoxicillin. Antibiotic prescribing was compared for the period 12-months prior and 90-days post AAT in those ‘de-labeled’.

Results

One hundred and forty-eight patients were referred, 80%(118/148) undertaking AAT. The median age was 59 (21,70), 37% male, 51% immunocompromised and 90% avoiding penicillins. From the 118 patients, 226 AALs were identified, 75% consistent with an immune mediated mechanism. Ninety-one percent had a revised AAL, 82% ‘de-labeled’. Eight-four percent (55/66) of penicillin allergy labels were removed. Comparing antibiotic usage pre-AAT versus post-AAT in those ‘de-labeled’, there was an increase in narrow spectrum penicillin (9% vs. 29%, p=0.0003) and beta-lactam/beta-lactamase inhibitor combination (5% vs. 20%, p=0.0002) antibiotic courses. A reduction in quinolone (15% vs. 4%, p=0.007), vancomycin (9% vs. 1%, p=0.01) and clindamycin use (9% vs. 0%, p=0.0001) post-AAT was noted. Inappropriate prescriptions were lower post AAT (35% vs. 5%, p=0.001)

Conclusions

A multidisciplinary AMS lead AAT model successfully removed AALs and impacted antibiotic prescribing; increasing narrow spectrum penicillin usage, reducing restricted antibiotic prescription and improving appropriateness. Implementation of AAT within AMS programs should be considered as a novel strategy to improve prescribing.

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An audit of melatonin prescribing for delirium treatment and prevention at a large tertiary care hospital

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Aim
Melatonin, an endogenous hormone, is involved in regulation of the circadian sleep-wake cycle. Dysregulation of the sleep-wake cycle is a hypothesised contributing cause of delirium, as well as a cardinal symptom. Pharmacotherapeutic options targeted at restoring the sleep-wake cycle include synthetic melatonin and ramelteon, a melatonin receptor agonist. Clinical trials of these agents have yielded mixed results. Nevertheless, they appear to have a favourable side effect profile compared to antipsychotics, which are often used for delirium treatment. Our aim was to describe the prescribing of melatonin for delirium across three inpatient units at a large tertiary care hospital.

Methods
A retrospective audit was undertaken of patients prescribed melatonin whilst an inpatient of the Orthopaedic, General Medicine and Geriatric units between January 2014 and December 2015. Patients were identified through pharmacy dispensing records. Data regarding previous melatonin use, indication, sex, age, comorbities and concurrent use of antipsychotic medication was collected from hospital medical records

Results
The number of inpatients prescribed melatonin increased from 32 in 2014 to 144 in 2015. Melatonin was newly prescribed during hospitalisation for 106/176 (60%) patients. 42/106 (40%) of new melatonin prescriptions were for delirium treatment and 2/106 (2%) were for delirium prevention, with 93% of these prescriptions written in 2015. Patients prescribed melatonin for delirium treatment had a mean of 6 comorbidities and 8 regular medications; 55% were female and 50% had a history of cognitive impairment or dementia. 28/42 (67%) of patients prescribed melatonin for delirium treatment also received a prescription for new antipsychotic medication. The most common dose of melatonin for patients with delirium was 2mg at night. Doses >2mg were used in 21% of cases.

Conclusion
Delirium was a common and increasing indication for initiating melatonin therapy. Further investigation of the efficacy and appropriate dose range of this treatment is warranted.

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A small molecule diminazene aceturate inhibits acute and chronic hepatobiliary fibrosis in mice

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Aim
A small molecule diminazene aceturate (DIZE) is a potential antihypertensive, anti-inflammatory and antifibrotic drug. Although it was shown that DIZE works by activation of angiotensin converting enzyme 2 (ACE2) of the renin angiotensin system (RAS), recent studies have confirmed that its action is ACE2 independent. However, no study has looked at DIZE's potential as an antifibrotic agent in hepatic fibrosis. Therefore, the present study was undertaken for the first time to determine the therapeutic efficacy of DIZE in both acute and chronic hepatobiliary fibrosis.

Methods
Treatment efficacy in acute and chronic hepatobiliary fibrosis was determined using bile duct ligated (BDL) C57BL/6 mice and Mdr2-KO mice, respectively. Mice in each treatment groups received continuous infusions of DIZE (10mg/kg/day) via subcutaneous osmotic minipumps for 2 weeks (BDL) and 4 weeks (Mdr2-KO). The diseased control groups received saline infusion. At completion liver tissues were collected to determine fibrosis by picrosirius red staining. Profibrotic, proinflammatory and ACE2 gene expressions were detected using real time qPCR. Liver ACE2 activity, and angiotensin II and angiotensin 1-7 peptide levels were also determined.

Results
DIZE significantly ($p<0.05$) reduced ALT, ALP and AST. The liver fibrosis was significantly reduced by DIZE (BDL=$p<0.01$, Mdr2-KO=$p<0.05$) compared to saline-infused groups. DIZE significantly downregulated the expression of collagen 1 (BDL and Mdr2-KO=$p<0.05$), profibrotic TGF-β1 (BDL=$p<0.05$, Mdr2-KO=$p<0.05$) and CTGF (BDL and Mdr2-KO=$p<0.05$), proinflammatory IL-6 (BDL=$p<0.05$, Mdr2-KO=$p<0.01$) and MCP-1 (BDL=$p<0.001$, Mdr2-KO=$p<0.01$) and hepatic myofibroblastic marker α-SMA (BDL and Mdr2-KO=$p<0.05$). However, there was no difference in ACE2 expression and activity and angiotensin II to angiotensin (1-7) ratio between the two groups.

Conclusion
In summary, DIZE-induced significant reduction in hepatic fibrosis was accompanied by reduced profibrotic and proinflmmatory cytokine levels without affecting ACE2 activity. We conclude that DIZE is a potent antifibrotic drug in mice and thus a potential therapeutic agent for hepatic fibrosis.

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ACE2-AAV gene therapy ameliorates severe biliary fibrosis in mice

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Aim
Most chronic biliary diseases including primary sclerosing cholangitis (PSC) has no therapy except for liver transplantation. We have recently shown that liver-specific adeno-associated viral (AAV) vector carrying angiotensin converting enzyme 2 (ACE2) markedly reduced biliary fibrosis in a short-term model of bile duct ligated mice(1). Therefore, the present study investigated the antifibrotic effect of ACE2 therapy in Mdr2-KO mice that produce pathological lesions closely resembling to those of PSC.

Methods
Single i.p. injection of ACE2-AAV or a control vector carrying human serum albumin (HSA-AAV) was administered to 7-month-old Mdr2-KO mice. Two months post-treatment, hepatic fibrosis was determined using picrosirius red staining and hydroxyproline assay. ACE2, pro-fibrotic and pro-inflammatory gene expressions and liver biochemistry were determined using qPCR and liver function test, respectively.

Results
ACE2 treatment in mice with severe biliary disease led to a 160-fold upregulation of ACE2 gene expression compared with that in HSA-treated animals. As a result, ACE2 therapy significantly reduced hepatobiliary fibrosis, as evidenced by reduced picrosirius red ($p<0.0001$, 4-folds) and hydroxyproline content ($p<0.05$). A significant reduction in collagen 1 ($p<0.05$), a major fibrosis marker gene, in ACE2-treated mice was associated with a significant reduction in alpha-SMA gene expression ($p<0.0001$), a marker of hepatic stellate cell activation. Consistent with this, ACE2 therapy significantly ($p<0.01$) reduced plasma ALT levels, suggesting that liver injury was also reduced in ACE2-treated Mdr2-KO mice compared with that in control mice.

Conclusion
In summary, ACE2 gene therapy ameliorates liver injury and severe biliary fibrosis in a mouse model of PSC. ACE2, the major enzyme in the alternate axis of the renin angiotensin system that cleaves the profibrotic peptide angiotensin II to antifibrotic peptide angiotensin (1-7), is thus responsible for the inhibition of biliary fibrosis. We conclude that liver-specific ACE2 over-expression could be a potential therapy in patients with severe biliary fibrosis such as PSC.

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Rajapaksha DIG, [1], Andrikopoulos S, [1], Angus PW, [1,2], Herath CB, [1],.

ACE2-AAV gene therapy ameliorates liver fibrosis in diabetic mice with non-alcoholic fatty liver disease

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Aim
Non-alcoholic fatty liver disease (NAFLD) is the most common liver disorder in developed countries including Australia. It is frequently associated with obesity and diabetes. However, there are no effective drugs to treat this condition. Angiotensin converting enzyme 2 (ACE2) is the major enzyme of the alternate axis of the renin angiotensin system that generates anti-fibrotic peptide angiotensin-(1-7) from pro-fibrotic peptide, angiotensin II. Because angiotensin II is implicated in liver fibrosis, we investigated the therapeutic potential of ACE2 in a dietary NAFLD model with diabetes.

Methods
C57BL/6 mice were fed high fat (20%) high cholesterol (2%) (HFHC) diet to induce NAFLD. They were rendered diabetic by two consecutive daily injections of streptozotocin (STZ) after 15 weeks of HFHC diet. Single i.p. injection of ACE2-AAV (ACE2-adeno associated virus) or a control vector carrying human serum albumin (HSA-AAV) was administered to mice 15 weeks post-STZ injection and the animals were sacrificed 10 weeks post-ACE2 therapy. Hepatic fibrosis was determined using picrosirius red staining. ACE2 and pro-fibrotic gene expressions were determined using qPCR.

Results
ACE2 therapy increased hepatic ACE2 gene expression by 75-folds ($p<0.01$) compared to the control vector injected group. This has led to a significant reduction ($p<0.01$) in hepatic fibrosis in diabetic NAFLD mice compared with that in the control vector injected mice. Reduced fibrosis in ACE2-treated mice was accompanied by significant reductions in gene expression of major fibrosis marker, collagen 1 ($p<0.01$), and hepatic stellate cell activation marker, alpha smooth muscle actin ($p<0.05$) compared with the control mice.

Conclusion
ACE2 gene therapy significantly ameliorated liver fibrosis in NAFLD mice with diabetes. This has major implications in diabetic patients with liver disease as diabetes is known to exacerbate liver injury. We therefore conclude that ACE2 gene therapy may be a novel therapeutic strategy to treat NAFLD in patients with diabetes.

Neutrophil-lymphocyte ratio is increased in diabetic kidney disease with albuminuria

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Introduction: Systemic inflammation has been linked with the development of diabetic kidney disease. Neutrophil-lymphocyte ratio (NLR) is a measure of systemic inflammation. We hypothesised that a higher NLR is associated with diabetic kidney disease with albuminuria.

Methods: 592 patients with either type 1 (n=114) or type 2 (n=478) diabetes attending an Austin Health Diabetes Clinic were recruited in a prospective study. For each clinic visit during the 2.5 year study period NLR was calculated by dividing total neutrophil count by total lymphocyte count as measured in the full blood examination. Albumin excretion rate from a 24h urine collection and estimated glomerular filtration rate (eGFR), calculated by the CKD-EPI formula, were recorded at the same time point. A multivariate regression analysis was undertaken to determine the associations between NLR and diabetic kidney disease with albuminuria (eGFR <60ml/min/1.73m^2 and albumin excretion rate ≥20ug/min) controlling for age, HbA1c, fasting cholesterol and C-reactive protein.

Results: NLR values were independently and significantly higher, (OR 1.44, 95% CI (1.01-2.05)), in patients with diabetic kidney disease with albuminuria (eGFR <60ml/min/1.73m^2 and albumin excretion rate ≥20ug/min) (p=0.046). There was no significant independent association seen between NLR and albumin excretion rate ≥20ug/min nor between NLR and eGFR <60ml/min/1.73m^2 individually.

Conclusion: Higher NLR is independently associated with diabetic kidney disease with albuminuria, suggesting the presence of systemic inflammation in these patients. Further interventional studies will be needed to investigate the nature of the relationship between these variables; whether cause, effect or association.

Key Words:
Neutrophil-lymphocyte ratio (NLR)
Diabetic kidney disease
Estimated glomerular filtration rate (eGFR)
Albumin excretion rate

Androgen action *via* the Androgen Receptor in the brain positively regulates muscle mass by actions in fast-twitch muscle fibres

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Androgens are one of the few agents proven to have anabolic effects in muscle, however, their mechanism of action is not completely understood.

Aim: To determine the contribution of androgens acting *via* the AR in neurons to regulate skeletal muscle mass and function.

Methods: We generated a mouse model in which the AR is deleted in neurons within the brain (neuron-ARKOs) by breeding our floxed AR mouse line with CamKIIα-iCre mice.

Results: Characterisation of our neuron-ARKO model shows that AR mRNA is undetectable in the cortex and olfactory bulb while deletion of the *AR* gene within the forebrain and hypothalamus is highly efficient at >99%. The AR is deleted to a lesser extent in the cerebellum and pituitary of neuron-ARKOs. Serum testosterone is increased 2-fold in neuron-ARKO male mice at 12 weeks of age ($P<0.05$), which is most likely caused by the disruption to the negative feedback of the hypothalamic-pituitary-gonadal axis as a result of AR deletion in the hypothalamus and pituitary. The increase in serum testosterone would be expected to increase muscle mass. However, despite elevated testosterone levels, neuron-ARKO males show a 13% decrease in gastrocnemius muscle mass ($P<0.05$) consisting of both fast and slow twitch fibres and an 11% decrease in the mass of the fast twitch muscle *extensor digitorum longus* ($P<0.001$). In contrast there is no change in the mass of the slow twitch *soleus* muscle. Preliminary analyses show a decrease in the cross-sectional area of the fast-twitch type 2B fibres in the neuron-ARKOs compared to WT controls ($P=0.07$).

Conclusion: These data provide the first evidence for a role of androgens, acting *via* the AR in the brain, to positively regulate muscle mass. Furthermore, these data suggest that the action of androgens on muscle mediated *via* the AR in the brain is directed towards fast-twitch muscles.

Title: Short and mid-term renal function in patients with type 1 and type 2 diabetes during and after pregnancy

Authors:

Cara Tanner, Jas-mine Seah, Christine Houlihan, Elif Ekinci

Introduction:

Pregnancy does not unfavourably effect renal function in the majority of women with type 1 (T1DM) and type 2 diabetes (T2DM). However, some women affected by moderate to severe diabetic kidney disease (DKD) experience an irreversible decline in renal function following pregnancy. We conducted an exploratory retrospective study of a single tertiary obstetric hospital with the aim to investigate the short- and mid-term changes in renal function associated with pregnancy in women with pre-existing T1DM, T2DM, and healthy controls. We hypothesize that normalisation of renal function occurs more rapidly in healthy controls.

Methods:

Biochemical characteristics of women with T1DM (n=91), T2DM (n=106) and healthy controls (n=119) were recorded across multiple time points 2 years pre- and post-pregnancy, and during each trimester of pregnancy from state-wide pathology services. Renal function was evaluated using the Chronic Kidney Disease Epidemiology Cohort (CKD-EPI) formula to estimate glomerular filtration rate (eGFR). Quantile regression with clustered data was used to assess pregnancy-associated changes in renal function over time in each group, using eGFR at 0 – 24 months pre-pregnancy as baseline renal function. Age and duration of diabetes were included in the analysis as independent variables.

Results:

All three groups of women demonstrated a physiological increase in eGFR during pregnancy, with renal function reaching a peak during the second trimester. The greatest rise was observed in healthy controls (25 mL/min/1.73m^2; p=0.001), which was significantly higher than in women with T1DM and T2DM. Compared to controls, the median rise in renal function was 17 mL/min/1.73m^2 (p <0.001) and 14 mL/min/1.73m^2 (p <0.001) lower in women with T1DM and T2DM, respectively. Normalisation of renal function to baseline occurred in all 3 groups by 6 months. Renal function returned to baseline quickest in healthy controls at a median rate of 0.08 mL/min/1.73m^2/day (p <0.001), followed by women with T1DM at a rate of 0.07 mL/min/1.73m^2/day (p <0.001). The slowest rate was observed in women with T2DM (0.04 mL/min/1.73m^2/day), which was statistically different from women with T1DM (p <0.001).

Conclusion:

Acknowledging the limitation of eGFR as a measure of renal function in pregnancy, the degree of hyperfiltration appears to be higher in controls than pregnancies affected by pre-existing diabetes. Normalisation of renal function in women with T2DM is significantly slower compared to healthy controls and women with T1DM, although the reason for this is unclear. Despite the slower recovery in renal function, pregnancy does not appear to be associated with worsening renal function in this cohort of T1DM and T2DM women with relatively preserved renal function.

Title Oestradiol depletion in premenopausal women with non-metastatic breast cancer is associated with severely deteriorated cortical and trabecular microstructure

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Key words cortical and trabecular microstructure; endocrine therapy for breast cancer

Aim Treatment of premenopausal women with breast cancer using ovarian suppression (OS) and aromatase inhibition (AI) causes more rapid and complete oestradiol depletion than natural menopause. Oestrogen deficiency increases remodelling rate, prolongs osteoclast lifespan, and shortens osteoblast life span.[1] Consequently, each of the many more remodelling events remove more bone, more rapidly. We therefore hypothesised that the remodelling imbalance produces severe microstructural deterioration while the rapid remodelling reduces matrix mineral density (MMD) of the reduced matrix volume.

Methods At this early stage of this case-control study, we have recruited 7 premenopausal women with breast cancer (mean age 45 years, range 38-51) treated with OS and AI for 38 months (range 11 – 118 months), 38 healthy age-matched premenopausal women and 38 healthy women at least ten years post natural menopause (mean age 62 years, range 60-65). Six cases had chemotherapy as part of their treatment. Women treated with tamoxifen for >6 months or anti-resorptives were excluded. Images of the distal radius and distal tibia were acquired using high-resolution peripheral quantitative computed tomography. Radial and tibial microstructure and MMD were quantified using StrAx1.0.[2] Independent t-tests were used to compare morphology. Interim analysis was performed using SPSS v22. Results are presented as mean difference (95% confidence interval).

Results Cases had 10.34% (5.45 to 15.24) higher cortical porosity than premenopausal age matched controls ($p<0.001$). Despite being nearly two decades younger than women 10 years post natural menopause, cases had comparable cortical porosity [4.38% (-1.61 to 10.37), $p = 0.15$]. Cases also had -2.53% (-4.24 to -0.81, $p = 0.002$) and -0.79% (-1.58 to -0.01, $p = 0.048$) lower trabecular bone volume relative to pre- and postmenopausal controls respectively, due to fewer, not thinner trabeculae, and -1.12% (-1.81 to -0.42, $p = 0.002$) and -0.79% (-1.58 to -0.01, $p = 0.048$) lower MMD than these controls respectively. Results at the tibia were similar (not shown).

Conclusions Severe and perhaps irreversible microstructural deterioration and the longevity of these women suggest that there is a need to investigate the role of early intervention to preserve bone strength.

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Improving the Transition of Care of Inpatients with Type 2 Diabetes

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Background:
Hyperglycaemia in inpatients with type 2 diabetes may necessitate initiation of injectable diabetes therapies during hospitalization to improve glycaemic control. Adapting to this intensification of therapy can be difficult for inpatients, and diabetes education performed in the hospital setting is subject to a number of factors which may limit its effectiveness. Home-based diabetes education is emerging as a tool that may facilitate effective diabetes education in patients commencing injectable diabetes therapies.
Aims:
A pilot feasibility randomised-controlled trial was conducted to determine whether diabetes care, comprising in-home diabetes education by a credentialed diabetes educator (CDE) and early post-discharge assessment by an endocrinologist, would safely enable transition from hospital to home on injectable diabetes therapies.

Methods:
Inpatients commencing injectable diabetes therapies were randomised to receive in-home diabetes education within 48 hours following discharge, or usual care. The intervention group had endocrinologist follow-up within 4 weeks and at 16 weeks post-randomization. The primary outcome was safety (hospital admission, emergency department presentation), and secondary outcomes were HbA1c, patient satisfaction with care (measured by DTSQ) and length of hospital stay.

Results:
103 inpatients were randomized to in-home diabetes education or usual care. After 16 weeks of follow-up, hospital presentations and readmissions did not differ between groups. There was one diabetes-related hospital presentation following discharge in each group. Preliminary statistical analysis found no difference in patient satisfaction or ΔHbA1c between groups.

Conclusion
For patients commencing injectable therapies, the results of this pilot feasibility RCT suggest that the use of a transitions diabetes team, comprising CDE for in home diabetes education and endocrinologist follow-up is a safe and acceptable model of care.

Tumour Necrosis Factor-alpha Receptor 1 and 2 are Reduced in patients with Type 1 Diabetes and Hyperfiltration

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Introduction

Soluble Tumour Necrosis Factor-alpha receptors (sTNF-aR) 1 and 2 may improve the prediction of future risk of progression to diabetic kidney disease (DKD) in patients with type 1 (T1DM) and type 2 diabetes (T2DM). sTNF-aR 1 and 2 may be associated with hyperfiltration, which has not been previously studied. In a prospective cross-sectional study, we aimed to determine the relationship between sTNF-aR 1 and 2 and measured glomerular filtration rate in patients with T1DM and renal hyperfiltration, defined as directly measured GFR (mGFR)≥120ml/min/1.73m^2, compared to those without.

Methods

29 patients with T1DM had mGFR determined using Tc-99m-diethylene-triamine-pentaacetate (DTPA) nuclear medicine GFR with Brochner-Mortensen correction. Serum sTNFaR1 and 2 were measured using the Luminex multiplex assay. Difference in sTNFaR1 and R2 values between patients with and without hyperfiltration were then compared.

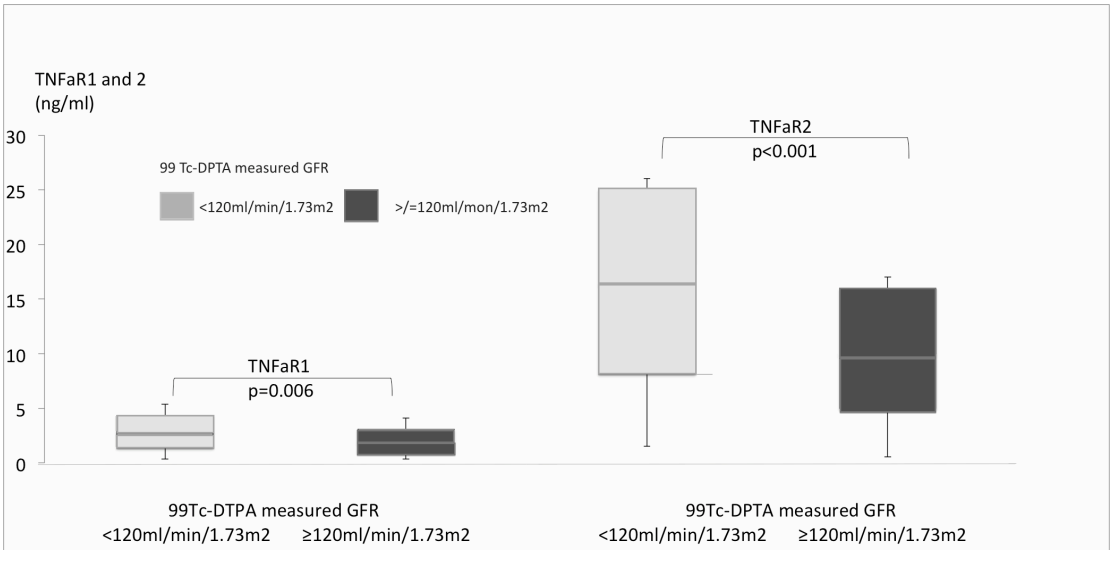
Results

sTNFR1 and 2 correlated well with mGFR (r^2 -0.7 and -0.8, respectively, p<0.001). The median mGFR was 124 (IQR 121-129) in the hyperfiltration group (n=10) and 94 (IQR 70-105, n=19) in the non hyperfiltration group (p<0.0001). Both sTNFaR1 and sTNFaR2 were significantly lower in the hyperfiltration group (sTNFaR1: median 1.2ng/ml (IQR 0.9, 1.4), p=0.006, and sTNFaR2: median 6.1ng/ml (IQR 4.8, 6.7) p=0.0004) compared to the non hyperfiltration group (sTNFaR1: median 1.6ng/ml (IQR 1.4, 2.6) and sTNFaR2: median 8.7ng/ml (IQR 8.0, 10.8), Figure).

Conclusion:

Serum TNFaR1 and 2 are lower in patients with type 1 diabetes and hyperfiltration. These results suggest that inflammatory processes are not associated with the state of hyperfiltration. However, lower levels of these receptors could also be related to their increased clearance in the hyperfiltering state.

Figure1: Soluble TNFaR1 and 2 in patients with hyperfiltration and non hyperfiltration



Testosterone Treatment Increases Loss of Body Fat and Prevents Loss of Lean Mass in Obese Men with Low Testosterone Levels on a Hypocaloric Diet: A randomized trial

. ClinicalTrials.gov NCT01616732

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Importance: Obesity is strongly associated with low testosterone levels in men. Whether testosterone treatment has benefits on body composition over and above caloric restriction is unknown.

Objective: To determine whether testosterone treatment augments diet-induced loss of fat mass and prevents loss of muscle mass.

Design: Randomised double-blind, placebo-controlled trial.

Participants: Obese men with a total testosterone level ≤12nmol/L.

Intervention: 100 participants receiving 10 weeks of a very low energy diet (VLED) followed by weight maintenance were randomised at baseline to 56 weeks of intramuscular testosterone undecanoate (n=49, cases) or placebo (n=51, controls).

Main Outcomes: The primary outcome was the between-group difference in fat mass at study end (56 weeks), quantified by dual-energy X-ray absorptiometry (DXA). Other main outcomes included change in lean mass, visceral fat and body weight.

Results: Cases and controls lost the same weight (testosterone -11.4kg; placebo -10.9kg) at study end (p=0.80). Cases had greater reductions in total fat, mean adjusted between-group difference (MAD) -2.9kg, p=0.04, and in visceral fat, MAD -2,678mm^2, p=0.04. Although both groups lost the same lean mass following VLED (cases -3.9kg; controls -4.8kg, p=0.36), cases regained lean mass (3.3kg, p<0.001) during weight maintenance, in contrast to controls, 0.8kg, p=0.29 so at study end, cases had an attenuated reduction in lean mass compared to controls, MAD 3.4kg, p=0.002.

Conclusions: Among obese men with lowered testosterone, testosterone treatment augmented diet-induced loss of total and visceral fat mass, and prevented diet-induced loss of lean mass. While men receiving placebo lost both fat and lean mass, the weight lost with testosterone treatment was almost exclusively due to loss of fat.

Disclosures

MNTF was supported by a postgraduate scholarship (1055305) and MG by a Career Development Fellowship (1024139) both from the NHMRC. BayerPharma provided testosterone, placebo and financial support to conduct investigations, but had no other role in the trial.

Dieting but not testosterone treatment improves androgen deficiency-like symptoms in obese men with lowered testosterone. ClinicalTrials.gov NCT01616732

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Importance: Obese men with modest reductions in circulating testosterone commonly report non-specific symptoms consistent with androgen deficiency. Whether testosterone treatment leads to improvements in androgen deficiency-like symptoms over and above the effects of dieting is unknown.

Objective: To determine whether testosterone treatment improves androgen deficiency-like symptoms among dieting men.

Design: Secondary analysis of a randomised double-blind, placebo-controlled trial.

Participants: Obese men with a total testosterone level ≤12nmol/L.

Intervention: 100 participants receiving 10 weeks of a very low energy diet (VLED) followed by weight maintenance were randomisedat baseline to 56 weeks of intramuscular testosterone undecanoate (n=49, cases) or placebo (n=51, controls).

Main Outcomes: The pre-specified outcomes were the between-group differences in Aging male symptoms score (AMS) and international index of erectile function (IIEF).

Results: Cases and controls lost the same weight after VLED (testosterone -12.0kg; placebo -13.5kg, p=0.40) and maintained this at study end (testosterone -11.4kg; placebo -10.9kg, p=0.80).There was no difference in AMS between groups after VLED (mean adjusted difference (MAD) -1.6, 95% CI -4.9; 1.8, p=0.35) or at study end (MAD -2.9, 95%CI -6.5; 0.8, p=0.12). Both cases and controls had improvements in AMS by approximately 20% after VLED (cases from 35.6 to 27.3 and controls from 34.6 to 27.9, both $p < 0.05$) which was maintained in cases (improved by 4.8 points, $p < 0.001$ relative to baseline) but not controls (improved by 1.9 points, $p = 0.15$) compared to baseline. Men had mild erectile dysfunction at baseline (IIEF cases 20.0, controls 19.3), with no between or within group differences during the study.

Conclusions: In relatively healthy obese men, androgen deficiency-like symptoms are primarily a consequence of excess weight rather than due to their reduced testosterone levels. For symptomatic benefit, weight loss rather than testosterone treatment should be the first line approach.

Disclosures

MNTF was supported by a postgraduate scholarship (1055305) and MG by a Career DevelopmentFellowship (1024139) both from the NHMRC.BayerPharmaprovided testosterone, placebo and financial support to conduct investigations, but had no other role in the trial.

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Pre-treatment with Dual Anti-platelet Therapy in STEMI – Does it Make Any Difference?

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Aim
International guidelines recommend that all patients presenting with STEMI receive aspirin and a P2Y12 inhibitor as early as possible. However, the safety and efficacy of pre-treatment with dual anti-platelet therapy before angiography is a matter of ongoing debate. We aim to ascertain whether pretreatment with dual antiplatelet therapy is associated with improved clinical outcomes

Methods
Consecutive patients from the Melbourne Interventional Group registry (2005-2014) who presented with STEMI and underwent primary PCI were included. Those who received any P2Y12 inhibitor prior to arrival in the catheterisation laboratory were included in the pre-treatment group; the remaining patients were included in the no pre-treatment group. The co-primary endpoints were TIMI flow grade, 12-month mortality, myocardial infarction and major adverse cardiac events. The safety endpoint was in-hospital bleeding.

Results
Of the 2,807 patients included 892 (31.8%) received pre-treatment. Clopidogrel was the most common P2Y12 inhibitor used (79.6%). Pre-treatment was associated with less thromboaspiration and GPIIb/IIIa-inhibitor use (both $p<0.01$) but there was no difference in initial TIMI flow grade or stent thrombosis. Pre-treatment was associated with lower 12-month mortality (4.7% vs. 7.0%, $p=0.02$), but similar rates of myocardial infarction (3.3% vs. 3.9%, $p=0.39$) and MACE (13.0% vs. 14.1%, $p=0.43$). There was no difference in in-hospital bleeding (3.6% vs. 3.9%, $p=0.67$). Multivariate analysis revealed pre-treatment was not an independent predictor of 12-month mortality (OR 0.79; 95% CI 0.5-1.3, $p=0.32$).

Conclusion
Pre-treatment with a P2Y12 inhibitor is safe and associated lower use of GPIIb/IIIa inhibitors and thromboaspiration devices. In this large real-world cohort, it was not an independent predictor of improved clinical outcomes at 12-months.

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Conservative oxygen therapy in cardiac surgery: A prospective before and after observational study

Introduction
The dominant approach to oxygen therapy for cardiac surgical patients is to target SpO2 levels >96%. While hypoxia is carefully avoided, there too are concerns over hyperoxia following cardiac surgery. A more conservative approach may feasibly and safely reduce exposure to hyperoxaemic states.

Method
We performed a before-and-after study to evaluate the introduction of a conservative approach to oxygen therapy (target SpO2 88-92% using the lowest FiO2) for cardiac surgical patients between January - October, 2013 (before period) and January – October, 2014 (after period). Our primary outcome was the proportion of arterial blood gases (ABGs) classified into hypoxaemia (PaO2 <60 mmHg), normoxaemia (PaO2 60-120 mmHg) and hyperoxaemia (PaO2 >120 mmHg) ranges for each period. Secondary outcomes were FiO2, mechanical ventilation (hrs), ICU and hospital length of stay and ICU mortality. Values are reported as median (IQR) or n (%).

Results
We studied 9599 ABGs (4519 before and 5080 after period) from 546 patients (547 before and 299 after) with a median age of 66 years (67 v 65 yrs, p=0.10). In the before and after period respectively, FiO2 was 30% (30, 40%) vs 30% (25, 40%) (p<0.01). PaO2 was 89.1 mmHg (73.6, 113 mmHg) vs 80.5 mmHg (69.4, 98.7 mmHg) (p<0.01). There were 175 (3.9%) vs 307 (6.0%) ABGs classified as hypoxaemic; 3418 (75.6%) vs 4118 (81.1%) as normoxaemic; and 926 (20.5%) vs 655 (12.9%) as hyperoxaemic (p<0.01). Duration of mechanical ventilation was 10 hrs (7, 15 hrs) vs 8 hrs (5, 13 hrs) (p<0.01). No significant differences were observed for ICU or hospital length of stay, or ICU mortality between groups.

Conclusion
Our findings provide preliminary evidence to support further investigations of conservative oxygen therapy and its impact on patient outcomes for cardiac patients undergoing cardiac surgery.

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NEAR-INFRARED SPECTROSCOPY IN ADULT CARDIAC SURGERY PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background/Aim
Despite the importance of cerebral tissue oxygen saturation ($SctO_2$), normal values of near-infrared spectroscopy (NIRS) derived $SctO_2$ in adult cardiac surgery patients have not been defined and the impact of peri-operative interventions to improve $SctO_2$ remains uncertain. Therefore, in adult cardiac surgical patients, we aimed to identify the normal NIRS-derived baseline range of $SctO_2$ and the nature and efficacy of peri-operative interventions designed to modulate $SctO_2$.

Methods
We performed a systematic review of randomised controlled trials (RCT) involving NIRS-based baseline $SctO_2$ readings in adult cardiac surgery patients (PROSPERO protocol: CRD42016038410). We searched MEDLINE, EMBASE and CENTRAL databases to April 15 2016 for full-length articles in English; collected data; and performed risk of bias assessment using a pre-piloted form adapted from the Cochrane Collaboration.

Results
We identified eleven RCTs with 953 participants, testing eight different interventions. The pooled mean baseline $SctO_2$ was 66.4% (95% CI: 65.0 - 67.7), generating a reference range of 51.0% - 81.8%. Five interventions (a $SctO_2$ monitoring protocol; normothermic CPB compared to hypothermic; glycerine trinitrate compared to placebo; midazolam compared to propofol for induction of anaesthesia; and sevoflurane-based anaesthesia compared to total intravenous anaesthesia) increased intra-operative $SctO_2$ across the majority of reported time points. Post-operative follow-up of $SctO_2$ occurred in only one study, and post-operative cognitive assessment correlating $SctO_2$ with cognitive function was applied in only four studies using variable methodology.

Conclusion
We have established that reference values for baseline $SctO_2$ in cardiac surgery patients are wide, and have identified interventions that modulate $SctO_2$. This information opens the door to standardised research and interventional studies in this field.

Plant L, [1], Taylor DMcD, [1,2], Johnson D, [3], Burrell L, [1,3], Worland T, [3], Puri A, [3].

Iatrogenic Acute Decompensated Heart Failure

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Aim
Acute decompensated heart failure (ADHF) can be precipitated by a number of conditions including inappropriate IV fluid or medication management in the ED or ward. We aimed to investigate the incidence, causes and outcomes of ADHF among adult patients

Method
We undertook a case-control study in the medical and surgical wards of a tertiary referral hospital between February 1 and May 31, 2016. Patients aged ≥18 years who developed ADHF during their inpatient stay were enrolled as cases. One control patient was matched to each case by age, gender, presenting complaint/surgery performed and co-morbidities. Cases and controls were compared across a range of clinical variables.

Results
80 cases were well-matched to 80 controls ($p>0.05$). ADHF precipitants comprised infection (30%), inappropriate IV fluid and medication management (23.8% and 8.8%, respectively), tachyarrhythmia (12.5%), myocardial ischaemia (8.8%), renal failure (1.3%) and other/unclear causes (15%). On days 2 and 1 prior to the ADHF and on the day of the ADHF, cases were administered significantly more median IV fluids volumes (ml) than controls: 2000 versus 751 ($p=0.03$), 2758 versus 975 ($p=0.001$) and 1165 versus 480 ($p=0.04$), respectively. Cases had significantly greater median length of stay (15 days versus 6 days, $p<0.001$) and mortality (12.5% versus 1.3%, $p=0.01$). Medications errors related to failure to restart regular medications.

Conclusion
New onset ADHF is common among hospital inpatients and associated with significant mortality. A substantial proportion (32.6%) of cases was iatrogenic, precipitated by inappropriate IV fluid or medication management. Interventions and education to prevent iatrogenic ADHF are recommended.

Sellar A, [1], Taylor DMcD, [1,2], Chen H, [1], Plant L, [1], Ross N, [1], Gavan R, [1], McLean D, [1], Berlingeri P, [1], Weiland T, [1,3], Knott J, [1,4]

Alternative Therapies used by adult Emergency Department patients

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3. Emergency Department, St Vincent's Hospital;
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5. Department of Respiratory Medicine, Austin Hospital.

Aim
The use of Alternative Therapies (AT) (e.g. chiropractic, homeopathy, naturopathy) by ED patients remains largely unknown. We aimed to determine the period prevalence, nature of AT use and perceptions of AT among adult ED patients

Methods
We undertook a prospective cross-sectional survey of a convenience sample of adult patients presenting to three EDs between February and June 2016. A validated, anonymous, self-administered questionnaire was completed by the patient or by a family member/friend proxy.

Results
674 patients were enrolled. In the previous 12 months, 500 (74.2%) patients had used at least one AT. AT users and non-users did not differ in gender, ancestry or chronic illness status ($p>0.05$). However, AT users were significantly younger and more likely to have private health insurance ($p<0.001$). 2049 AT courses of 55 different AT had been taken including massage (75% of users), meditation (35%), chiropractic (32.6%), acupuncture (32%) and yoga (30.6%). AT users were significantly more likely ($p<0.01$) to believe that AT can prevent illness, treat illness, are more effective than prescription medicines, can assist prescription medications, are safe and provide a more holistic approach. 41 (6.1%) patients used AT for their ED presenting condition. However, only 14 (34.1%) of these notified their ED physician of this.

Conclusion
The period prevalence of AT use among ED patients was high. ED physicians need to know that their patients may also be using AT for their presenting complaint and should inquire about their use.

Ross N, [1], Taylor DMcD, [1,2], Sellar A, [1], Chen H, [1], Plant L, [1], Gavan R, [1], McLean D, [1], Berlingeri P, [1], Weiland T, [1,3], Knott J, [1,4], McDonald C, [1,5].

Outpatient asthma management of Emergency Department patients

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Aim
Best-practice asthma management requires good patient education, follow up and appropriate medication. We aimed to determine whether the outpatient management of ED asthma patients is compliant with Australia's national guidelines

Methods
We undertook a cross-sectional survey in the EDs of three tertiary referral hospitals between February and June 2016. A convenience sample of patients aged 18-65 years with a history of asthma diagnosis or treatment were enrolled. Three asthma severity groups were identified using Asthma Control Test scores (well controlled, not well controlled, poorly controlled) and compared.

Results
Fifty one patients were enrolled: 17 (34%), 15 (29.4) and 19 (37.3%) patients were in the well, not well and poorly controlled groups, respectively. Fourteen (27.5%) patients smoked and 21 (41.2%) reported passive smoking. The GPs of 36 (70.6%) patients provided asthma care although 35 (68.6%) never had routine check-ups. 21 (41.2%) patients had good understanding of an action plan although only 15 (29.4%) owned one. 14 (27.5%) patients had no preventer medication. The patients were only able to identify a mean of 3.4 asthma triggers and 1.0 patho-physiological changes that occur during an attack. Significantly more poorly controlled patients had been vaccinated against influenza ($p=0.03$) and had >6 exacerbations in the previous year ($p=0.02$). There was a moderate-good correlation (coefficient 0.58, $p<0.001$) between the patients' actual and perceived asthma control status.

Conclusion
These results suggest that patient asthma knowledge is poor and that their outpatient management is non-compliant with national guidelines.

Chen H, [1], Taylor DMcD, [1,2], Taylor SE, [3], Harding A, [3]

Accuracy of information sources used to determine the medication history in the ED

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Aim
Ascertaining a patient's best possible medication history (BPMH) at the community-hospital interface is essential for safe and effective practice. We aimed to assess the accuracy of multiple BPMH information sources.

Methods
We conducted a prospective, observational study. Adult patients taking ≥1 regular medication were enrolled. The BPMH was ascertained using an informed patient/carer interview and confirmed with ≥1 other source. For residential care facility (RCF) patients, the BPMH was determined from the RCF chart and another source. Seven sources of information were compared with the PBMH: the patient's medication list (PML), GP letter, patient's own medications (POM), medications stored and recorded in dose administration aids (DAAs), community pharmacy dispensing history and the RCF chart.

Results
455 enrolled patients took a median of five 'regular' and two 'prn' medications. The accuracy of the sources differed significantly ($p<0.001$). For 'regular' medications, the median accuracies for drug names and dosages were PML 77.8%, DAA stored medications 77.4%, DAA recorded medications 75%, community pharmacy 61.5%, GP list 61.3%)and POM 42.9%. The PML was the most accurate for 'prn' medications (16.7%). The RCF chart was 100% accurate for both 'regular' and 'prn' drugs. Many inaccuracies were potentially serious e.g. omission of thyroxine (GP letter) and warfarin (POM).

Conclusion
A combination of sources is needed to ascertain the BPMH. The PML is the most accurate information for both 'regular' and 'prn' medications and should form a key component of the BPMH.

Taylor DMcD, [1,2], Yap CYL, [3], Knott JC, [2,4], Taylor SE, [1], Phillips GA, [2,5], Karro J, [5], Chan EW, [6], Kong DCM, [3], Castle DJ, [2,7]

Intravenous midazolam-droperidol (combination), droperidol (only) or olanzapine (only) for the acutely agitated patient: A multi-centred, randomised, double-blind, triple-dummy, clinical trial

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Aim
We aimed to determine the most efficacious of three currently used drug regimens for the sedation of acutely agitated patients in the emergency department (ED).

Methods
We undertook a randomised, double-blind, triple-dummy, clinical trial in two metropolitan EDs (October 2014-August 2015). Patients, aged 18-65 years, requiring intravenous (IV) drug sedation for acute agitation were enrolled. Each was randomised to an IV bolus of either midazolam 5mg-droperidol 5mg, droperidol 10mg or olanzapine 10mg. Two top up doses were administered, if required: midazolam 5mg, droperidol 5mg or olanzapine 5mg, respectively. The primary outcome was time to adequate sedation.

Results
349 patients were enrolled. The baseline characteristics of the groups (age, gender, triage category, drug/alcohol intoxication) did not differ ($p>0.05$). However, the median (IQR) times to adequate sedation (minutes) differed significantly ($p<0.001$): midazolam-droperidol group 5 (8), droperidol 11 (17), olanzapine 11 (20). Five minutes after the initial sedative administration, 55.9%, 24.3% and 29.2% of patients were adequately sedated, respectively, ($p<0.001$). At all other times, significantly more patients in the midazolam-droperidol group were adequately sedated ($p<0.01$). Significantly fewer patients in the midazolam-droperidol group required top-up doses (28.0%, 59.5% and 60.8%, respectively, $p<0.001$) or rescue medication (1.7%, 13.5% and 25.8%, respectively, $p<0.001$). The proportion of patients in each group who experienced an adverse event did not differ (22.0%, 17.1% and 20.8%, respectively, $p=0.63$).

Conclusion
The midazolam-droperidol combination is the best drug regimen for sedation of the acutely agitated ED patient. These findings will inform best-practice guidelines for the management of this difficult patient group.

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Taboo or not taboo: Advance Care Planning in the Chinese-Australian community

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Aim: The aim of this study is to identify factors that influence the engagement of Advance Care Planning (ACP) amongst Chinese-Australians. ACP has been shown to improve the end-of-life care (EoLC) received by dying patients and reduce stress in their family members. Despite its benefits, people from non-English speaking backgrounds in Australia have been excluded from ACP consultations and research.

Methods: In this qualitative descriptive study, semi-structured interviews were conducted in-language to explore the views of a purposive sample of 30 community-dwelling elderly Chinese-Australians within Victoria, Australia. Transcripts were translated and qualitative thematic analysis was used to analyse the data for themes.

Results: Three key themes were identified: knowledge, attitude and needs of ACP amongst the Chinese-Australians. There was a low awareness of ACP amongst the participants and some confusion regarding the concept. Most participants reported positive attitudes towards ACP but mentioned that some Chinese people may be uncomfortable discussing about death-related topics. Many participants would want to know the true status of their health and plan ahead in consultation with family members to reduce burden and suffering. The predominant barrier to ACP with Chinese-Australians is the language barrier and this has to be overcome to increase its awareness. General practitioners (GPs) were identified to be key in the dissemination of ACP information as they are respected and viewed as authoritative.

Conclusion: Discussions about ACP and death may not be culturally inappropriate. The participants of this study were open to the concept of future planning around EoLC, suggesting the low uptake of ACP amongst Chinese-Australians is not culturally motivated. The lack of knowledge surrounding ACP highlights the need to provide appropriate in-language resources and promotion of ACP by health professionals to improve the access to this service amongst Chinese-Australians and potentially other culturally and linguistically diverse groups.

Does mode of presentation to hospital in ST-segment elevation myocardial infarction (STEMI) impact on total ischaemic time and health outcomes?

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Introduction: Prompt diagnosis and timely treatment is fundamental to outcomes in ST-segment Elevation Myocardial Infarction (STEMI). There has been an emphasis on improving the in-hospital components of STEMI management such as door-to-balloon-time (DTBT), with pre-hospital time delay largely overlooked.
Aim: To examine clinical characteristics by mode of arrival to hospital, and the effect on total ischaemic time and health outcomes.
Methods: A six-year review was undertaken on 614 consecutive STEMI patients treated with primary percutaneous coronary intervention (PPCI). Data was categorized according to mode of hospital arrival; self-presentation or ambulance presentation, with or without pre-hospital notification (PHN). Symptom onset-first ECG, DTBT and total ischaemic time were prospectively collected. Inferential statistics were used to examine relationships between groups.
Results: Patients who self-presented to hospital had the longest total ischaemic time, were more likely to be younger and male**.** Patients who arrived via ambulance without pre-hospital notification were older, more often women and had higher clinical risk scores. Medium-term mortality was higher in this group.

N=614	**Self present (n=99)**	**Amb with no PHN(n=202)**	**Amb with PHN(n=313)**	***p-value***
Age (mean±*SD*)	58±*12*	67±*13*	62±*13*	p<0.001
Female	12%	29%	19%	p<0.001
TIMI Risk >5	17%	40%	24%	p<0.001
Anterior STEMI	41%	49%	40%	p=0.15
Diabetes	40%	47%	35%	p=0.04
Out Hour	57%	55%	62%	p=0.32
Symptom-ECG	$175_{73\text{-}480}$	$128_{88\text{-}303}$	$80_{46\text{-}154}$	p<0.001
DTBT	$89_{73\text{-}113}$	$86_{69\text{-}113}$	$47_{35\text{-}66}$	p<0.001
Total ischaemic time	$265_{156\text{-}567}$	$214_{67\text{-}386}$	$164_{122\text{-}237}$	p<0.001
Normal LVEF	17%	9%	19%	p=0.98
IH mortality	1.0%	13.8%	3.1%	p<0.001
365-mortality	1.0%	15.9%	5.1%	p<0.001

Conclusion: Careful conclusions are drawn with heterogeneity between groups for baseline clinical characteristics. Total ischaemic time is longer for those that self present to hospital, with poorer health outcomes for those that arrive via ambulance with no pre-hospital notification. Further analysis is required to determine whether comorbid condition determines mode of transportation or vice versa, and whether this impacts on the ability to deliver timely STEMI treatment.

Activated clotting time (ACT) guided transradial (TR) band removal post coronary angiography: a pilot study.

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Background:
Radial coronary angiography is increasingly used as the vascular access site for coronary angiography. Heparin is administered during the procedure to prevent radial artery occlusion. Transradial bands (TR) band are applied to the wrist post sheath removal as a haemostatic device. Manufacturer guidelines recommend deflation of the TR band over 4 hours (usual care).

Aim: We sought to ascertain whether using Activated Clotting Time (ACT) as a guide to deflate a TR Band decreased total time to wean (TTW) safely with no increased bleeding rates, compared to usual care.

Method: This study examined 60 consecutive patients having radial coronary angiography as a day procedure. Patients were randomised to a control or treatment group. The control group followed the usual care post TR band application, and the treatment group followed an ACT guided TR band deflation protocol with band removal at 2 hours. Baseline clinical characteristics, demographics and procedural characteristics were collected. Complication rates such as bleeding, radial access site haematoma and pain were recorded post procedure. Statistical analysis was carried out to ascertain any differences between the two groups.

Results: No statistical difference was found between the control and treatment groups for baseline clinical characteristics. There was a statistically significant reduction in total time to wean the TR band in the treatment group 152 $\pm$ 59 vs 231 $\pm$ 26 (mean $\pm$ SD minutes); $p<0.001$. The reduction in deflation time with the new protocol was not associated with a statistically significant increase in radial access site bleeding (treatment 7% vs control 0%; $p=0.31$).

Conclusion: Removal of the TR band at 2 hours is a safe strategy and does not increase bleeding rates. This has led to the implementation of a new protocol at Austin Health, where patients are discharged after 2 hours post TR band application. We will continue to monitor for complications using this protocol and expand this study to include patients having percutaneous coronary intervention.

Clinical Characteristics and Predictors of Readmissions in Heart Failure Patients Admitted Under General Medicine

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Aim: The incidence and prevalence of heart failure progressively increases with ageing. We sought to analyse the clinical characteristics and determine the predictors of readmission amongst older heart failure patients admitted under General Medicine at a tertiary hospital.

Methods: We evaluated the clinical and echocardiographic data for 102 consecutive heart failure patients admitted under General Medicine and undertook multivariate analysis to determine independent predictors of the 30-day hospital readmission rates. Standard definitions were used for binary variables. Depression was only diagnosed if there had been a history of depression +/or use of anti-depressant medication.

Results: Mean age was 81.5 ± 10.3 years. Of the 102 patients, 54% were female and 28% were from a non-English speaking background. Hypertension, chronic renal impairment, atrial fibrillation, and anemia were the most common comorbidities (90%, 78%, 73%, and 52% respectively). Of the 92 patients that survived to hospital discharge, 16 (18%) were readmitted within 30 days. Patients with and without a 30-day readmission were similar with regards to age ($p = 0.71$), female gender ($p = 0.09$) and proportion with impaired LVEF ($p = 0.97$). Readmitted patients were more likely to have depression (50.0% vs. 20.8%, $p = 0.015$), this being the only significant independent predictor of heart failure readmission (OR 3.9, 95%CI 1.2, 12.3, $p = 0.02$).

Conclusion: Elderly patients with heart failure are a complex cohort. Depression seems to be an under recognised, yet powerful predictor of heart failure morbidity. More studies are needed to examine if improved treatment of depression would reduce readmissions.

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The 6 minute walk test improves exercise confidence in chronic heart failure patients

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Aim

Chronic heart failure (CHF) patients have poor adherence to self-care behaviours, particularly exercise. Patient confidence in their physical abilities is a known predictor of exercise adherence. However, factors influencing confidence are poorly understood and the efficacy of simple interventions to increase such confidence is not known. The aim of this single-site, repeated measures study was to evaluate the effects of a 6-minute walk test (6MWT) on exercise confidence in CHF patients.

Methodology

CHF patients attending an out-patient heart failure clinic were prospectively enrolled to perform a 6MWT according to American Thoracic Society Guidelines. Consenting participants completed the Cardiac Depression Scale (CDS) at baseline and an Exercise Confidence Survey (range 0-100; higher scores indicate greater confidence) at baseline and following completion of a 6MWT. Baseline demographics, including CHF characteristics, were obtained from hospital medical records.

Results

Fifty-seven CHF patients were enrolled to the study (81% males, mean age = 63±13 years). Most patients (68%) had non-ischemic CHF aetiology and were NYHA class II or III. Over one quarter of patients (28%) were depressed (CDS ≥ 95). Baseline Total Exercise Confidence (mean 66±24) was inversely associated with age ($p<0.01$), NYHA class ($p<0.001$), and depression ($p<0.001$). Distance walked on 6MWT (mean = 400 ± 123 metres) was positively correlated with Baseline Total Exercise Confidence ($p<0.001$) and with each of the baseline Exercise Confidence sub-scales (ie., Walking, Running, Climbing and Lifting Confidence; $p<0.001$). Following the 6MWT, a significant improvement in Total Exercise Confidence ($F_{(1, 49)} = 7.26$, $p<0.01$) and Running Confidence ($F_{(1,51)} = 4.77$, $p<0.05$) adjusted for age, CDS score and NYHA class, was observed.

Conclusions

These findings suggest that the 6MWT is a simple and effective intervention to improve exercise confidence in chronic heart failure patients. Future research should monitor whether improvements in exercise confidence are persistent and translate to changes in exercise behaviours.

The short-term effect of right ventricular mid-septal pacing on right ventricular function

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Background: Right ventricular (RV) apical pacing is associated with left ventricular (LV) dyssynchrony and dysfunction. However, the effect of pacing on RV function, in particular with leads positioned in the RV mid-septum, remains unknown. We investigated the short-term effect of pacing on RV function.

Methods: We enrolled 24 patients with normal baseline LV and RV function requiring permanent pacemaker insertion. Echocardiography was performed prior to implantation (baseline) and at 1 month. We assessed RV tricuspid annular plane systolic excursion (TAPSE), tricuspid annular tissue Doppler-derived systolic velocity (S'), RV fractional area change (FAC) and RV global longitudinal strain (GLS) using speckle tracking.

Results: Mean age was 73.8 ± 9.5 years. 1-month percent ventricular pacing average was 32% (range 0-100%). 17 patients had atrioventricular nodal dysfunction and 7 had sick sinus syndrome. There was a small but statistically significant decline in RV GLS 1 month following pacemaker insertion(Table). There was also a trend towards decline of RV function on all other measured parameters.

Variables	Baseline (Mean ± SD)	1 Month (Mean ± SD)	p-value
TAPSE (cm/second)	22.5 ± 5.2	21.9 ± 3.2	0.3
RV S' (cm)	13.5 ± 2.5	12.3 ± 1.9	0.2
FAC (%)	48.1 ± 10.3	46.1 ± 7.9	0.2
GLS	-25.3 ± 4.6	-22.5 ± 3.8	<0.0001

Conclusions: RV mid-septal pacing may be associated with a slight decline of RV function early after pacemaker insertion, which may be identified by strain analysis. Longer-term follow-up is under way to assess if this predicts long-term RV dysfunction.

Is Percutaneous Coronary Intervention to Complex Lesions Associated with Worse Long-term Mortality?

Background: The ACC/AHA coronary lesion classification was developed to quantify lesion complexity and has become a predictor of procedural success. The long-term prognostic significance of percutaneous coronary intervention (PCI) to complex coronary lesions in stable coronary artery disease is unknown. We aim to assess whether PCI to complex lesions is associated with higher long-term mortality.

Methods: Clinical and procedural characteristics of 682 consecutive patients with stable coronary artery disease (CAD) who underwent elective percutaneous coronary intervention (PCI) between May 2007 and January 2011 were prospectively collected. All patients were dichotomised as either simple (A and B1) or complex (B2 and C) based on the ACC/AHA classification of the lesion undergoing PCI. The primary endpoint was all-cause mortality determined via the Australian National Death Index**.**

Results: Of the 682 patients, 287 (42%) underwent PCI to a complex lesion. There was no significant difference in baseline clinical characteristics between the groups. In the complex PCI group, there were 67 (24%) bifurcations, 63 (22%) chronic total occlusions and 30 (11%) ostial lesions. Complex lesions were associated with significantly lower procedural success (94.1% vs. 99.2%, $p<0.01$). At mean follow-up of 5.5 years, there were 35 (12.2%) deaths in the complex PCI group and 41 (10.4%) in the simple PCI group (log-rank $p=0.31$).

Conclusion: Complex coronary lesions are associated with lower PCI success rates, even in the contemporary PCI era. However, patients with complex lesions do not appear to have higher long-term mortality.

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Prescribing of Mandated Medications in HF-rEF

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Introduction

The use of evidence-based pharmacotherapies in heart failure with reduced ejection fraction (HF*r*EF) can improve clinical outcomes. However, translation of evidence into clinical practice is often limited. The American Heart Association's 2013 guidelines[1] recommend ACEi/ARB, beta-blockers and loop diuretics for all NYHA class II-IV HF*r*EF patients with mineralocorticoid antagonists (MRA) in those with sufficient renal function.

Method

We prospectively collected data on all patients admitted to Austin Health with decompensated HF over two one month periods in 2014/2015 as part of the VCOR HF snapshot. All patients were followed up for 30 days.

Results

In total, 115 patients were admitted with ADHF. 59 had echo-confirmed HF-*r*EF. In total, 115 patients were admitted with ADHF. 59 (51.3%) had echo-confirmed HF-*r*EF. 34 (57.6%) were male. Average age was 74.8 years. 36 (61.0%) had sufficient renal function for MRA use.

Table: Prescribing patterns in HF*r*EF 2014-2015

Medication	Admitted on	Discharged on	Change	p-value
Loop diuretic	41 (69.5%)	54 (91.5%)	13 (22.0%)	<0.05
ACEi/ARB	34 (57.6%)	34 (57.6%)	0	1.00
Beta-blocker	42 (71.2%)	46 (78.0%)	4 (6.8%)	0.526
MRA (if applicable)	19 (52.8%)	27 (75.0%)	8 (22.2%)	0.085
Recommended regime*	13 (22.0%)	19 (32.2%)	6 (10.2%)	0.301

*Loop diuretic, ARB/ACEi and beta-blocker, with MRA if K^+ <5 and eGFR >30.

Conclusion

With only a third of patients being on the recommended pharmacotherapy regime at discharge, there is room for improvement in prescribing mandated medication for HF-*r*EF. Significantly greater prescription of loop diuretics may indicate a clinician focus on symptom, rather than pathophysiological, management.

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Should All Patients Presenting with STEMI Be Screened for Familial Hypercholesterolaemia?

Background: Familial Hypercholesterolaemia (FH) is a common autosomal dominant genetic disorder associated with premature coronary artery disease. FH is under-recognised in the general population and often its first manifestation is acute myocardial infarction. We aim to ascertain the proportion of patients with STEMI who could be diagnosed with possible or probable FH.

Method: Clinical and procedural characteristics of 412 consecutive patients presenting with STEMI who underwent primary percutaneous coronary intervention (PCI) at a major tertiary centre were prospectively collected. Patients were dichotomised according to the Dutch Lipid Clinic Network Score (DLCNS) into; possible/probable FH if their score was ≥3; or unlikely FH if their score was <3. The DLCNS is a validated FH screening tool that incorporates history, physical examination and LDL-cholesterol levels.

Results: Of the 286 patients, 58 (20.3%) have possible or probable FH. This is likely an underrepresentation given the poor documentation of family history of premature vascular disease and presence/absence of clinical findings suggestive of FH. Patients with possible/probable FH are likely to be younger (51±8 vs. 66±13 years, $p<0.01$), male gender (90% vs. 77%, $p=0.04$), have a family history of premature CAD (86% vs. 24%, $p<0.01$) and have higher LDL-C levels (3.2±0.9 vs. 2.7±1.2, $p<0.01$). There was no difference in statin or ezetimibe discharge prescription between the groups.

Conclusion: Given the significant proportion of patients presenting with STEMI who could be diagnosed with possible FH, screening should be strongly considered to enhance management of the index case and to facilitate family screening.

Is a Family History of Premature Coronary Artery Disease Associated with Worse Long-term Mortality in Patients with Stable CAD?

Background: A family history (FH) of premature coronary artery disease (CAD) is a well described independent risk factor for developing CAD. However, it is still unclear whether FH has a significant impact on long-term mortality in patients with established CAD. We aim to examine the effect FH on long-term survival of patients with stable CAD.

Method: Clinical and procedural characteristics of 682 consecutive patients with stable coronary artery disease (CAD) who underwent elective percutaneous coronary intervention (PCI) between May 2007 and January 2011 were prospectively collected. Patients were stratified based on the presence or absence of a self-reported FH of premature CAD. The primary endpoint was all-cause mortality determined via linkage with the Australian National Death Index.

Results: Of the 682 patients, 292 (42.8%) had a FH of premature CAD. Baseline characteristics were similar between the two groups except patients with a FH were more likely to have preserved renal function (84.9% vs. 78.5%, p=0.04) and be smokers (14% vs. 7%, p<0.01). At mean follow-up of 5.5 years, there were 28 (9.6%) deaths in the FH group and 49 (12.6%) deaths in the no FH group (p=0.27).

Conclusion: Patients with known stable CAD and a positive FH of premature CAD do not appear to have worse long-term prognosis. Whether this is due to early detection and consequent effective secondary prevention therapy is yet to be determined.

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Unscheduled emergency department presentations by cancer patients ¶

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Introduction
People with cancer who present to the Emergency Department (ED) for disease or treatment related side effects have worse outcomes than those who do not (1, 2). With a rising incidence of cancer and more patients being treated in the outpatient setting, more cancer patients are accessing emergency services for disease and treatment related symptoms (3).

Aim
The aim of the PhD study is to identify the number of patients who present to an ED after receiving anti-cancer drug treatment in a Chemotherapy Day Unit (CDU) setting. Additionally, this study will describe the patient population and identify potentially modifiable risk factors for ED presentation.

Methods
Twelve months of retrospective data was collected from medical records at a large tertiary hospital in Melbourne, Australia. Eligible records include patients who received anti-cancer drug treatment in the CDU between July 2014 and June 2015. Frequency and descriptive statistics were initially undertaken using SPSS 14.0 (SPSS, Chicago, I11, USA). Bivariate analysis using chi-square statistics was used to determine differences in ED service use and subsequent admission based on demographic and clinical variables.

Results
Three hundred and seventy-nine patients made a total of 624 ED presentations during the study period. The main reasons for presentation were fever (n=103), feeling general unwell (n=52) and pain (n=35). Preliminary data reveals that 393 (62%) patient attendances were allocated a triage category of between 3 and 5 (where 1 is most severe and 5 least). Four hundred and forty-six (71%) were admitted to the short stay unit or the inpatient area for further care.

Conclusion
Identifying risk factors that are potentially modifiable will inform cancer service innovations to help prevent unscheduled ED presentations for cancer patients. Future research should focus on evaluation of new system level interventions that will prevent patients with low levels of clinical risk from presenting to ED services.

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Schimmelbusch K,[1] Preston J, [1]

Post operative hypotension MER calls reduce as a result of a multidisciplinary education.

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Aim
Hypotension is a common postoperative complication typically treated with a fluid bolus during initial resuscitation efforts. The aim of this study was to investigate whether a multidisciplinary education program on postoperative fluid resuscitation would reduce the number of hypotensive-triggered Medical Emergency Response (MER) calls at The Surgery Centre (TSC) in-patient unit at The Austin Repatriation Campus.

Methods
In our before and after study we evaluated the impact of a specifically designed 30-minute in-service education session that focused on the recommended IV fluid and volume used during the initial resuscitation for post-operative hypotension. We measured the number of hypotensive-triggered MER calls in the 12-months prior to January 2105 and 12-months following March 2015, the education sessions as well as staff opinion of the dedicated session.

Results
Thirty-five staff (4 medical, 31 nursing) attended four education sessions provided during the month of February 2015. There were 25 hypotensive-triggered MER calls in 9222 patients during the pre-period and 15 hypotensive-triggered MER calls in 10657 patients in the post-period. Staff feedback indicated a knowledge increase regarding initial fluid resuscitation of postoperative hypotension. Nursing and medical staff also commented that the existing collaborative management of MER calls was further enhanced following the education intervention.

Conclusion
Despite an increase number of patients admitted to TSC, there was an overall reduction in hypotensive MER calls. A multidisciplinary education program on the recommended IV fluids and volume during the initial resuscitation of a postoperative MER call was identified as reducing MER calls.

Nurse-led titration of angiotensin converting enzyme inhibitors and beta-adrenergic blocking agents for patients with heart failure with reduced ejection fraction: a meta-analysis

Andrea Driscoll, Judy Currey, Henry Krum, Andrew Tonkin ,

Background
Angiotensin converting enzyme inhibitors (ACEIs) and beta-adrenergic blocking (BB) agents can improve survival and reduce hospital readmissions in patients diagnosed with heart failure with reduced ejection fraction (HFrEF). Evidence shows there is a dose-dependent relationship of these medications with improved patient outcomes. Nurse-led titration (NLT) may be a novel strategy to facilitate this up-titration.

Methods
A literature search of randomised controlled trials comparing NLT of BBs and ACEIs comparing the optimisation of these medications by a nurse to optimisation by another health professional, in patients with HFrEF with endpoints focussing on patient outcomes and safety, was conducted.

Main results
A pooled analysis of seven studies (1924 participants) found that participants in the NLT group were 21% less likely to experience a hospital admission for any cause (95% CI 0.71-0.88) and 39% for a heart failure hospitalisation (95%CI 0.36-0.72). All-cause mortality was lower in the NLT group (RR 0.66, 95% CI 0.48-0.92) compared to usual care. Approximately 27 deaths could be avoided for every 1000 people receiving NLT of BBs and/or ACEIs. The number of participants reaching target dose of BBs was higher in the NLT group compared to usual care (RR 1.94, 95%CI 1.02-3.69) and they reached maximal dose in half the time. No adverse events related to NLT were reported.

Conclusions
Participants in the NLT group experienced less hospital admissions, an increase in survival and number of participants reaching target dose earlier. NLT is a potential and viable strategy to improve the optimisation of BBs to enhance patient outcomes.

In-patient heart failure nurse practitioner service significantly increases mandated medications and reduces re-hospitalisation rates.

Driscoll A, Asker K, Johnson D, Farouque O, Burrell L, Jones E, Jones N, Al-Kaisey A, Hare DL

Background/Introduction: Hospitalisations are the major contributor of costs for heart failure (HF). Early HF readmissions increase substantially when inpatient care is not optimised. Ideally patients admitted to hospital with acute decompensated heart failure (ADHF) should be managed by a specialist heart failure team. However, access to such a team is not always feasible. Heart failure nurse practitioners (HF NP) are an emerging component of the HF specialist workforce and to date their impact on improving patient outcomes is untested, particularly in an inpatient setting.

Purpose: The aim of this study was to determine the effect of an inpatient HF NP service on improving patient outcomes in patients admitted with ADHF.

Methods: A pre and post-test design was used. The study recruited 300 patients admitted to hospital with acute decompensated heart failure (ADHF) and discharged home (150 patients in the historical control and 150 in the prospective HF NP group). Patients in the HF NP group received education about their heart failure and self-management strategies, prescribing and titration of key therapeutic agents, referrals to appropriate health professionals and referral for follow-up in a home visit heart failure program or exercise program, and outpatient clinic.

Results: Among the 300 patients admitted with ADHF, mean age was 78±11 years and 61% were male. Overall, 42% of patients had heart failure with reduced ejection fraction (HFrEF), 40% were NYHA class III and 55% class IV. There was no significant difference between the two groups for NYHA class, HFrEF vs heart failure with preserved ejection fraction, precipitants for admission, and co-morbidities. There was a higher prescription rate of beta blockers (80% vs 73%) and mineralocorticord receptor antagonists (50% vs 23%) in patients with HFrEF enrolled in the HF NP service, compared to the historical control group. Referrals to HF home visit program were also higher in patients in the HF NP service (90% vs 35%, $p<0.0001$) but this was not a significant predictor of 90-day hospital readmissions in a multivariate model. Ninety-day hospital readmission rates were significantly lower in the HF NP service compared to the historical control group (48% vs 64%, $p=0.02$) with no mortality. Patients seen in the HF NP service were 51% less likely to be readmitted within 90 days (adjusted HR 0.49, 95% CI 0.3-0.81, $p<0.0001$).

Conclusion: A HF NP service improved the quality of care for patients admitted with ADHF. This was reflected by an increase in adherence to evidence-based practice and a significant reduction in 90 day hospital readmissions.

Preston J,[1], Schimmelbusch K,[1]

Nurse led medical orientation program improves patient outcomes

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Aim

The aim of this study was to determine compliance with the 500 mL fluid bolus recommendation during hypotensive Medical Emergency Response (MER) calls, at The Surgery Centre (TSC) inpatient ward, Heidelberg Repatriation Hospital[1].

Method

Medical staff were provided with an orientation program by the TSC Clinical Support Nurse. A component of this was an article and a follow-up email on fluid volume resuscitation recommendations for postoperative hypotension. An explanation was also provided if the doctor was not working night shifts. To determine the compliance with these recommendations, fluid volumes administered during hypotensive MER calls were compared 12 months prior and 12 months post the nurse initiated medical orientation program.

Results

The number of patients admitted to TSC inpatient ward increased from 9 222 12 months pre intervention to 10 657 12 months post intervention. 25 doctors rotated through the TSC inpatient ward during the post-intervention phase of which 12 (48%) were night residents. The frequency of a 500 mL fluid bolus during a hypotensive MER call increased from 52% pre-intervention to 94% post-intervention. There was a reduction in the number of hypotensive MER call from 25 to 15 over the 2-year period.

Conclusion

The nurse initiated medical orientation program was identified as improving compliance with the fluid volume resuscitation recommendations during hypotensive MER calls at TSC inpatient ward. A reduction in hypotensive MER calls also occurred despite an increased number of inpatient admissions.

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Purcell R[1], Knott C, Haines K[1], LoPresti R [1]

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Learner evaluation of a tertiary hospital inter-professional simulation faculty education development program

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Aim

Implementing vocationally based simulation education in a tertiary hospital requires more than high-quality simulation facilities[1]. Access to simulation education expertise is crucial. In our tertiary hospital, simulation expertise was limited to a small number of staff, which reflected an unsustainable model. There is limited literature around inter-professional faculty development aimed at fostering organisational capacity for high-quality vocational simulation. This program focused on developing skills necessary to deliver simulation within and across disciplines. We evaluated the program participant's perception of the change in their knowledge of simulation.¶

Methods

Single site, pre-post design evaluating a comprehensive simulation faculty education development program. Inter-professional participants attended three practical workshops which covered these domains: introduction to simulation pedagogy, scenario development, and debriefing skills. Participants self-rated their pre- and post-program simulation skills in these domains (5 point scale, range: 1 = Low, 3 = Medium, 5 = High) and acceptability of program (5 point scale, range: Strongly Disagree to Strongly Agree) using a locally designed tool.¶

Results

This program was run twice in 2015, with a total of 24 unique participants (10 Allied Health, 8 Nurses, 6 Doctors), who were experienced professionals (59% were >10 years qualified). The average rating for all domains (knowledge of simulation pedagogy; ability to develop a scenario; ability to conduct a debriefing session) was 2 pre-program and 4 post-program. The majority (58%) of participants 'Strongly Agreed' the inter-professional design of the program enhanced their learning. Furthermore, 58% 'Strongly Agreed' the format of the program was appropriate to their learning needs.

¶

Conclusion

This program increased vocational clinician-educators' skills to deliver future simulation. The inter-professional nature of the program enhanced learning and the program format, incorporating face-to-face teaching and expert knowledge sharing, was acceptable to participants. The program has initiated the process of developing a skilled simulation faculty to a sustainable level.

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Ian Baldwin[1], Julia De Marchi[2], Nigel Fealy[1], Paula Carty[1]

An evaluation of a smart phone application for post graduate nurses in Intensive Care Specialty Training

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Background: Smart phones are becoming more common place for communication and accessing information related to work, as well as in learning domains. Free web based applications have become readily available and suitable for this setting.

Aim: We sought to trial a sporting team application for post graduate intensive care training in a tertiary referral intensive care unit (ICU). Team App is a free Australian built application and easily modifiable for the health care setting and allows for instant chat, document upload, event scheduling, social media, photos, notifications and news alerts.

Method: Nine post graduate nurses were established as the team and following training for the use of the application the team consented into an evaluation for use over one year.

Results: There were seven females and two males, with an age range 25 – 34 yrs. Eight used smart phones and one nurse accessed the application via desktop computer. Application usage saw 41 % using the application twice per week and 16% greater than three times per week respectively. The evaluation showed that chat was the highest used feature (83%) followed by education documents and web links (27%). There were 192 chat messages logged throughout the year which included topics on roster swaps, university work and positive appraisal.

Discussion: The education managers considered the application highly effective for communication 24/7. It assisted in bringing attention to important documents and encouraged more reliable tutorial attendance throughout the teaching year. Software reliability was excellent and never failed.

Conclusions: Team App is a free and very functional education tool for post graduate nursing within the ICU or any health care team setting. From this study we have established that this application can be used effectively in an education and health care environment and has the potential for further development.

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Creating a Culture of Research in Nursing at HRH – Phase One Early Graduate Year (EGY) Nurse Quality Projects

Research in nursing is important but is often seen as difficult in the clinical area due to workload demands. The aim of this project was to have nurses working on projects in double staffing time that would make a difference to patient care. There are clinical champions on each continuing care ward at HRH aligned to the National Safety and Quality Healthcare Standards. When graduates commence in the area they are expected to do an audit related to one of the standards in collaboration with the ward based clinical champion and the nursing education team. They then look at the audit results and come up with improvement strategies if required. A number of audits have been done during the first rotation of 2016. These have provided valuable information for improving patient care. One graduates audit looked at the 7 rights of medication administration and identified some issues. The clinical champion and the education team are now looking at strategies for improvement. Another audit looked at patient footwear and came up with a strategy of assessing footwear on admission and recommending correct footwear for the carer to bring in for the patient. This may prevent falls. The graduate nurses reported that these projects made them feel part of the team and that they felt they could make a positive difference to patient care. In the future this project may be rolled out o other wards at Austin Health.

Rust A,[1], Preston J,[2]

Mission impossible? Ceasing routine commencement of oxygen therapy in a recovery unit.

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2. *Clinical Education Unit, Austin Health, Heidelberg, Victoria*

Aim

The aim of this study was to determine whether a multidisciplinary education campaign would cease the current practise of routinely commencing oxygen therapy in a recovery unit.

Method

Nursing staff conducted in-service education and sent email notifications to nurses and anaesthetists at The Surgery Centre (TSC) recovery unit regarding the rationale for ceasing the routine commencement of oxygen therapy [1-4]. Instead, oxygen therapy was to be commence when a patient's oxygen saturation was persistently below Urgent Clinical Review (UCR) criteria (SaO_2 < 94%). Compliance with the new criteria was determined by an 8-week post-intervention oxygen therapy commencement audit.

Results

103 patients were audited. Of these, 19 (18%) required supplemental oxygen for 30 minutes or less. The main reason cited by nursing staff for commencing supplemental oxygen therapy was hypoventilation due opioid analgesia administration. Only 6 patients (5.8%) returned to the ward with supplemental oxygen therapy in-situ. A cost saving of $42 was calculated by not routinely using oxygen masks for oxygen delivery during this 8-week period.

Conclusion

The multidisciplinary education campaign was successful in ceasing the routine commencement of oxygen therapy in the recovery unit. Financial savings also occurred. The flow on effect of reducing environmental waste and the cost associated with the disposal of the masks would also ensue.

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Exploring nurse's ability to correctly stage pressure Injuries

Joey Ting RN Austin Health Fran Pearce Education Coordinator Austin Health

Abstract

It is estimated that between 15-25 per cent of patients in the health system develop pressure ulcers.

Accurate assessment of patients with pressure ulcers is essential to plan effective prevention and management strategies. There is evidence within the literature internationally that nurses have difficulty staging pressure injuries and are often unable to Differentiate wounds of other aetiologies such as Incontinence associated dermatitis

Aim

The aim of this quality activity is to explore nurse's ability to correctly stage pressure Injuries.

Method

A group of nurses ranging from novice to expert nurses within a rehabilitation unit were asked to stage digital photographs of pressure validated by The European Pressure Ulcer Advisory Panel & National Pressure Ulcer Advisory Panel.

Results

Results indicated a lack of consensus among staff across all range of clinical and academic experience. This project offers an opportunity to identify potential learning needs to ensure accurate assessment and effective management for patients with a pressure injury.

Is the patient experiences of caring and person-centredness associated with perceived nursing care quality?

Fran Pearce [1] Elizabeth Watt[2], David Edvardsson [2]
Austin Health, Melbourne [1]. La Trobe University, Melbourne[2]

Introduction: In-patient experiences have had limited attention in health care quality policy and standards, as well as quality assessments in practice. The impact of central nursing concepts such as caring and person-centredness on patient ratings of quality is largely unknown.

Aims: The study aimed to explore the extent to which caring and person-centredness contribute to perceived nursing care quality by acute care hospital in-patients.

Design: A cross-sectional survey design was used to collect data from a sample of Australian acute hospital in-patients (n=210).

Methods: The study collected self-report patient data through a study survey including demographic data and the Caring Behaviours Inventory, the Person-centred Climate Questionnaire, the SF-36, and the Distress thermometer. Descriptive and inferential statistics were used to explore sampling characteristics the associations between study variables after controlling for confounders.

Findings: The results indicate that the caring behaviours of staff and the extent to which the ward was perceived as person-centred accounted for more than half of the total variance in nursing care quality as rated by patients. Knowledgeable and communicable staff, timeliness of assistance and environmental support stood out as most significantly related to quality

Conclusions: Patient ratings of caring and person-centredness were highly associated with perceived nursing care quality in a tertiary acute hospital. Patient experiences of the extent to which nursing manifests caring and person-centredness seem to have an influential role in ratings of nursing care quality. Assessments of health service and nursing care quality can benefit from increasingly including direct data on patient experiences.

Tom Kupfer[1], Benjamin Harris[1], Kym Rykers[1]

Employing statistical process control charts as evidence for improving linac isocentre quality control and frequency optimisation†

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†*abstract accepted at EPSM conference 2016, 6-11 November 2016, Sydney.*

Introduction

Process control charts are quality assurance (QA) tools that provide succinct graphical representations of process stability.[1] One such chart was implemented for QA of an Elekta Infinity linear accelerator, to characterise isocentric stability and inform optimal QA frequency.

Method

An image-based, semi-automated and robust Winston-Lutz-type QA process was established that measures to sub-millimetre accuracy (a) the positioning accuracy of the Elekta Precise Table, (b) the coincidence of radiation isocentre and imaging isocentre, and (c) the size of the radiation isocentre with gantry rotation, defined as the greatest distance between individual radiation field centres along the major X-, Y- and Z-axes.[5] A macro-enabled in-house MSExcel spreadsheet facilitated graphical presentation and statistical analysis of the QA results. Action thresholds were based on published recommendations.[6,7]

Results

From data gathered over 12 months, the table positioning accuracy along X- and Y-axis was 0.0±0.5mm (mean±2SD) and -0.2±1.0mm in Z-axis. For the latter, the data was not normally distributed. The coincidence of imaging and radiation isocentre along any axis was stable at <|0.2|±0.2 mm. The size of the radiation isocentre in the Y-axis was stable at 0.86±0.11. However, on two occasions after radiation beam steering, the mean size changed by more than 0.35 mm (>3 SD) in the X-axis and Z-axis. This magnitude was obvious on the charts, in one instance prompting corrective action.

Conclusion

Control charts revealed how beam tuning affects the size of the radiation isocenter and elegantly captured the linac's isocentric stability. These results provided justification for reducing the frequency of comprehensive linac isocentre checks, as well as evidence for when corrective action was required. Similar benefits are anticipated as control charts are applied to other linac QA processes.

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Sensitivity, specificity and predictors of positive ^{68}Ga-PSMA PET in advanced prostate cancer: a systematic review and meta-analysis

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Context: ^{68}Ga PSMA-PET is an emerging imaging modality introduced to assess the burden of prostate cancer, typically in biochemically recurrent or advanced disease. ^{68}Ga PSMA-PET provides the ability to selectively identify and localize metastatic prostate cancer cells and subsequently change patient management. Due to its limited history, robust sensitivity and specificity data outlining ^{68}Ga PSMA-PET positive scans are not available. We undertook a systematic review and meta-analysis of reported predictors of positive ^{68}Ga PSMA-PET and respective sensitivity and specificity profiles.
Methods: We performed critical reviews of MEDLINE, EMBASE, ScienceDirect, Cochrane Libraries and Web of Science databases in April 2016 according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement. Quality assessment was performed using Quality Assessment if Diagnostic Accuracy Studies-2 tool. Meta-analysis and meta-regression of proportions were performed using a random-effects model with pre-PET PSA levels as the dependent variable. Summary sensitivity and specificity values were obtained by fitting bivariate hierarchical regression models.
Results: Sixteen articles including 1,309 patients were analysed. Overall percentage of positive ^{68}Ga PSMA-PET was 40% (95% CI: 19-64%) for primary staging patients and 76% (95% CI: 66-85%) for biochemical recurrence (BCR) patients. Positive ^{68}Ga PSMA-PET scans for BCR patients increased with higher pre-PET PSA. For PSA categories 0-0.2ng/ml, 0.2-1ng/ml, 1-2 ng/ml and > 2 ng/ml, the percentage positive were 42%, 58%, 76% and 95% respectively. Shorter PSA doubling time increased ^{68}Ga PSMA-PET positivity. On per-patient analysis, summary sensitivity and specificity were both 86%. On per-lesion analysis, summary sensitivity and specificity were 80% and 97% respectively.
Conclusions: In the setting of biochemically recurrent prostate cancer, pre-PET PSA predicts the risk of positive ^{68}Ga PSMA-PET. Pooled data identifies favourable sensitivity and specificity profiles compared to choline-based PET imaging techniques.

Renal tubular sodium transporter expression and phosphorylation is altered in pre-eclampsia

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Background:
In pre-eclampsia, suppression of the renin-angiotensin-aldosterone system and changes in blood volume contribute to the development of hypertension (1). Limited studies have examined the role of renal tubular salt transporters in the pathogenesis of pre-eclampsia. Analysis of proteins found in urinary exosomes provides a non-invasive technique for detection of changes in renal tubular sodium transporter activity *in vivo* (2).

Aim:
To characterise the phosphorylation and expression of tubular sodium transporters, detectable in urinary exosomes, in pre-eclamptic, normotensive pregnant and normotensive non-pregnant females.

Methods:
A cross-sectional study of 8 pre-eclamptic, 18 normotensive pregnant patients and 19 non-pregnant female controls was conducted. Expression and activating phosphorylation of sodium transporters in urinary exosomes isolated by ultracentrifugation were analysed by Western Blot. We studied the following proteins; (i) NKCC2, the drug target for frusemide, (ii) NCC, the drug target for thiazide diuretics, and (iii) ENaC, the drug target for amiloride.

Results:
There was a 5.3-fold increase in phosphorylation of the S130 residue on NKCC2 and a 3.0-fold increase in total NKCC2 expression in pre-eclamptic patients compared to normotensive pregnant patients ($p=0.0013$ and $p=0.0051$, respectively). However, in pre-eclamptic patients, phosphorylation of the T105 residues on NKCC2 ($p=0.0042$) and the T60 residue on NCC ($p=0.0092$) was significantly reduced compared to normotensive pregnant patients (68.6% and 75.9%, respectively). Expression of the α ($p=0.0111$) and γ ($p=0.0229$) subunits of ENaC was increased by 14-fold and 2.6-fold, respectively, in pre-eclamptic patients. There was no significant difference between normotensive pregnant and non-pregnant subjects in expression and phosphorylation levels of NKCC2 and NCC, or expression of the α and γ subunits of ENaC.

Conclusions:
The data suggest that sodium transporter expression and phosphorylation are unchanged in the third trimester of pregnancy compared to non-pregnant females. By contrast, expression of NKCC2 and ENaC, and activating phosphorylation of NKCC2 and NCC, were significantly altered in pre-eclampsia. This is the first evidence of a change in renal sodium transporter expression and phosphorylation in pre-eclampsia. It suggests the existence of novel activation pathways affecting salt transporters in pre-eclampsia and may lead to the development of a non-invasive biomarker.

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Physiologic fluid optimisation algorithm improves outcomes in patients undergoing pancreaticoduodenectomy: a prospective multicentre randomized controlled trial

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Supervisor:
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Introduction:
Enhanced Recovery After Surgery programmes for pancreaticoduodenectomy can be effectively implemented without compromising patient safety or increasing length of hospital stay. However, the additional impact of a surgery-specific cardiac output-guided algorithm on perioperative outcomes has never been evaluated in this group of patients. Therefore we evaluated if an intraoperative goal directed therapy algorithm (GDT) improves outcomes in patients undergoing pancreaticoduodenectomy.

Methods:
After Ethics approval we conducted a multicentre, randomised trial. Patients undergoing pancreaticoduodenectomy were randomised to a standardised Enhanced Recovery After Surgery programme (Usual care group), or an Enhanced Recovery After Surgery programme in combination with a surgery-specific cardiac output-guided algorithm (GDT group). The primary outcome was length of stay. Secondary outcomes included perioperative fluid intervention, and rate and severity of complications (Clavien-Dindo classification).

Results:
Fifty-six patients were recruited from four hospitals (GDT group: 26 patients, Usual care group: 26 patients). Baseline patient characteristics were similar in both groups. Median (Interquartile range) duration of surgery was 8.6 hours (7.1:9.6) in the GDT group vs. 7.8 hours (6.8:9.0) in the Usual care group (p=0.20). Patients in the GDT group had lower intraoperative fluid balances: 1005mL (475:1873) vs. 3300mL (2474:3874); p=<0.0001, and lower volume of fluid administered intraoperatively: 2050mL (1313:2700) vs. 4088mL (3400:4525); p<0.0001. Fewer complications occurred in the GDT group compared to the Usual care group, (44 vs. 92; p=0.001). There were no significant differences in proportions of patients experiencing complications (p=0.179) or in rate of worst complications (p=0.432) between groups. Median length of stay was lower in the GDT group 9.5 days (7:14.3) vs. 12.5 days (9:22.3) in the Usual care group; p=0.002.

Conclusion:
An intraoperative physiologic fluid optimisation algorithm combined with Enhanced Recovery After Surgery programme reduced length of hospital stay and number of complications compared to Enhanced Recovery After Surgery programme alone. Our findings support the notion that non-operative management is an important determinant of complications for patients undergoing pancreaticoduodenectomy.

Goal-Directed Fluid Therapy is Associated with Improved Outcomes in Patients Undergoing Pancreaticoduodenectomy

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Introduction: The judicious use of intravenous (IV) fluids through a goal-directed therapy (GDT) algorithm in major abdominal surgery is associated with improved patient outcomes. Few studies specifically examine IV fluid use and outcomes in patients undergoing pancreaticoduodenectomy (PD). The objective of this study was to assess the relationship between GDT and PD patients.

Methods: We tested our hypotheses by conducting a retrospective observational study. 147 consecutive patients undergoing PD at Austin Hospital were evaluated. Multiple logistic regression models were used to determine factors associated with IV fluid use, vasoactive medication requirements, development of complications and length of hospital stay.

Results: Groups were similar with respect to demographics and baseline hemodynamic variables. Patients receiving GDT received significantly less intravenous fluid compared to usual care. Median total intraoperative fluid was 3000 ml (IQR: 2050:4175) in the GDT group compared to 4500 ml (IQR: 3275-5325) in the Usual care group; p<0.0001. With adjustment for covariates, pre-operative albumin, length of surgery time and epidural anaesthesia, intra-operative fluid balance remained less in the GDT group, p<0.0001. Noradrenaline and dopamine were more likely to be administered in GDT group; p=0.002 and p<0.0001 respectively. Postoperative complications were common and occurred at similar frequencies amongst the GDT and Usual care groups [64% vs. 68%; p=0.71. Cardiogenic pulmonary oedema and pulmonary atelectasis were more common in the Usual care group; p=0.0087, OR (95%CI): 0.07 (0.00:1.26) and p=0.035, OR (95%CI): 0.14 (0.02:1.06) respectively. Median length of hospital stay was 10 days (IQR: 8.0:14.0) in the GDT group compared to 13 days (IQR: 8.8:21.3) in the Usual Care group; p=0.01.

Conclusions: Our findings show that GDT using a surgery-specific cardiac output algorithm is associated with reduced IV fluid administration and cardiorespiratory complications, and shortens length of hospital stay after PD. We have defined both a need for improved care and the necessary background data for power calculations needed to design prospective trials to evaluate protective strategies that may improve patient centered outcomes in this setting.

Authors. David J Berlowitz[1,2] for the COSAQ collaborative

A randomized controlled trial of auto-titrating continuous positive airway pressure treatment for obstructive sleep apnoea after acute quadriplegia (COSAQ).

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Quadriplegia is a severe, catastrophic injury that acutely causes obstructive sleep apnoea alongside lifelong physical disability. Treatment with nasal continuous positive airway pressure (CPAP) is particularly challenging in this group. We hypothesised that 3 months of auto-titrating CPAP would improve neuropsychological function, sleepiness, quality of life, anxiety and depression more than usual care in acute quadriplegia.
Methods. 11 spinal cord injury centres across Australia, New Zealand, Canada and the UK screened 1628 people (July 2009-October 2015) who sustained a new, traumatic quadriplegia. 337 people met the inclusion criteria and underwent full, portable polysomnography. 265 had an apnoea hypopnoea index greater than 10, were classified as “OSA positive” and proceeded to a 3 night CPAP trial. 160 tolerated at least 4 hours of CPAP during run-in and were randomized.
Results. 149 participants (134 men, age 46±34, 81±57 days post-injury) completed the trial. Linear modelling revealed no differences in improvement in attention and information processing, as measured by the Paced Auditory Serial Addition Task, on intention-to-treat (p=.59; mean difference 2.6, 95% CI, -6.9 to 12.1) or per protocol for adherence (primary outcome). Intention-to-treat analyses revealed that CPAP significantly improved the secondary outcome of sleepiness (p=0.01, 1.17, -2.1 to -.25).
Discussion: CPAP significantly improved sleepiness after acute quadriplegia but did not improve neurocognition beyond that seen with post-injury, spontaneous recovery.

Trial registration: Australian New Zealand Clinical Trial Registry ACTRN12605000799651

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The Impact of Tele-Monitoring CPAP on Adherence in a Clinical Setting: A Pilot Study.

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Abstract

Background.

Continuous Positive Airway Pressure (CPAP) is an effective treatment for Obstructive Sleep Apnoea, although suboptimal treatment adherence is a significant issue. Tele-monitoring CPAP (TCPAP) is a device that allows for daily automatic transmission of detailed information to the clinician and for settings to be remotely changed, potentially enhancing the ability of clinicians to provide targeted helpful timely assistance. TCPAP has been shown to improve adherence[1], although its broader clinical utility is not well understood. We report initial results of a pilot study examining whether TCPAP improves CPAP adherence by allowing early appropriate targeting and intervention.

Aim.

To compare CPAP adherence at three months in patients implemented with tele-CPAP who were initially not adherent with those that were.

Methods.

Consecutive patients eligible for government funded CPAP that underwent CPAP implementation in November 2015 were provided with TCPAP devices. Patients were contacted when low adherence, residual events or leak were observed in a weekly data check; or where patients initiated contact. Patients with poor week 1 mean nightly adherence (<4hr) were identified. Adherence measured at 3 months is the 11-12 weeks average.

Results.

11 participants with median (range) age 66.5 (30-77) years, BMI 41 (29-51) kg/m2 and AHI 62 (31-105) /hr were included. 8 participants were adherent initially and 3 were not.

	n	at 1 week	at 3 months
Non-Adherent	3	1.3(1.3)	4.3(3.2)
Adherent	8	6.4(1.3)	4.7(2.5)

Table: mean (SD) adherence (hrs/night)

Discussion/ Conclusion.

The results of this small pilot study suggest an increased usage trend in the initially non-adherent group at 3 months, and for the initially adherent group to maintain adherence. If these trends are confirmed in a larger, prospective trial, it would support the notion that TCPAP with the targeted clinical interventions it facilitates may improve CPAP adherence.

Reference

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Churchward T[1,3], Dalic L[2], Edmonds M[2], Worsnop C[1,3], Carney P[2], Rochford P[1,3]

Combined Full EEG with Polysomnography in a clinical setting: a review.

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2. *Dept of Neurodiagnostics, Austin Health*
3. *Dept Respiratory and Sleep Medicine, Austin Health*

Introduction

Combined Polysomnography (PSG) with full EEG (PSG+EEG) is indicated where patients have relevant differential / multiple neurological and sleep disorders and PSG+EEG may better inform clinical practice, including where diseases may interact. Patients may benefit from clinical decisions based on such combined data, including by seeing temporal interactions between diseases. More broadly, the inter-department collaborative nature of these tests may enhance multi-disciplinary knowledge. Potential disadvantages include that these tests are more logistically complex to set up and report: possibly delaying diagnosis and treatment.

Aim

To review PSG+EEG utility and outcomes.

Methods

Retrospective analysis of consecutive PSG+EEG over 5 years from June 2011 was conducted and test diagnoses reviewed. The value of individual combined test results on clinical decisions was also described.

Results/Discussion

59 subjects (25 male) had a median (range) age 43 (17-75) years, BMI 28 (17-52) kg/m^2, and AHI 5 (0-72) events /hr.

Finding	% of studies
1 only	3%
2 only	6%
3 only	31%
4 only	6%
1 and 3	9%
2 and 3	16%
3 and 4	6%
1 and 3 and 4	3%

Key:	
1	Parasomnia
2	Seizure or significant EEG abnormality
3	Sleep disordered breathing
4	PLMD, or unexplained sleep fragmentation

Table 1. Post test diagnoses

Consensus of test value to inform clinical practice showed 90% of tests being informative, after consideration of test findings and previous diagnoses. Approximately 2/3 of studies with seizure-related diagnoses revealed comorbid sleep disordered breathing.

Jennifer M Cori,[1,2] Therese Thornton,[1,2,] Fergal J O'Donoghue,[1,2,] Peter D Rochford[2], John Trinder[1], Amy S Jordan[1,2]

Arousal induced hypocapnia does not reduce genioglossus muscle activity on return to sleep in obstructive sleep apnea.

1. University of Melbourne, Parkville, Vic., Australia;
2. Institute for Breathing and Sleep, Heidelberg, Vic., Australia;

Aim
To investigate whether a large ventilatory response to arousal in obstructive sleep apnea (OSA), promotes further obstruction by inducing hypocapnia and a subsequent reduction in upper airway dilator muscle activity on return to sleep.

Methods
30 OSA patients slept untreated whilst instrumented with: EEG, EOG, sub-mental EMG, airflow, end-tidal CO_2, epiglottic pressure catheter and intramuscular genioglossus EMG (EMGgg). Post-study, NREM respiratory arousals were identified and designated an end-arousal CO_2 value, which was the difference between an individual's waking CO_2 and their CO_2 on the last breath of arousal. Linear models determined whether there was an association between the end-arousal CO_2 and peak and tonic EMGgg on each of the first five breaths following the return to sleep.

Results
1137 arousals were analysed from 24 participants. The median end-arousal CO_2 was -0.72mmHg below waking CO_2 (range= -8.8mmHg to 11.5mmHg). There was a significant ($p<0.05$) negative association that approximated an exponential function between end-arousal CO_2 and peak EMGgg on all breaths (except breath 4) following the return to sleep (see Figure 1 for an example). A 1mmHg decrease in end-arousal CO_2 was associated with a 2% increase in peak EMGgg. Therefore arousals with the lowest CO_2 had the highest peak EMGgg. Tonic EMGgg was similar. These results are inconsistent with traditional respiratory control theory which would predict that low CO_2 post-arousal, would subsequently result in low muscle activity post-arousal.

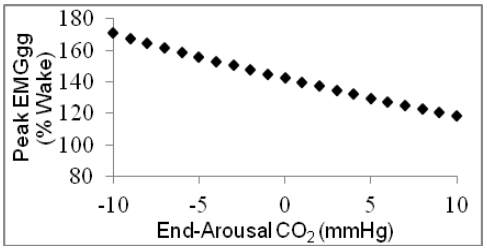

Figure 1. End-arousal CO_2 and peak EMGgg on sleep breath 5

Conclusion
Arousal induced hypocapnia does not reduce upper airway dilator muscle activity on return to sleep. Rather, arousals with low end-arousal CO_2 had increased genioglossus activity. Therefore, arousals are unlikely to perpetuate OSA via reduced dilator muscle activity as commonly stated in the arousal literature. These findings may explain why studies that have attempted to reduce incidence of arousal have had mixed efficacy in treating OSA.

Jennifer Cori, [1,2], Fergal O'Donoghue[1,2], Peter Rochford[1] John Trinder[2] and Amy Jordan[1,2]

Upper airway dilator muscle after-discharge occurs following arousal from sleep but is reduced by hypocapnia.

1. Institute for Breathing and Sleep, Heidelberg, Vic., Australia;
2. University of Melbourne, Parkville, Vic., Australia;

Aim

Arousal from sleep produces an abrupt increase in upper airway dilator muscle activity(1). Following the return to sleep muscle activity gradually decays back towards pre-arousal levels. This process is attributed to after-discharge. We assessed whether upper airway dilator muscle after-discharge is affected by hypocapnia which is also induced by arousal from sleep(1).

Methods

24 healthy individuals (6 female) had measurement of EEG, EOG, EMG, airflow, $P_{ET}CO_2$ and intramuscular EMG of the genioglossus (EMG_{GG}). During sleep, hypocapnia was induced via mechanical hyperventilation ($P_{ET}CO_2$ reduced ≥2mmHg below normocapnia). To induce normocapnia for comparison, ventilator settings remained unchanged and CO_2 was added. Tones were played to induce arousals during hypocapnia and normocapnia following two minutes of stable sleep. Repeated measures ANOVA compared the return to sleep EMG_{GG} between the hypocapnic and normocapnic conditions. Significance was set at $p<.05$.

Results

11 participants (4 female) had useable data. Pre-arousal $P_{ET}CO_2$ was significantly less during hypocapnia (40.74±2.37) than normocapnia (43.82±2.89). EMG_{GG} was significantly elevated above pre-arousal levels for two breaths following return to sleep during hypocapnia and six breaths during normocapnia. This finding is novel as the effect of hypocapnia on dilator muscle after-discharge has not previously been assessed. It is consistent with literature which demonstrates an inhibitory effect of hypocapnia on ventilatory after-discharge during sleep. In patients with obstructive sleep apnea who frequently experience episodes of upper airway collapse terminated by arousal, the resulting after-discharge may offer protection to upper airway patency following the return to sleep. However, if the ventilatory response to arousal is large and induces hypocapnia, dilator muscle after-discharge may be diminished, leaving the upper airway vulnerable to further collapse following the return to sleep.

Conclusion

In healthy individuals arousal from sleep induces dilator muscle after-discharge but the duration of after-discharge is reduced with hypocapnia.

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The direction of the relationship between symptoms of insomnia, depression and anxiety in adolescents

Authors

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Aim

This study assessed the direction of the relationship between symptoms of insomnia disorder, depression, various anxiety disorders and obsessive compulsive disorder (OCD) in adolescents after controlling for age, gender, chronotype, and outcome variable at baseline.

Method

Data was collected in eight high schools in Adelaide, South Australia, at two time-points approximately 6 months apart. The study was completed by 318 and 255 high school students at baseline and follow-up, respectively, aged 12 – 18 (M= 14.96, SD= 1.34) in grades 7 to 11 at baseline. Hierarchical regression analyses were used to assess each relationship, the first model controlling for age, gender and chronotype, and the second controlling for outcome variable at baseline.

Results

Insomnia symptoms predicted and were predicted by symptoms of each psychiatric disorder in model 1. In model 2, insomnia symptoms predicted symptoms of depression, and vice-versa. Symptoms of insomnia also predicted symptoms of separation anxiety disorder (SAD) but not vice-versa, in model 2. Symptoms of obsessive compulsive disorder (OCD) and social phobia (SP) predicted symptoms of insomnia disorder in model 2, but not vice-versa. Insomnia symptoms were no longer related to symptoms of other anxiety disorders in model 2. In general, the study found that symptoms of insomnia and psychiatric disorders are strongly associated in adolescents, but the direction of the relationship differs across psychiatric disorders.

Conclusion

Symptoms of insomnia disorder are bidirectionally related to depressive symptoms independent from baseline symptoms, and unidirectionally related to symptoms of OCD and SP where OCD and SP are independent risk-factors of the development of insomnia symptoms.

Continuous Positive Airway Pressure (CPAP) for management of Obstructive Sleep Apnoea (OSA) following acute, traumatic tetraplegia: adherence rates and factors influencing adherence.

Graco, M[1 2]; Schembri, R[1 3]; Berlowitz, DJ[1 2]

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Introduction

Prevalence of OSA following acute tetraplegia is reportedly 83%. CPAP is the first-line treatment however effectiveness is limited by poor adherence. Little is known about CPAP adherence in people with acute tetraplegia.

Aims

To determine the rate of CPAP adherence in people with acute tetraplegia and the associated factors.

Methods

Analysis of CPAP adherence in a randomized controlled trial of auto-titrating CPAP for OSA after acute quadriplegia (COSAQ). Participants who tolerated CPAP for >4 hours on 1 of 3 nights were randomised. Those in the CPAP arm were “adherent” if they tolerated CPAP for >4 hours per night for 5-7 nights/week for at least 50% of the 13-week study. Univariate analyses determined associations between baseline factors and adherence.

Results

11 centres participated in the study and 149 participants (134 men, age 46$\pm$34, 81$\pm$57 days post-injury) completed the study. 78% of participants with an Apnoea Hypopnoea Index (AHI) $\geq$10 passed the initial 3 night CPAP trial (164/211) and were randomized to CPAP or usual care. Of the 79 participants receiving CPAP, 23 (29%) were adherent. Assuming those who did not pass the initial trial would not have been adherent, the overall CPAP adherence rate was 18% (23/126). Factors associated with CPAP adherence included higher AHI (p=0.01), higher abdominal girth (p=0.003) and study site (p=0.02).

Conclusion

Adherence to CPAP following acute, traumatic quadriplegia is poor. Those with a higher AHI and abdominal girth are more likely to adhere. Clinician support and expertise with CPAP implementation is also likely to be important.

Title:
Use of the Montgomery Cannula ™ as an interim step in high risk tracheostomy decannulation.

Introduction: The Montgomery Cannula ™ (MC) is a hollow silicon tube sitting securely in the tracheostoma maintaining patency without impinging on the tracheal lumen. Initially designed primarily to treat obstructive sleep apnea (OSA), the MC allows evaluation of decannulation tolerance; maintenance of stoma patency and allows prompt and non-traumatic tracheostomy re-insertion if required.

Design, setting and participants: A case series of patients who received a MC from March 2013-February 2016 under the care of the Tracheostomy Review and Management Service (TRAMS) at a quaternary healthcare centre in Melbourne, Australia.

Intervention:
Eight patients received a MC as an adjunct to decannulation

- Airway patency in doubt (n=3)
- Risk of sputum retention (n=2)
- Assessment of mask ventilation (n=1)
- Medically unstable (n=1)
- Non-closing tracheostoma (n=1)

Results: Five patients had the MC removed after a period of stabilization, one patient still has the MC in situ for ongoing evaluation of fluctuating airway patency, one patient (Y) had the MC permanently placed for stoma occlusion, and one patient (X) removed their own MC which was recorded as an adverse event. There were three adverse events in total, patient X removed their own MC whilst confused but did not require tracheostomy or MC reinsertion. Patient Y had their MC dislodged accidently at home, it was re-introduced in the Emergency Department with no ongoing issues. The last case involved a patient coughing the cannula out inadvertently, reinsertion was not required.

Conclusion: The MC was a useful adjunct in cases where doubt existed over a patient's ability to safely tolerate decannulation. The MC may not be suitable for use in confused patients at risk of removing their own tube accidentally. The MC also provided a novel solution for a patient with failed tracheostoma closure.

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A CPAP intervention program to improve treatment adherence and self-efficacy in patients with Obstructive Sleep Apnoea

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Aim

Continuous Positive Airway Pressure (CPAP) is the mainstay treatment for Obstructive Sleep Apnoea (OSA), but adherence to treatment is poor. Group cognitive behavioural therapy (CBT) has been shown to improve CPAP uptake and adherence[1], however it is unclear if this is through an improvement in sleep apnoea self-efficacy. The aims of this study are to determine whether a CPAP intervention program improves 1) CPAP usage, and 2) scores on the Self-Efficacy Measure for Sleep Apnea[2] (SEMSA) questionnaire, compared to a treatment as usual program.

Methods

Thirty OSA patients commencing CPAP were randomised into 2 groups: treatment as usual (TAU; N=15) or a novel CPAP intervention program (CPAP; N=15). TAU participants underwent the usual laboratory protocol to commence CPAP, consisting of an education session, mask fitting, CPAP trial and in-laboratory CPAP titration. CPAP participants underwent the same protocol, plus (i) a 1.5 hour intervention program, 2 weeks prior to CPAP titration; and (ii) follow-up calls 1 and 7 nights post CPAP titration. The intervention consisted of a standardised education session and discussion of OSA, CPAP and general health. All participants completed the SEMSA at baseline and on the evening of their CPAP titration. SEMSA subscales are risk perception, outcome expectancies and treatment self-efficacy. CPAP usage data were downloaded 7 days after titration.

¶

Results

The CPAP group had significantly higher CPAP usage at 1 week compared to the TAU group (mean±SD=5.6±2.4hrs vs 3.4±1.9hrs; $p=0.01$). A significant interaction was found, with risk perception ($p=0.006$) and outcome expectancies ($p<0.001$) subscale scores improving from baseline to post intervention in the CPAP group only, but not scores on the treatment self-efficacy subscale ($p=0.35$).

¶

Conclusion

CPAP adherence at 7 days was higher in the CPAP group compared to the TAU group. Perceptions of health risks and outcome expectancies, but not treatment self-efficacy, improved with a CPAP intervention program.

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Getting informed about consent: Clinicians' perspectives on informed consent in a public child and adolescent mental health service

Joshua Rosen*, Cameron Dawson*, Dr Hanna Cheng†
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Abstract

Introduction

Informed consent is a crucial element of ensuring autonomy, patient-centred care and patients' rights. While it is clear that many clinicians see informed consent as ethically and legally important, there has been little research into how this translates into their everyday practice in an Australian child and adolescent mental health setting. This study aims to identify the broad themes of these clinicians' perspectives.

Methods

20 allied health and medical clinicians from inpatient and outpatient teams at Austin Child and Adolescent Mental Health Service (CAMHS) were approached between February and June, 2016 to participate in semi-structured interviews which were recorded and transcribed. The transcripts were evaluated for both inductive (pre-established) and deductive (emergent) codes and themes using the Framework approach. 10 inpatient and outpatient clinical files were audited through scanned medical records to evaluate documentation of informed consent.

Results

Four main themes were identified:

1. Ethics: Almost all clinicians agreed that ethics underpinned informed consent.
2. Information: Clinicians differed significantly in the information they provided routinely to clients and families. Reasons such as the effect on the therapeutic alliance were discussed by some clinicians.
3. Pragmatism: Case vignettes highlighted a common response of complying with a pragmatic approach in a family setting rather than dealing in ethical ideals.
4. Assent, consent and adolescents: Several views on this issue were apparent, including some confusion between assent and consent.

Conclusions

This study highlighted four key themes in perspectives on informed consent from child and adolescent mental health. This data will allow clinicians and managers to reflect and compare their own practices with those clinicians studied. For individual clinicians this may allow them to better rationalise their informed consent processes to be more aligned with their own ethical ideals. Managers may find these results and themes useful in tailoring training and auditing. Researches will be able to use this data as a springboard for additional research into informed consent in a child and adolescent mental health setting.

Keywords
Child and adolescent psychiatry, child and adolescent mental health, informed consent, clinicians.

Eleanor Pilioussis

Abstract: PTSD and Dissociation

Introduction

The dissociative subtype of Post-Traumatic Stress Disorder (PTSD) in DSM-5 is characterised by derealisation, depersonalisation and emotional numbing. Theory suggests that dissociation may limit treatment response by reducing fear activation. Research has not supported this theory, though only a few small studies have addressed the issue to date. The present study will examine the relationship between dissociative symptoms and treatment outcomes for a longstanding psychological treatment program. We predicted that dissociation would be correlated with overall PTSD severity, but would not correlate with response to treatment.

Methods

Participants were former Australian Defence Force personnel with PTSD (n=238), of mean age 50.7 years. All had completed the 12-week cognitive behavioural therapy, trauma-focused treatment program at the Psychological Trauma Recovery Service in Melbourne, Australia.

Data was collected upon admission to the Program and at 12 months after treatment commencement. Key outcome measures were the PTSD Checklist (PCL) and the Dissociative Experiences Scale (DES), with additional measures of anxiety, depression and anger. Paired t-tests, correlations and stepwise multiple regression were conducted to determine associations between variables of interest and treatment response.

Results

Mean pre-treatment PCL score significantly improved from 65.36 (SD 9.06) to 59.15 (11.37) post-treatment ($p<.001$), though DES scores did not change. Both dissociation and anger were associated with overall pre-treatment severity of PTSD (Pearson correlation = .362, $p<.001$ and .303, $p<.001$ respectively).

There was no correlation between dissociation and PTSD treatment response (Pearson correlation = .004, $p=.970$). Stepwise multiple regression analysis revealed that both anger and pre-treatment PCL score explained a significant proportion of the variance in treatment response ($F(2,103) = 13.794$, $p<.001$), with an R^2 of .211.

Conclusion

The present study supports the recent research findings that dissociation does not affect response to trauma-focused cognitive behavioural therapy. Further research into the role of anger as a correlate of severity, and a predictor of treatment response appears warranted.

Khumra S[1,2], Chan J[3], Worland T[4], Urbancic K[1,2], Angus P[5], Jones B[5], Grayson M.L[2,6], Trubiano J[2,6]

A comparative analysis between antibiotic allergy labels and non-antibiotic allergy labels in liver transplant recipients

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4. Department of General Medicine,
5. Liver transplant unit,
6. Department of Medicine, University of Melbourne

Aim
Antibiotic allergy labels (AA) are associated with suboptimal prescribing and inferior clinical outcomes. The effect of labelling in liver transplant recipients (LTR) is unknown. We aim to determine the prevalence and nature of AA and their impact on antibiotic use and clinical outcomes.

Methods
A retrospective cohort study was conducted over a 5-year period (2010-2015). Using a departmental liver transplant database, recipients with AA were identified. An equal number of matched controls (LTR without an antibiotic allergy label; NAA) were selected for comparison. AA were defined as Type A adverse drug reactions ([ADRs], non-immune mediated), Type B ADRs (immune mediated) or unknown. Baseline demographics, transplant history and infection-related admissions were recorded. Antibiotics administered during liver transplant and subsequent infection-related admissions were recorded: agent(s) and duration. Re-admission, ICU-admission, *Clostridium difficile* infection (CDI) and mortality rate were captured.

Results
From 313 LTR, 51 (16%) had ≥ 1 AA label. These were matched with 52 controls. Female predominated in the AA group (65% vs. 25%, p=0.002). No other statistical differences in baseline demographic, transplant history or clinical outcomes (p > 0.05) demonstrated. Seventy-seven ADRs were recorded: 16 (21%) Type A, 56 (73%) Type B and 5 (6%) unknown. Main antibiotic classes implicated included beta-lactams (53%), sulphonamides (21%) and fluoroquinolones (9%). AA patients were associated with higher cephalosporin usage (107/354 courses vs. 75/328 courses, p=0.03), a trend toward increased glycopeptide use (78/354 courses vs. 76/328 courses, p=0.08) and CDI (9 cases vs. 3 cases, p= 0.07).

Conclusion
High AA prevalence in LTR was identified. Many reported ADRs consistent with side effects amendable to pharmacist-led ‘de-labelling’. AA associated with increased cephalosporin and reduced trimethoprim-sulfamethoxazole (Co-T) courses. Reluctance to employ Co-T has potential implications for

prophylaxis strategies. Increased glycopeptide and CDI rates are common antimicrobial stewardship program targets.

Taylor L, [1], Leroi M,[1]

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Phenotypic identification of multiple β-lactamases in extensively resistant Enterobacteriaceae

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1.Department of Microbiology, Austin Pathology, Austin Health, Heidelberg, Vic., Australia;

¶

Aim

To evaluate a modification of a phenotypic screening method for the detection of extended spectrum β-lactamases (ESBLS) and carbapenemases¶

Methods

Current CLSI guidelines recommend a differential zone size measurement method[1] for the detection of ESBLs. Limitations with this method may occur when other superimposed β- lactamases preclude interpretation. A modification of this method with the addition of β- lactamase enzyme inhibitor reagents to each disc offers the potential for improved detection of β- lactamases[2]. This method also permits limited characterisation of carbapenemases by use of meropenem as a substrate.

Reference and routine laboratory isolated gram negative organisms with molecular characterisation were selected for testing. Molecular results were used as the comparative standard.

¶

Results

46 isolates were evaluated with 17 carbapenemase and 39 ESBL tests performed respectively.

Table 1: Carbapenemase detection

Modified CLSI screen		PCR reference result	
		Positive	Negative
POS	10	10	0
NEG	7	3	4

13/17 isolates were found to have a carbapenemase.10 of these were detected by both CLSI and PCR methods. Of the three isolates that were negative using the CLSI method two were OXA metallo-β lactamases and one strain had a VIM. There were no false positives.

Table 2: ESBL detection

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Modified CLSI screen		PCR reference result (CTX-M)	
		Positive	Negative
POS	18	17	1
NEG	21	0	21

17/18 isolates with a positive CLSI screening test had molecular evidence of a CTX-M linage ESBL. The single discordant positive result was found on sequencing to be due to a SHV lineage ESBL (SHV-5).

Conclusion

The modified CLSI method accurately identified ESBLs in organisms with multiple β lactamases. It was less successful in detecting some carbapenemase enzyme types.

References

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McGrath A, [1] Loo W [1]

Comparison of medication prescription safety and quality using an electronic medication management system to paper-based prescribing systems nationally.

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Aim

To compare the safety and quality of patient medication prescriptions placed using an electronic medication management system (eMMS) to aggregate data from audits of paper-based systems conducted in hospitals across Australia in 2014.[1]

Methods

A random sample of 52 patients from 18 Austin Health (AH) ward areas was selected in April 2016. All medication orders for these patients were reviewed for up to seven days. Data collected included patient identification details, weight, allergies and venous thromboembolism prophylaxis. The safety and quality of prescribing was assessed against criteria adapted from the Australian Commission for Safety and Quality in Healthcare audit tool for paper medication charts in Australian hospitals. Clarity of medication name, route, dose and frequency were independently assessed by two investigators (an intern pharmacist and a senior medication safety pharmacist).

Results

Overall 891 electronic medication orders were evaluated.

- Identification requirements were complete for all AH patients, compared with 42.3% on paper charts nationally ($p<0.01$).
- Over 67% of AH patients had a weight recorded compared with 27.5% on paper charts ($p<0.01$).
- One (0.1%) electronic order was unclear for medication name, compared with 3% nationally ($p<0.01$). This order was deemed low risk for patient harm.
- Two (0.2%) route errors were observed compared with 10.4% nationally ($p<0.01$).
- Within AH orders, no frequency errors, dose errors or error-prone abbreviations were observed.
- Prescriber name was clear for all AH orders compared with 71.6% nationally ($p<0.01$).

Conclusion

This audit of the AH eMMS demonstrates a superior level of clarity and completeness of patient specific and medication order details, compared with national audits of paper-based systems in other Australian hospitals. Some errors still occur with an eMMS, therefore real time monitoring of medication orders remains important to maximise safety and quality of prescribing and related medication documentation.

References

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Taylor SE,[1] McLauchlan R,[1] Chan J,[2] Chau A,[2] Goldblatt C[2]

So what are we waiting for? Outpatient clinic patient perceptions and expectations of outpatient pharmacy services.

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2. *Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Vic., Australia*

Background
Increasingly, hospital outpatient pharmacy departments are dispensing highly specialised medicines including oral chemotherapy, complex antimicrobial and transplantation regimens.

Aim
In response to a number of complaints about the timeliness of prescription dispensing, we sought to evaluate patient perceptions and expectations of an outpatient pharmacy service.

Methods
We conducted a series of 50 structured interviews with a random selection of patients or their carers attending an outpatient clinic of a metropolitan tertiary referral hospital. Interviews were conducted face-to-face in the clinic waiting area. To achieve a good spread of responses across the different clinics up to two patients were recruited from an individual clinic and up to five clinics were focused on each day for one week in November 2015. Qualitative data was analysed thematically by one investigator by coding significant statements into themes. These themes were reviewed by a second investigator and discrepancies were discussed to achieve consensus.

Results
The most important factors that the patients considered when selecting a pharmacy were convenience (40%), best explanations about the medicines (22%), stock availability (14%), dispensing speed (8%) and lowest price (4%). Most patients expected that their prescriptions should be dispensed within 10-15 minutes. Generally patients had a limited understanding of what is involved in dispensing a prescription after they present it to the pharmacy and felt that there would be no differences in the complexity of prescriptions dispensed in a hospital compared to a community pharmacy.

Conclusions
Patients valued convenience and provision of thorough medicines information but they also expected medicines to be dispensed within a short time period. Interventions are required to increase patient awareness of the steps involved in dispensing their medicines and the complexity of newer medication therapies.

Review of the prescribing of oxycodone on discharge from a metropolitan hospital.

Authors: Emily O'Halloran (intern Pharmacist Austin Health), Jade Eyles (QUM Pharmacist Austin Health), Anne McGrath (Medication Safety Pharmacist Austin Health).

Aim: To determine the quantity of oxycodone that is currently being prescribed to patients and whether a plan for the duration of its use is communicated on discharge.

Methods: All oxycodone dispensing on discharge over a two-week period was reviewed. Oxycodone dispensings on discharge were assessed for the quantity supplied, pharmacist intervention to adjust the quantity, comment about the duration of use for controlled release products, pharmacist documentation of the provision of additional information, and communication of a management plan for controlled release products to the general practitioner (GP).

Results: The immediate release (IR) and controlled release (CR) products were analysed separately. Of the 277 IR oxycodone dispensings on discharge the pharmacist reduced the quantity supplied in 28 (10.1%) cases and provided additional information on 30 (10.8%) occasions. Eighty-nine CR dispensings were included, of these the pharmacist reduced the quantity in 6 (6.7%) cases and documented the provision of information 12 (13.5%) times. A stop date was included on only 23 (25.8%) labels and a plan for the intended duration included in 30 (33.7%) discharge summaries. Of note, the emergency department and short stay wards showed higher rates of pharmacist intervention (17.4% compared to 9.4%) and provision of information (69.6% compared to 5.50%) for the dispensing of IR oxycodone when compared to the rest of the hospital.

Conclusion: This review has demonstrated that patients are regularly prescribed a reduced quantity (i.e. less than a full pack) of oxycodone on discharge from hospital, but that there is room for improvement in the provision of information about the plan for oxycodone use to both the patient and their GP.

Chow A,[1] Loo W, [1] Cheung S, [1] McLauchlan R, [1] Taylor S[1]

Successful implementation of an electronic Controlled Drug Register in a major public hospital pharmacy department.

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Background

Historically, all transactions of Controlled (Schedule 8) Drugs have been recorded using a paper-based register, a system with several shortcomings:

- Difficulties in investigating discrepancies, due to concurrent use of multiple books throughout a large organisation.
- Archival storage required to store bulky books for three years.
- Risk of health-professional diversion going undetected, posing significant patient and staff safety risks.

We have therefore developed an electronic system (e-Register) for documenting controlled drug (CD) transactions.

Aim

To describe the development, implementation and evaluation of a computerized CD e-Register within a major hospital pharmacy department.

Methods

1. An electronic system for obtaining, supplying, recording, disposing and monitoring of CD was developed and tested. This system sits within the pharmacy dispensing program.
2. In the absence of national uniform specifications for e-Registers, we evaluated our e-Register against criteria developed by NSW Health that e-Registers must meet to comply with NSW legislative requirements.
3. The e-Register was progressively implemented throughout our department. A survey of pharmacist perceptions was undertaken and the time to process CD transactions pre- and post-implementation of the e-Register were measured.

Results

We are satisfied that our new e-Register complies with best practice guidance as specified by the NSW Health criteria. Rollout of the e-Register began in May 2016. It has been well received by pharmacists, who have noted reduced time to address discrepancies and efficiencies due to auto-population of prescription and requisition details. Pharmacists have recommended rolling the system out to include ward CD transactions, to fully close the CD supply loop.

Conclusion

Implementation of an e-Register for CD has improved efficiency, accuracy, staff satisfaction and minimized the risk of drug diversion within a hospital pharmacy. Further roll-out to wards requires the dispensing system to link more closely with our electronic clinical documentation system.

Taylor SE,[1] McLauchlan R,[1] Chan J,[2] Chau A,[2] Goldblatt C[2], Morey S[1]

Listening to the voice of the patient to inform outpatient pharmacy dispensary service quality improvements.

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2. *Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Vic., Australia*

Background
The quality of care provided by the hospital is important and so too are our patients' perceptions of this care. The Australian Council on Healthcare Standards states that hospitals should ensure that patients' feedback can contribute to the hospital's quality improvement programs.

Aim
To develop a quality improvement tool to evaluate patient perceptions of an outpatient pharmacy service and how the service might be improved.

Methods
A survey tool to assess satisfaction with the outpatient pharmacy service and recommendations for improvement was adapted from a previously published questionnaire. The tool included questions in five main domains; performance, responsiveness, tangibles, courtesy, security and direct service questions. One hundred randomly selected patients who received an outpatient prescription from the outpatient pharmacy during a single week in November 2015 were invited to participate in a 5-minute telephone interview.

Results
The mean age of participants was 58 years and 58% were male. Patients attended a broad range of outpatient clinics. Overall, 95% of patients reported that the outpatient pharmacy service was good or excellent, 90% reported that questions about the medicines were answered well or very well and 98% reported that staff helpfulness and friendliness were good or excellent. Patients' recommendations for improvement included configuration of the front glass window, particularly for elderly and hearing impaired patients and more comfortable chairs and music in the waiting area.

Conclusion
Overall, patients are highly satisfied with the services provided by the outpatient dispensary. It is intended that such interviews will be conducted at 3-6 monthly intervals to evaluate incremental changes made to the service and inform future service improvement interventions.

Hurren, F, [1], Fang, YT,[1], Chua, K, [1]

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The Carbapenem Inactivation Method (CIM) for the detection of OXA enzymes in Gram-Negative Bacteria.

¶

1.Department of Microbiology, Austin Hospital, Heidelberg, Vic., Australia

¶

Aim

The emergence of carbapenem-producing Gram-negative bacteria is an emerging public health concern. Current phenotypic methods, such as the Carba NP test[1], provide a rapid assay able to detect carbapenemase activity in *Enterobacteriaceae* isolates. However, this method has provided challenges in the detection of Oxa containing enzymes for a number of laboratories. The CIM method[2] provides an alternative phenotypic screening method that can reliably detect carbapenemase activity.

¶

Methods

The CIM was performed by suspending two 10µl inoculation loops of culture taken from a blood agar plate in 1mL of saline. Aliquots of this suspension were added to two eppendorf tubes. A 10µg meropenem disk was added to the suspensions and incubated at 35°C for 8 hours and 24 hours respectively. After incubation the disks were removed from the suspension and placed on a Mueller-Hinton agar plate inoculated with a susceptible *Escherichia coli* ATCC 25922 strain and subsequently incubated at 35°C for 16-18 hours with an initial read at 8 hours. If the test isolate produced a carbapenemase, the meropenem in the disk was inactivated thus allowing growth of the susceptible *E. coli* strain. A clear zone of inhibition was observed in isolates that do not harbour carbapenemases.

Results

A total of 20 clinical and screening isolates (15 *Acinetobacter baumanni*, 2 *E. coli*, 1 *Klebsiella pneumoniae*, 1 *Pseudomonas aeruginosa*) together with control strains were tested in parallel with the Carba NP test. 19 test isolates yielded a positive CIM result at both an 8 hour and 16-18 hour read. Only one *A. baumannii* isolate demonstrated a positive Carba NP test result, but this isolate contained both OXA and NDM genes. 19 of test isolates were shown to carry various OXA genes by PCR.

Conclusion

The CIM method is a reliable phenotypic tool to detect Gram-negative bacteria harbouring OXA containing genes compared to the Carba NP method.

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2. Van der Zwaluw et al. PLOS ONE 2015 10: 1371

What is the significance of a positive central venous catheter blood culture without a concordantly positive peripheral blood culture? – a prospective study in uninfected Haematology patients

Authors:

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Abstract

Background: Catheter related bloodstream infections (CRBSI) are an important source of morbidity and mortality for patients with in-dwelling central venous catheters (CVC). Some diagnostic criteria consider a positive CVC blood culture (CVCBC) a CRBSI despite negative peripheral blood cultures (PBC). This definition has not been systematically evaluated. Theoretically it would have high sensitivity but may have poor specificity due to growth of contaminating flora from the device. This poses an issue in overcalling infection rates, with consequences for inappropriate antibiotic administration and line removal. This study is an ongoing project that examines the contamination rate of CVCBC to assess the specificity of this definition.

Methods: This is an ongoing, single site, prospective observational study. 'Well' haematology patients with long-term (≥3 days) in-dwelling central lines (Hickman catheters, Port-a-Cath, PICC) were invited to participate. Participants had a paired set of blood cultures taken, one set from the CVC and another from a peripheral vein, and these were cultured for any microbial growth. Participants were then reviewed at 72 hours for evidence of infection to ensure any microbial growth represented true contaminants. Samples were considered true contaminants if there was a positive CVCBC but negative PBC and no clinical signs of infection at 72 hours.

Results: Out of 16 paired sets of cultures, no contaminants were detected. All participants were well at 72 hours of follow up. One participant was treated with antibiotics within the 72 hour follow up period and their sample had to be excluded from the study – leaving 15 sets of cultures included for review. There was one unplanned emergency admission within 7 days following enrolment but this was not due to an infectious cause. Final results are pending.

Conclusion: Initial findings indicate that the contamination rate of CVCBCs is low. However, the current sample size is too small for any meaningful statistical analysis to be performed. Further blood samples would be required before a conclusion could be made.

Keywords:

Contamination rate, false positive rate, central venous catheter blood culture, peripheral blood culture, catheter-related bloodstream infection

Fields: Tumour Immunology, T-Cell development

TCR beta sequencing to determine clonal T-cell populations in melanoma patients undergoing immunotherapy

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The adaptive immune system elicits clonal expansion of tumour-infiltrating lymphocytes (TILs) in melanoma[1]. Immunotherapeutics targeting immune suppressive receptors such as CTLA-4 and PD-1 have been shown to influence prognosis with a correlated increase in TILs[2,3]. However, immune-checkpoint inhibition can also prompt immune-related adverse events such as rare instances of acute inflammation including complications like cytomegalovirus (CMV) pneumonia[4]. Assessing clonality and TIL numbers is therefore of interest in solid tumours. Next Generation Sequencing (NGS) assays designed across the V, D and J regions of the *TCRB* gene can be used to infer T-cell clonality. The immunoSEQ hsTCRB kit from Adaptive Biotechnologies utilizes an initial VDJ gene-specific amplification with a proprietary set of primers, followed by adapter ligation and sequencing on an Illumina platform. The sensitivity of the assay was assessed by spiking in a single clone population, isolated using NY-ESO-1 derived peptides in proportions with healthy donor peripheral blood mononuclear cell (PBMC) DNA. It was shown that genomes derived from healthy donor PBMCs contain 85% unique clones of TCR, and we were able to detect our clone spiked at 0.01%. This ability to detect specific clones of lymphocytic DNA indicates that the immunoSEQ NGS assay is readily adapted to the study of clonal T-cell populations and will be sensitive enough to target limited lymphocytic DNA in FFPE from tumour tissues including serial studies of patients undergoing immunotherapy. Following sequencing Individual clones can also be monitored using uniquely designed qPCR assays utilising rearrangement specific primers.

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Jessica Duarte[1], Janique Peyper[2], Katherine Woods[1], Simon Chang-Hao Tsao[1], Georgina Long[3], Richard Kefford[4], Richard Scolyer[3], Jonathan Cebon[1], Jonathan Blackburn[2]

Protein Microarrays for the Immunological Profiling of Melanoma

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Aim
There is substantial evidence that the aberrant expression of cancer-testis (CT) antigens - a family of ca. 150 proteins that are both auto-immunogenic and mainly restricted to tumours in various types of human cancers - makes them attractive immunotherapy targets, as well as possible cancer diagnostic and therapeutic monitoring markers. Therefore, we aimed to measure differences in CT antigen-specific antibody repertoires between pre- and post-treatment melanoma patient samples, and assess whether these could correlate with the likelihood, nature and extent of response of these individual patients to a given therapeutic treatment.

Methods
In order to detect and quantify CT-antigen-specific antibodies circulating in the serum of cancer patients, we co-developed a novel CT antigen microarray platform. This tool represents a high-throughput means of profiling antibody repertoires against over 100 cancer-restricted antigens in a highly reproducible, sensitive and specific manner. We carried out a retrospective serological study of antibody titres across a cohort of thirty-six advanced malignant melanoma patients prior to and following kinase inhibitor treatment, using archived human serum samples.

Results
We observed statistically significant changes in antibody titres to treatment across 81% of the cohort, and successfully identified abundant antibody titers towards two leading CT antigens – NY-ESO-1 and MAGEB1 – which were present across 61% and 56% of this cohort, respectively, with reported therapeutic target potential. Furthermore, our CT antigen array data suggested preliminary evidence of direct correlation between our observed antibody responses and the clinically reported ones across a subset of patients (approximately 35% of the cohort).

Conclusion
In conclusion, we showed that our novel protein microarray platform represents a sensitive, high-throughput and readily customizable means to detect and quantify the presence of large panels of cancer-specific human antibodies in serum, obtaining consistently robust, high quality and reproducible data, and demonstrating its potential feasibility and inferred biological significance.

King D, [1,2], Liu Z,[1,3,] , Ramsland PA[4], Burvenich IJG[1,3] Scott AM[1,3]

Implications of Fc-engineering to a humanised anti-Le^y antibody on receptor binding and cellular effector function

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Aim
The interaction between the immunoglobulin G (IgG) Fc region and Fcγ receptors (FcγRs) is the primary mechanism linking antibody-mediated immune responses with cellular effector functions. The majority of this research has been aimed at enhancement of interactions with FcγRIIIa, which is the key mediator in natural killer (NK) cell antibody-dependent cell-mediated cytotoxicity (ADCC). Through ligation of FcγRIIIa, NK cells not only induce tumour cell death via ADCC but also induce expression of the costimulatory receptor CD137 which can be targeted for further enhancement of effector function.
Method
Here, we describe a set of novel Fc variants of anti-Lewis Y (Le^y) antibody (hu3S193) generated through amino acid engineering. These novel variants were first determined by *in silico* methods from crystal structures and then produced in a mammalian expression system for further analysis. Binding of variant Fc domains to human Fc receptors (FcRs) was determined via ELISA and SPR measurements on Biacore. ADCC assays were performed with various Le^y positive tumour cell lines using PBMCs and purified NK cells as effector cells and CD137 expression on NK cells was evaluated through flow cytometry.
Results
Binding analysis of Fc domains to FcRs showed mutants with enhanced binding to FcRs and some mutants even showed completely abrogated binding. ADCC results confirmed FcγRIIIa binding profiles seen with hu3S193 variants. The Fc mutants with enhanced binding to FcγRIIIa, S239D and S298A, show enhanced ADCC and ability to stimulate CD137 expression on purified NK cells.
Conclusion
The novel Fc variants of hu3S193 show altered binding to FcRs and some demonstrated improved effector functions on NK cells. The two variants S239D and S298A enhanced ADCC and increased CD137 expression on NK cells. These findings highlight the importance of these Fc amino acids in binding to FcRs, and demonstrate the ability to engineer therapeutic antibodies to further enhance antitumour efficacy.

The EHF transcription factor is downregulated in poorly differentiated colorectal cancers and inhibits cell migration

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Background:

The loss of differentiation is a key characteristic of colorectal cancer, and is associated with increased propensity for metastasis. Understanding the mechanistic basis for the loss of differentiation in colorectal cancer may inform strategies for re-inducing differentiation and consequently inhibiting metastatic spread. The goal of this study was to determine the role of the Ets Homology Factor (EHF) transcription factor in the regulation of differentiation status and migration of colorectal cancer cells. EHF is a member of E26 transformation specific (ETS) transcription factors are important regulators of differentiation and developmental programs in many tissues.

Methods:

Affymetrix microarrays were used to identify transcription factors which are significantly differentially expressed between moderately and poorly differentiated colorectal cancer cell lines. Differential gene expression was confirmed by q-RT-PCR and western blot. The moderately differentiated colorectal cancer cell line SW948was transfected with EHF targeting siRNAs using lipofectamine. The poorly differentiated colon cancer cell line HCT116 was transfected with an exogenous EHF construct and single cell clones were selected by G418 resistance. Migration potential was analysed using the Boyden-Chamber assay and stained for migrated cells.

Results:

Analysis of microarray data demonstrated that EHF expression was significantly downregulated in poorly differentiated colorectal cancer cell lines compared to moderately differentiated lines. Knockdown of EHF in moderately differentiated SW948 colorectal cancer cells enhanced cell migration while conversely, EHF overexpression in poorly differentiated HCT116 cells inhibited cell migration.

Conclusion:

This study identifies a novel role for the EHF transcription factor in the regulation of migration of colorectal cancer cells.

Targeting Jak Kinases to treat Colon Cancer

Colon Cancer is one of the most prevalent forms of cancer in Australia, resulting in 15 000 cases and over 4000 deaths per year. Late presentation of the disease is associated with poor prognosis and a 5-year survival rate as low as 5%.

Over 80% of colon cancers are caused by aberrant activation of the Wnt/β-Catenin pathway. This is primarily a consequence of homozygous loss or inactivation of the tumour suppressor gene APC. However inhibition of the Wnt/β-Catenin pathway is likely to result in on-target toxicity. Interestingly, APC-mutant intestinal epithelium, but not normal epithelium, requires continuous signalling through the gp130-Jak-STAT3 pathway. This suggests that the gp130-Jak-STAT3 pathway can be rate-limiting for the proliferation of the intestinal epithelium in the presence of excessive Wnt/β-Catenin signalling. Pro-inflammatory cytokines Interleukin 6/11 (IL-6/-11) activate the gp130-Jak-STAT3 pathway. Excessive secretion of these cytokines results in increased activity of the Signal Transducer and Activator of Transcription (STAT). Janus Kinases (JAKs) are important upstream tyrosine kinases that phosphorylate STAT3. Therapeutic inhibition of JAKs can limit STAT3 activation and therefore reduce the role it plays in proliferation, survival and invasion.

We have used in vitro techniques to analyse the role JAKs play in colon cancer. Firstly we determined which JAKs are expressed in a panel of colon cancer cell lines. We then determined the role that Jaks play in STAT3 activation and colony formation using a system of inducible shRNA-mediated down-regulation of specific members of the JAK family. We have determined that Jak1 is the predominant kinase in colon cancer cell lines and it plays a vital role in the ability of these cells to form colonies in 3D culture systems, whereas Jak2 is not required. Furthermore experimental Jak1/2 specific inhibitors AZD-1480 and CYT-387 both significantly impaired the ability of cancer cells to form colonies.

We use the inducible, colon-specific cdx2-cre^{ERT2} model of colon cancer to assess the efficacy of these inhibitors. To most accurately represent human colon cancer, this mouse model has a loss of Apc, an activating oncogenic mutation in Kras and loss of a p53 allele. Tumours develop quickly in these mice and represent an aggressive, advanced form of the disease. A Jak1 specific inhibitor will be used in addition to AZD-1480 and CYT-387, which will confirm that inhibiting Jak1 is a potential therapeutic target in the treatment of colon cancer. Looking ahead, we will also analyse the immune system in these mice to assess the impact of Jak inhibition and investigate whether immune checkpoint blockade may be possible in this model.

Targeted combination therapeutics to overcome acquired resistance to single targeted therapeutic in FGFR3 aberrant metastatic bladder cancer

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Introduction

New therapies are required for patients with metastatic urothelial cancer (mUC), which has a median overall survival of 12-18 months. Mutations and gene fusions in the *Fibroblast Growth Factor Receptor* 3 (*FGFR3)* gene occur in 20-30% of patients with mUC. A clinical trial which assessed activity of the pan-FGFR inhibitor BGJ398 (Novartis) demonstrated responses in 30% of patients with mUC and *FGFR3* gene mutations or fusions and a median PFS of 4 months. This was lower than that reported for other targeted therapeutics, and suggestive of both innate and acquired resistance mechanisms to therapy. To address this, we generated cell lines with acquired resistance to BGJ398 by long term culture of two human bladder cancer cell lines with *FGFR3* fusions (RT4, SW780) with this agent. Analysis of these lines identified increased expression of pHER3 and pAXL in the resistant lines. The aim of this Honours project was first, to determine whether combination treatment of BGJ398 with HER3 and AXL inhibitors can further inhibit tumour cell growth and second, to explore the mechanism and time course over which BGJ398 induces pHER3 and pAXL.

Methods

RT4 and SW780 cell lines were treated with BGJ398 alone or combination with either AZD8931 (Her3 inhibitor) or R428 (AXL inhibitor). For comparison, we also assessed response to these agents in the FGFR3 WT UC cell line T24 (negative control) and the FGFR2-amplified gastric cancer cell line Kato III (positive control). Cell viability was assessed after 96 hours using the CellTiter-Glo® luminescent assay (Promega) and apoptosis was determined by measuring the sub-G1 population by Flow Cytometry. Synergy between agents was determined by calculation of the R-index. Changes in protein expression of pHER3, HER3, pAXL and AXL following drug treatment were determined by Western Blot analysis over 96 hours. Changes in mRNA expression of HER3, AXL and relevant FGFR3 downstream pathway components (Myc and Fra1) were assessed by qPCR over the same time course.

Results

Treatment of the FGFR3-fusion harboring cell lines RT4, SW780 with BGJ398 significantly inhibited cell proliferation. Treatment of these lines with the HER3 inhibitor AZD8931 alone had minimal effect on cell proliferation however combination treatment with BGJ398 resulted in further inhibition of cell proliferation. Furthermore combination treatment induced apoptosis in these cell lines. Similar effects were observed in the FGFR2-amplifed Kato III cell line but not in FGFR-WT T24 cells. In contrast treatment of these cell lines with the AXL inhibitor R428 had minimal effect on cell proliferation when treated alone and failed to enhance BGJ398 induced cell proliferation. Assessment of activity of these combinations in the acquired resistant cell lines is currently underway.

Exploration of the mechanism and time course over which BGJ398 induces pHER3 and pAXL are currently being assessed in SW780 and RT4 cells treated with BGJ398 over 96 hours and assessment of changes in HER3 and AXL mRNA and protein expression.

Discussion/Future Directions

Acquired resistance to FGFR3 inhibition is associated with increased pHER3 and pAXL. Combination treatment with BGJ398 with the HER3 inhibitor AZD8931 enhanced the effect of BGJ398. In contrast AXL inhibition failed to enhance the growth inhibitory effect of BGJ398. These findings identify a novel strategy for enhancing the therapeutic activity of BGJ398 in FGFR3-fusion harboring mUC.

Garwood MJ[1], Hawkes EA[2,3], Chong G[2]

Safety and efficacy of high-dose methotrexate as central nervous system prophylaxis in diffuse large B-cell lymphoma

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Aims: Systemic high-dose methotrexate (HDMTX) is utilized as a prophylactic agent for central nervous system (CNS) relapse in diffuse large B cell lymphoma (DLBCL). However, its efficacy is undetermined. Patient selection for HDMTX is largely based on historical risk factors. The German high-grade non-Hodgkin lymphoma study group (DSHNHL) prognostic model separates patients with aggressive B-cell lymphoma into three risk groups for CNS disease. The aims of this study were to evaluate the toxicity of HDMTX, determine HDMTX efficacy in preventing CNS relapse and define if HDMTX and non-HDMTX patients differ according to the DSHNHL model.

Methods: Patients diagnosed with DLBCL between 2004 and 2014, initially treated with RCHOP-like chemotherapy and given HDMTX for CNS prophylaxis were identified by pharmacy records at Austin and Box Hill hospitals. DLBCL patients diagnosed between 2007 and 2014, initially treated with RCHOP-like chemotherapy and not given HDMTX were identified by pharmacy records at Austin hospital. Patient records were retrospectively reviewed for HDMTX toxicity, CNS disease risk factors as specified in the DSHNHL model and CNS relapse.

Results: 72% of patients given HDMTX did not experience nephrotoxicity, and none progressed to grade 4 nephrotoxicity. 97% of HDMTX patients experienced anaemia and 75% experienced neutropenia. 1 patient had grade 3/4 anaemia, 11 patients had grade 3/4 neutropenia and there was one episode of febrile neutropenia. Comparison of 24 HDMTX patients matched to 24 non-HDMTX patients showed no significant difference in CNS relapse rate (p-value 0.489). Comparison of the DSHNHL model score for 24 HDMTX patients and 122 non-HDMTX patients showed no significant difference.

Conclusion: HDMTX was well-tolerated by patients, therefore can safely be used as a prophylactic agent. Larger studies are required to determine the efficacy of HDMTX as CNS prophylaxis. Tools like the DSHNHL prognostic model maybe useful in providing objective methods for identifying patients at risk of CNS relapse.

Mikeska T [1,2], Do H [1,2], Witkowski T [1], Musafer A [1], Zapparoli G [1], Dobrovic A [1,2]

Accredited *MGMT* Methylation Analysis for use in Molecular Diagnostics

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Aims:
Methylation of the promoter region of *MGMT* occurs frequently in glioma, in particular glioblastoma and *IDH*-mutated low-grade glioma. *MGMT* methylation status has prognostic as well as predictive value. The value of testing for MGMT protein expression by immunohistochemistry staining as an alternative is controversial, and *MGMT* methylation remains the gold standard for clinical decision making. We thus have established a workflow for DNA methylation analysis of *MGMT* suitable for use in molecular diagnostics to support neuro-oncologists in their decision making processes.

Methods:
Tumour-rich and tumour-free areas are identified by a pathologist on H&E stained sections of formalin-fixed, paraffin-embedded (FFPE) tumours. DNA is extracted from the macrodissected material and bisulfite-modified for DNA methylation analysis. The sample is then tested for DNA methylation in the promoter region of the *MGMT* gene using methylation sensitive-high resolution melting analysis (MS-HRM). A quantitative score can be obtained using bisulfite pyrosequencing after MS-HRM if required.

Results:
MS-HRM allows the reliable detection of *MGMT* methylation in FFPE-derived DNA and gives results consistent with bisulfite pyrosequencing. The assay allows an easy and unambiguous interpretation of results, even when methylation patterns are clearly heterogeneous.

Conclusions:
The workflow established for *MGMT* methylation analysis meets the requirements for routine use in molecular diagnostics. An independent study showed that this assay outperformed methylation-specific PCR in predicting progression-free survival and overall survival for high-grade glioma patients. Standardised testing procedures and stringent quality control procedures ensure high-quality and reproducible results as well as a fast turn-around-time. Our laboratory at the Olivia Newton-John Cancer Research Institute is NATA accredited for performing *MGMT* methylation testing.

Inflammation mediates profound changes to the immunopeptidome of melanoma.

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Aim:
Degradation of cellular proteins by the proteasome is critical for generation of MHC-associated peptides. The constitutive proteasome and the IFNγ-induced immunoproteasome differ in three catalytic subunits, altering production of MHC class I epitopes. The potential for a disparate repertoire of epitopes between inflammatory/non-inflammatory tumors therefore arises. We previously demonstrated this as a mechanism of escape from T lymphocyte killing targeting a single melanoma antigen (Woods et al., 2016). We investigated whether inflammation caused wholescale change to the immunopeptidome, and whether this was a mechanism of tumour immune escape via subsequent change in $CD8^+$ T lymphocyte tumor recognition.
Methods:
We used a sensitive mass spectrometry approach (DIA-SWATH) to characterize changes to the immunopeptidome of melanoma, dependent on the proteasome subtype expressed by the cell.
Results:
We present the first study demonstrating the effect of IFNɣ mediated inflammation on composition of the immunopeptidome in melanoma. Significantly, we demonstrate that while the immunopeptidome had similar overall immunogenicity in presence or absence of IFNɣ, there were changes in $CD8^+$ T cells recognition of altered epitopes. In *in vivo* animal models we manipulated melanoma cells to switch proteasome subtype following treatments which induced IFNγ at the tumor site. In human biopsies we demonstrated a direct correlation between the presence of tumor infiltrating lymphocytes, and expression of immunoproteasome specific subunits.
Conclusions:
This study highlights the effect of changes in inflammation at the tumor microenvironment as a potential mechanism of significant immune escape from T lymphocyte mediated tumor targeting. Awareness of tumor immunopeptidome plasticity may be critical to inform development of therapies involving cancer vaccination, adoptive T-lymphocyte transfer, or combination treatments including these.

Woods, K., Knights, A.J., Anaka, M., Schittenhelm, R.B., Purcell, A.W., Behren, A., and Cebon, J. (2016). Mismatch in epitope specificities between IFNgamma inflamed and uninflamed conditions leads to escape from T lymphocyte killing in melanoma. J Immunother Cancer *4*, 10.

Reehorst C[1,2], Nightingale R[1], Mariadason J[1,2]

The *in vivo* effect of Ets homologous factor (EHF) on intestinal homeostasis

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Aim

Colorectal cancer (CRC) arises due to uncontrolled cell division, failure of cells to undergo cell death (apoptosis) and loss of cellular differentiation. Poor cellular differentiation status in colorectal tumours has been associated with worse patient outcome. The EHF transcription factor is highly expressed in the colonic epithelium, and down-regulated in poorly differentiated colorectal cancer cell lines and primary tumours. The role of EHF in regulating colon cell differentiation *in vivo* is unknown. The aim of this study was to determine the role of EHF on intestinal cell differentiation and homeostasis *in vivo*.

Methods

The mouse strain $EHF^{lox/lox}$ $Villin^{CreER}$ was developed where the DNA-binding domain of EHF can be selectively deleted in the intestinal epithelium by administering intra-peritoneal injections of tamoxifen. Mice were monitored and weighed weekly while given food and water ab libitum until the day of sacrifice. The effect of EHF deletion on intestinal cell differentiation, proliferation and homeostasis was determined by quantitative RT-PCR and immunohistochemistry.

Results

Specific deletion of EHF in the intestinal epithelium was confirmed at the DNA and mRNA level in $EHF^{lox/lox}$ $Villin^{CreER}$ mice treated with tamoxifen, while EHF remained intact in $EHF^{lox/lox}$ $Villin^{CreER}$ mice treated with vehicle only. Assessment of cell proliferation by Ki67 and BrdU staining revealed no differences between tamoxifen and vehicle-treated groups. Similarly, no differences in the composition of the different intestinal epithelial cell lineages or expression of markers of intestinal epithelial cell maturation were observed between the two groups.

Conclusion

EHF does not play a vital role in normal intestinal epithelial cell homeostasis; however the effect of EHF inactivation in cancer development and metastasis is yet to be determined.

Loh Z, [1,2], Estacio O,[1,2], Grigg A[2], Chong G[2], Hawkes E[2]

Routine Blood Investigations Have Limited Utility in the Follow-up of Aggressive Lymphomas

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Aim:
After attaining complete remission (CR) with first-line therapy, patients with aggressive lymphoma undergo close surveillance to detect early relapse. Current global guidelines recommend routine follow-up blood tests but evidence supporting this practice is limited. This study evaluates the utility of laboratory tests in detecting relapse after treatment.

Methods:
We conducted a retrospective review of all patients diagnosed with Hodgkin lymphoma or aggressive non-Hodgkin lymphoma who attained CR after first-line chemotherapy. Clinical records were reviewed to determine follow-up and relapse details. An abnormal blood test was defined as any new and unexplained abnormality for full blood examination, white cell differential, lactate dehydrogenase or erythrocyte sedimentation rate.

Results:
246 eligible patients were identified between 2000-2015 who underwent 2383 outpatient visits. Median follow-up was 37months (range 3-1358). Laboratory tests were performed at 91% of appointments. Forty-three (17%) patients had documented relapse. Routine laboratory testing detected asymptomatic relapse in only 2/43 patients (5%); in the remaining patients, relapse was suspected clinically 33/43 (77%) or detected by imaging 8/43 (19%).

The sensitivity, specificity, PPV and NPV of all routine laboratory tests in detecting relapse was 80%, 60%, 9% and 99% respectively. In addition, an abnormal blood test result prompted a change in management for only 16% of asymptomatic patients, compared to 61% of those with concurrent symptoms or signs. Falsely positive blood tests prompted unnecessary further investigations at 47 appointments.

No significant difference in survival was shown between patients who had a blood test performed within 3 months of relapse versus patients who did not (p=0.454).

Conclusion:
The majority of relapses are detected by patient-reported symptoms, often at unscheduled visits, and blood tests demonstrate unacceptably poor performance characteristics with no survival benefit. This suggests that routine blood tests have limited utility in the surveillance of asymptomatic patients in CR after primary chemotherapy.

Investigating Epithelial-Mesenchymal Plasticity in Circulating Tumour Cells from Breast Cancer Xenograft Models

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Introduction: Metastasis is the major cause of cancer mortality. A strong link between metastatic behaviour and epithelial-mesenchymal plasticity (EMP) has been demonstrated in human breast cancer (BC). EMP can provide carcinoma cells with invasive ability to leave the primary tumour, enter into the circulation as circulating tumour cells (CTCs), arrive at a distant organ and ultimately form a metastasis. This project aims to investigate EMP in BC CTCs by first comparing EMP-associated gene expression profile of CTCs and primary tumours.

Materials and methods: A human-specific tandem nested RT-qPCR was successfully developed to characterise and compare the expression profiles of forty-one human genes in pooled CTCs and primary tumours from two human BC xenograft-bearing mouse models, MDA-MB-468 and ED03. These genes include EMP markers, BC stem cell markers, hormonal receptors, hypoxia and cellular metabolism genes. A direct lysis method, which minimises RNA loss, was also optimised and incorporated into the pipeline to study gene expression of CTCs at the single cell level.

Results: Two replicate experiments of at least ten mice were performed and results were consistent across replicates. In pooled CTCs relative to primary tumours from both xenograft models, a significant increase in expression of mesenchymal markers (*SNAIL1, VIM, SERPINE1 and TNC*), and surprisingly of a prototypic epithelial marker *CDH1* were observed. A decrease/loss of *EpCAM* was reproducibly observed in CTCs of both models, while decreased *CD24* and *EGFR* in CTCs were only seen in the MDA-MB-468 model. Analysis of single CTCs revealed examples of concordance in single cells with the results obtained with the pooled CTCs.

Conclusion: The complex yet consistent alteration in both epithelial and mesenchymal markers in CTCs across the two models is suggestive of a 'hybrid' EMP phenotype in CTCs, which can play significant role in cancer progression and metastasis.

Arielle van Mourik, 2016

Cerebral toxoplasmosis in a patient with prolonged CD4 lymphopenia post autologous haemopoietic stem cell transplant.

Introduction:
Toxoplasma gondii is a ubiquitous protozoan parasite which infects approximately one third to one half of the world's population. In the immunocompetent host, it typically causes a self limiting and asymptomatic infection before entering a lifelong latent phase. Reactivation and disseminated toxoplasmosis occur in the setting of impaired cellular immunity as described in patients with acquired immunodeficiency syndrome (AIDS) secondary to human immunodeficiency virus (HIV) infection and patients receiving prolonged immunosuppression post solid organ transplant (SOT) or allogeneic haematopoietic stem cell transplant (alloHSCT). Toxoplasmosis post autograft has been rarely described. We present a case of toxoplasma encephalitis in a patient with persistent CD4 lymphopenia post autograft for peripheral T-cell lymphoma (PTCL).

Case summary:

A 64y HIV negative female was diagnosed with autoimmune haemolytic anaemia (AIHA) and idiopathic thrombocytopenic purpura (ITP) in 2012 and 2013, treated with IVIg, a total 4 months of prednisolone (two separate courses, average dose 30mg/day), a single dose of 375mg/m^2 rituximab and 6 months of azathioprine 100mg/day. The lymphocyte count prior to AIHA was normal (2.9 x 10^9/L; normal range 1-4 x10^9/L) Her subsequent course was complicated by a persistent lymphopenia (0.3-0.7x10^9/L,) and cutaneous mycobacterium kansasii infection. PTCL was diagnosed in February 2015 and treated with 6 cycles of high dose chemotherapy (CHEOP) followed by an autograft in July 2015 with BEAM conditioning. Lymphocyte counts at 3, 7 and 9 and 12 months post transplant were 0.4, 0.5 ,0.8 and 0.3 x 10^9/L respectively. Dapsone for pneumocystis jirovecii pneumonia (PJP) prophylaxis was provided, cotrimoxazole was contraindicated due to a rash. Twelve months post autograft she developed left leg weakness and intermittent headache. A MRI brain showed 4 x enhancing cerebral lesions, of which histology demonstrated toxoplasma tachyzoites in neutrophils confirmed by PCR. Toxoplasma serology was IgG positive but IgM negative. The CD4 count was severely reduced 0.09 x 10^9/L (normal 0.65-2.0 x 10^9/L) Treatment with pyrimethamine (25mg daily) and sulfadiazine (1g QID) was commenced with some improvement in neurology prior to discharge for rehabilitation.

Discussion:
Toxoplasmosis occurring > 2 months post autograft is very rare, with to the best of our knowledge only 8 cases previously reported. Of these, 5 of the 7 evaluable had at least one other risk factor for toxoplasmosis reactivation including persistent lymphopenia, delayed immune reconstitution and high dose steroids. Normally after autograft, CD3 counts (reflective of total T cell count) are initially decreased but return to baseline by three months. CD4 counts reach a nadir at day 15 and take at least 12 months to return to baseline, while CD8 cells rise rapidly to supranormal levels in the first month and may remain elevated for up to 12 months. The inversion of CD4:CD8 ratio is thought to explain the increased risk of infection in this period. In our patient, however, CD4:CD8 ratio had normalised and all counts remained low, suggesting another pathology underlying the lymphopenia.

Currently, prophylaxis for toxoplasmosis post autograft is only recommended for patients at increased risk, such as those on high dose steroid therapy. When warranted, the drug of choice is cotrimoxazole, which is often concurrently administered for PJP prophylaxis, but frequently not given due to its myelosuppressive effects and replaced by dapsone which is not proven to be effective prophylaxis for toxoplasmosis. This case highlights the importance of identifying patients at high risk of reactivation post autograft (i.e. persistent lymphopenia and/or high dose steroid therapy) and ensuring adequate prophylaxis with cotrimoxazole or other agents such as combinations of pyrimethamine / sulfadiazine or pyrimethamine / clindamycin.

Treatment of Solitary Adrenal Metastases using Stereotactic Ablative Body Radiotherapy: a Case Study

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Purpose: Renal Cell Carcinoma (RCC) including adrenal is the 9th most common cancer in Australia with a median age at diagnosis of 65 years. Surgery is the standard of care, but significant co-morbidities in this patient group often preclude the use of surgery as a treatment option. Stereotactic Ablative Radiotherapy (SABR) is an alternative treatment option which delivers large doses of radiation in a small number of treatments, which results in a highly potent biological effective dose. Specialised care is taken in the planning and treatment of these patients due to respiratory motion influencing target position. The experience of planning and treating this technique is described.

Method: A 61 year old male presented with a right adrenal nodule detected on PET highly suspicious of metastases from RCC. The patient was to receive 26Gy in 1 treatment using SABR. For radiotherapy simulation, a Four Dimensional Computed Tomography scan was performed to obtain accurate information on movement of the tumour and normal anatomy at all phases of the breathing cycle. An Elekta™ Bodyfix™ consisting of a vacuum bag shaped to the patient and vacuum drape were used. This was used to ensure the patient was stable and respiratory motion was similar for CT and treatment.

Planning and Treatment: A plan was created using four 360 degree co-planar arcs using a Volumetric Arc Therapy technique. The radiation dose was optimised around the Planning Target Volume (PTV). A number of quality indices and dose constraints were used for organs at risk and the PTV to ensure high plan quality. Verification using Elekta™ Four Dimensional Cone Beam Computed Tomography scan was used at treatment to validate setup position and patient's respiratory pattern.

Correlation of PD-L1 expression with immune cell infiltrates, genome-wide copy number aberrations and survival in mesothelioma.

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Introduction:
Recent clinical studies using immune checkpoint inhibitors in mesothelioma (MM) have shown promise in shifting treatment paradigms. However, the immune environment and targets of these treatments such as program death receptor 1 (PD-1) and its ligand PD-L1 have not been well characterised in MM. Using a large cohort of patients, we investigated PD-L1 expression, the surrounding immune infiltrate and genome-wide copy number status and correlated these parameters to clinicopathological features.

Patients and methods:
Tissue microarrays (TMA) were constructed and stained with PD-L1 (E1L3N,CST, Massachusetts), CD4, CD8 and Foxp3 antibodies. PD-L1 positivity (PD-L1+) was defined as >5% membranous staining regardless of intensity and high positive as >50%. Genomic DNA was obtained from tumour cores of a representative subset (68 patients) and used for genome-wide copy number analysis (CNA) using Affymetrix's OncoScan platform. Percent Genome Aberrated (PGA) was computed for each sample as the total number of base pairs within altered regions, divided by the total number of base pairs in each region included in the array.

Results:
Amongst 329 patients evaluated, the median age was 67 years and most were male 274(83.2%).Epithelioid histology (N=203; 62.9%) was the commonest. PD-L1+ was seen in 41.7% with high positivity in 9.6%. PD-L1+ correlated with non–epitheloid histology (P=<0.0001) and increased infiltration with CD4, CD8 and FOXP3 lymphocytes. High PD-L1 expression correlated with worse prognosis (HR=2.37; 95%CI: 1.57-3.56; P=<0.0001) on univariate analysis. On multivariate analysis histology, stage, Neutrophil-Lymphocyte ratio (NLR) and ECOG status were found to be independently associated with survival, but not PD-L1+. PD-L1 gene (CD274) copy number gains were seen in seven (11.2%) of patients but did not correlate with PD-L1 expression. Higher PGA was seen in epithelioid histology, was not associated with PD-L1 expression but trended towards poorer survival (HR=1.5; 95%CI: 0.89-2.68; P=0.14).

Conclusion:
High PD-L1 expression was associated with non-epithelioid MM, poor clinical outcome and increased immunological infiltrates. Interestingly, increased genomic alterations did not correlate with PD-L1 expression but was associated with poorer survival.

Wookey PJ[1], Furness SGB[2], Kourakis A[1], Hare DL[1].

The switch between the pre-apoptotic cell stress response and apoptosis seen through new rose-tinted glasses

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Aim
Apoptosis is a form of programmed cell death (PCD), which is an important process in most diseases and in normal tissue homeostasis. Cancers survive and thrive because of the upregulation of mechanisms that bypass PCD, in a state equivalent to the pre-apoptotic cell stress response. Here we demonstrate a novel role for the calcitonin receptor (CTR) in this response.

Methods
Using a unique antibody:fluorophore (AF568-red channel) conjugate developed in our laboratory, which recognises an extracellular epitope of human calcitonin receptor (CTR), we demonstrate high fluorescence events (HFEs) associated with apoptopic cells using confocal microscopy and flow cytometry.

Results
The HFEs are generated in dying cells induced with cytotoxins and coincides with binding of annexin V to the plasma membrane, which detects phosphatidylserine exposed on the outer face, an event linked with commitment to apoptosis. This was recorded in all cell types tested using either multi-channel confocal microscopy or flow cytometry of Jurkat cells. Extensive use of negative controls helped substantiate this discovery.

Conclusions
An HFE results from mobilisation of CTR from intracellular compartments in response to cytotoxin during the pre-apoptotic cell stress response. Exposure of the receptor on the plasma membrane is followed by the internalisation of the antibody:fluorophore with apoptosis and condensation in the perinuclear region. This discovery is relevant to our understanding of the pre-apoptotic cell stress response and the switch to apoptosis.

Furness SGB, Hare DL, Kourakis A, Turnley AM, Wookey PJ. (2016) A novel ligand of calcitonin receptor reveals a potential new sensor that modulates programmed cell death. **Cell Death Discovery**, accepted for publication, July 2016.

Wookey PJ[1], Gilabert-Oriol R[2], Furness SGB[3], Kourakis A[1], Hare DL[1].

Recalcitrant tumours require powerful medicine: a comparison of the potency of immunotoxins and an antibody:drug conjugate to kill glioma stem cells.

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Aim
We have previously reported that calcitonin receptor (CTR) is highly expressed in the lethal brain tumour *glioblastoma* by malignant glioma cells and glioma stem cells. A monoclonal antibody (mAb2C4) against a linear epitope within the extracellular domain of hCTR was chemically conjugated to either plant ribosome-inactivating proteins (RIPs) or the drug monomethyl auristatin E (MMAE), an antibody:drug conjugate (ADC). The relative potencies of these drugs were compared against established lines of glioma stem cells and U87MG derived from *glioblastoma*.

Methods
The efficacy of the immunotoxins was improved by several log values with co-administration of an enhancer purified from plants, namely the triterpene saponin SO-1861. The potencies (EC_{50}) of immunotoxins mAb2C4:saporin, mAb2C4:dianthin and mAb2C4:gelonin were compared to mAb2C4:MMAE in 4 cell lines of glioma stem cell and the line U87MG using release of LDH in 96-well plates. Each of the conjugates had been purified by two-step chromatography.

Results
Detailed statistical analysis was performed with the line SB2b comparing mAb2C4:dianthin (EC_{50} = 7.8pM) with mAb2C4:MMAE (EC_{50} = 2000pM), which is approximately 250-fold less potent. Several other glioma stem cell lines and the cell line U87MG were tested and the efficacy of mAb2C4:RIP (immunotoxins, EC_{50} range 5-47pM) compared to the ADC (EC_{50} range 2000-2500pM).

Conclusions
These results demonstrate that CTR is an effective target found to be expressed by a large proportion of glioma stem cell lines and U87MG, and that the immunotoxins are approximately 250 times more potent than an equivalent ADC.

Gilabert-Oriol R, Furness SGB, Stringer BW, Day BW, Kourakis A, Boyd AW, Hare DL, Fuchs H, Weng A, Thakur M, Johns TG, Wookey PJ. (2016) Dianthin-30, gelonin or saporin versus monomethyl auristatin E, each configured with an anti-calcitonin receptor antibody, differentially promote cell death *in vitro* of high grade glioma cell lines derived from glioblastoma. **J Control Release**, under review, July 2016.

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Phytophenols improves inflammation and insulin resistance associated with gestational diabetes mellitus.

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Introduction: Gestational diabetes mellitus (GDM) is a global health issue that imposes serious health problems for both mother and baby. Infection and/or inflammation are key regulators of insulin resistance associated with GDM. Phytophenols such as nobiletin and resveratrol decrease inflammation and improve insulin sensitivity in animal models of diabetes. Using bacterial and viral products (LPS and poly(I:C), respectively) and the pro-inflammatory cytokine TNF-α as models of GDM, we examined the effects of nobiletin and resveratrol on: inflammation in placenta and adipose tissue, and insulin resistance in skeletal muscle tissue from pregnant women. We also studied the *in vivo* effects of nobiletin and resveratrol on the pregnant db/+ GDM mouse model.

Methods: Pro-inflammatory cytokine mRNA expression and were determined by qRT-PCR and ELISA, respectively. Insulin signalling components was determined by Western blotting and glucose uptake assays. Resveratrol and nobiletin were administered daily to pregnant mice and tissues were collected at d18.

Results: In vitro, nobiletin and resveratrol significantly reduced LPS, poly(I:C) and TNF-α-stimulated IL-6, IL-8, IL-1α/β and MCP-1 mRNA expression and release from human placenta and adipose tissue. In human skeletal muscle tissue, nobiletin and resveratrol restored insulin-mediated glucose uptake impaired by LPS, poly(I:C) and TNF-α. Our in vivo studies found nobiletin and resveratrol significantly improved inflammation in GDM mice. Nobiletin also significantly decreased maternal adiposity in GDM mice.

Conclusion: Nobiletin and resveratrol can reduce inflammation in placenta and adipose tissue and improve skeletal muscle glucose uptake. These exciting findings suggest that phytophenols can disrupt key pathways involved in the pathogenesis of GDM. Longer term studies on offspring growth and development are currently underway; however, our findings indicate that phytophenols may have potential benefits in the prevention of GDM.

Prevention of mother-to-child transmission of hepatitis B virus: Successful implementation of new management guidelines for hepatitis B virus positive women in a hospital with a specialized clinical service

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Background & Aims: Vertical transmission of hepatitis B virus is the leading mode of transmission with perinatal transmission accounting for half the global chronic hepatitis B burden. Risk of perinatal transmission is proportional to maternal viral load. Antenatal antiviral therapy is emerging as a therapeutic option that reduces the risk of mother to child transmission of hepatitis B for women with a high viral load. Risk stratification according to viral replicative status helps guide clinical implementation of antepartum antiviral therapy in high-risk cases. We evaluated the introduction of new management guidelines and a specialized clinic for hepatitis B positive women in a level three maternity hospital.

Methods: Retrospective audit of clinical management and maternal and infant outcomes of hepatits B positive women who delivered in a single maternity hospital over a two-year period (Jan 2014 to Dec 2015). Maternal and infant outcomes for all hepatitis B positive women were collected. Women with high viral load (> 200,000 IU/mL) were referred to a perinatal infectious diseases clinic for consideration of antiviral therapy with tenofovir to reduce mother to child transmission risk.

Results: A total of 11497 women gave birth during the study period, of which 101 women (0.88%) were hepatitis B positive. The vast majority of hepatitis B positive women were born in Asia (74.3%). Viral load testing was performed in 99/101 of hepatitis B positive women, of which 30 (30.3%) had a viral load > 200,000 IU/mL. Twenty-six women accepted tenofovir therapy to reduce mother to child transmission; 23/26 had a successful treatment response recorded and 2 had missing data. There were no cessations of tenofovir due to side effects. There were no significant differences in the rates of breastfeeding (p = 0.15) or mean birthweight (p = 0.079) between infants born to hepatitis B positive women on or off tenofovir. Of the 99 live infants at discharge, 99% (n=98) received the hepatitis B vaccine and immunoglobulin.

Conclusions: Our results demonstrate the effectiveness of defined clinical pathways and a specialized clinical service in the implementation of strategies to reduce mother-to-child transmission of hepatitis B virus.

Key words: hepatitis B, pregnancy, viral load, perinatal transmission, mother-to-child transmission, antiviral therapy, tenofovir.

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New medical therapeutics for ectopic pregnancy.

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Aim
Ectopic pregnancy represents a serious gynaecological emergency that can erode the maternal vasculature and cause fatal haemorrhage. While methotrexate injections can resolve small ectopic pregnancies, most are too large and require surgery. Our objective was to identify a more potent therapeutic than methotrexate to treat ectopic pregnancy.

Methods and Results
Twelve chemotherapeutics and molecularly targeted tyrosine kinase inhibitors were screened in JEG3 and HTR8 cell lines using an MTS viability assay. Vinorelbine**,** a vinca alkaloid, was a clear outlier with surprising efficacy. 10 nM of Vinorelbine reduced cell viability significantly more than 100,000 nM of methotrexate. We confirmed the potency of vinorelbine using the xCELLigence system and using flow cytometry, where we demonstrated vinorelbine significantly increased apoptosis and necrosis.
For in-vivo studies, JEG3 xenografts were implanted subcutaneously in to SCID mice, and vinorelbine or vehicle was administered intravenously, with placental tumour volume measured over 14 days. Vinorelbine induced a significant decrease in JEG3 xenograft tumour volume ($p<0.001$), tumour weight ($p<0.001$) and circulating hCG, with a dose of 5mg/kg inducing complete placental tumour regression.

Conclusion
This data suggests that vinorelbine is highly efficacious at inducing placental cell death both in-vitro and in-vivo.

Steroid sulfatase mRNA is upregulated in the placenta and maternal whole blood of preterm preeclamptic women

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Aim: Preeclampsia is a serious complication of pregnancy affecting 5% of pregnancies worldwide. The placenta is central to preeclampsia. Our team identified 137 genes highly expressed in placenta relative to other human tissues. A custom microarray of 45 these placental specific genes identified Steroid Sulfatase (STS) as one of twelve genes significantly increased in a cohort of preeclamptic placentas relative to gestation-matched normotensive controls. We explored a role for STS in preeclampsia by characterising STS expression in placenta and maternal whole blood and investigating the functional role of STS in primary placental trophoblasts.

Methods: STS characterisation was performed on severe early-onset preeclamptic (n= 29) and gestation-matched normotensive controls (n=15). We characterised placental and maternal whole blood STS mRNA and placental protein expression via qRT-PCR, immunohistochemistry and Western Blot. To assess the functional contribution to sFlt1 secretion, primary placental trophoblasts were isolated from term placentas and siRNA targeting STS administered. sFlt1 secretion and sFlt1 variant (sFlt1-e15a and sFlt1-i13) expression was assessed after treatment via ELISA and qRT-PCR. The effect of STS on trophoblast differentiation (syncytialisation) was assessed via hCG ELISA and Western Blot for E-Cadherin.

Results: STS mRNA expression was significantly elevated in preeclamptic placentas ($p \leq 0.0001$). STS protein localises to the placental syncytiotrophoblast. Functional analysis showed significantly ($p \leq 0.05$) reduced sFlt1 secretion when STS was silenced. sFlt1 variant analysis showed a significant ($p \leq 0.01$) decrease in sFlt1-i13 expression, but no change in membrane-bound Flt1 or sFlt1-e15a mRNA expression. Silencing STS had no affect on hCG secretion or E-cadherin expression in treated trophoblasts.

Conclusion: This study has confirmed that STS is increased in preeclamptic placentas and that this increase is detectable in maternal whole blood. Functional analysis suggests that STS may affect placental sFlt1 secretion in preeclampsia by regulating sFlt1-i13 expression and not via mechanisms related to syncytialisation of the placenta.

New generation antiplatelet therapies to prevent preeclampsia

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Introduction: Preeclampsia is a serious complication of pregnancy. Responsible for thousands of maternal and fetal deaths worldwide, there is no cure. Key pathophysiological steps in preeclampsia include 1) placental damage and oxidative stress, 2) elevated sFlt1 and soluble endoglin (sEng) and 3) endothelial dysfunction. While the antiplatelet drug aspirin is used clinically to prevent preeclampsia, its effectiveness, if any, remains limited. New generation antiplatelet therapies (Clopidogrel, Prasugrel and Ticagrelor) have health benefits beyond anti-thrombus formation (they reduce oxidative damage, inflammation and endothelial dysfunction) and thus may be more effective to prevent preeclampsia. We examined whether new generation antiplatelet agents can counter the pathophysiological steps in human preeclampsia models and compared their efficacy directly to aspirin.

Methods: Primary human trophoblast, placental explants and endothelial cells (human umbilical vein endothelial cells (HUVECs) and uterine microvascular cells (UtMVs)) were treated with increasing doses of Aspirin, Clopidogrel, Prasugrel or Ticagrelor (0-100μM). Endothelial dysfunction was induced by addition of the pro-inflammatory cytokine Tumor Necrosis Factor (TNF)-α (10μg/mL) stimulation of endothelial cells (antiplatelet agents were titrated in). Peripheral blood monocytes were isolated and applied to stimulated HUVECs; their adhesion was assessed flurometrically. Media and cell lysates were collected to assess 1) antioxidant response element signaling pathways, 2) anti-angiogenic factors (sFlt1/sEng) and the pro-angiogenic factor PlGF and 3) endothelial dysfunction (vascular cell adhesion molecule-1 (VCAM1) and endothelin-1 (ET-1)).

Results: New generation antiplatelet agents induced nuclear Nrf2 translocation (antioxidant transcription factor) and increased antioxidant gene expression: HO-1, NQO1 and GCLC. In contrast, aspirin did not affect antioxidant pathways. Furthermore Clopidogrel, Prasugrel and Ticagrelor potently reduced sFlt1 secretion from both placental and endothelial cells; and sEng secretion from endothelial cells. In contrast, aspirin did not affect sFlt or sEng secretion. PlGF mRNA expression was significantly enhanced with new generation anti-platelet treatment. Clopidogrel and Prasugrel rescued endothelial dysfunction, mitigating TNFα induced monocyte-endothelial adhesion, as well as VCAM1 and ET-1 mRNA and protein expression. Again aspirin had no effect.

Conclusions: New generation antiplatelet therapies potently upregulate anti-oxidant defences, decrease sFlt1/sEng secretion and counter endothelial dysfunction in human models of preeclampsia. Given they are classified as category B/C drugs, they represent exciting candidate therapies to prevent preeclampsia.

Jeannette Milgrom[1,2,3], Christopher J Holt[1], Charlene Holt[1,2], Jessica Ross[1,2] & Jennifer Ericksen[1,2], Alan W Gemmill[1]

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Randomised Trial of Antenatal Depression Treatment - Impact on Early Child Developmental Outcomes

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¶

Aim

Substantial evidence links antenatal depression, anxiety and stress with negative effects on fetal development, resulting in enduring negative impacts on child development. Despite this, there is a paucity of research on intervention programs designed to address depression and anxiety in pregnancy, and none that report on the potential of treatment for improving child outcomes. We aimed to evaluate the efficacy of a brief treatment for maternal depression and anxiety in pregnancy in a sample of women with a diagnosed depressive disorder.

¶

Methods

We developed a cognitive behavioural therapy treatment for antenatal depression and anxiety and evaluated it in a feasibility trial. This was followed by a pilot randomised controlled trial (RCT) which collected data on the efficacy of the brief intervention and follow-up data on infant development.

¶

Results

The feasibility study (n = 25) yielded promising results for adherence, acceptability and improvements in depression and anxiety (Beck Depression Inventory and Beck Anxiety Inventory). The RCT (n = 54) again showed excellent adherence and acceptability and supported the efficacy of the treatment. Strong reductions in anxiety were observed during pregnancy and improvements in depression were maintained at nine months representing a moderately large effect size. Nine-month infant outcomes showed several medium-to-large effects favouring the intervention in domains including problem solving, self-regulation, and stress reactivity, which were statistically independent of maternal postnatal mood.¶

Conclusion

Treating severe depression and anxiety during pregnancy with a brief CBT intervention appears feasible and effective. Results regarding a positive effect of treatment on infant outcomes are encouraging. The cohort is being followed longitudinally and preliminary data on child outcomes at 2 years of age will be presented. To reliably detect clinically meaningful effects on later child outcomes, larger RCTs are likely to be required.

Reference

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Desneves K [1], Rafferty J[1], Rodi H [1], Panisset M [2], Nunn A [3], Davies P [4], Ward L [4], Galea M [2]

Title of abstract Energy requirements and body composition in acute spinal cord injury

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Aim
This study aimed to determine the most appropriate equation to predict total energy expenditure (TEE) using doubly labelled water (DLW), and to validate the use of bioelectrical impedance spectroscopy (BIS) to assess body composition. Estimation of energy requirements following acute spinal cord injury (SCI) is challenging due to metabolic, physical activity and fat free mass (FFM) changes and lack of validated equations to predict energy requirements.
Methods
Twenty participants completed DLW, and BIS assessments. Thirteen also underwent dual x-ray absorptiometry (DEXA) scans. Five published population-specific equations to predict FFM from BIS were tested. Dietary Intake was assessed by twenty-four hour recall and energy requirements estimated using predictive equations.
Results
Median TEE was 9,721kJ/day (IQR 8.6-10.8). Energy intake was 107% of TEE. There was poor agreement between measured TEE using DLW and that estimated by predictive equations. The level of agreement was not improved when fat free mass was used in the population specific Buchholz equation. The mean difference and limits of agreement (±2 standard deviations) compared with DLW was -1.71(-12.35,-4.6)kg for the DEXA and -0.90(-9.50,-3.25)kg using the equation from Kocina and Heyward (1997) for measures of FFM.
Conclusion
Equations used to estimate energy expenditure in acute SCI patients were inaccurate compared with the gold standard DLW. BIS provides a valid measure of FFM using the population-specific equation of Kocina and Heyward (1997) and can be undertaken at bedside using a portable BIS device. A prediction equation to estimate energy requirements in acute SCI remains elusive.

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Georgie Hollingsworth[1], Emily Mountier[2], Deepak Gill[3], Suzanne Davis[4], Charuta Joshi[5], Catherine DeVille[6], Manju Kurian[6], DDD study, Katherine C. Nickels[7], Gemma Carvill[8], Candace T. Myers[8], Heather C. Mefford[8], Lynette G Sadleir[2], Ingrid E. Scheffer[1,9,10,11]

Novel *SCN1A* phenotype: Early Profound Developmental Epileptic Encephalopathy with Movement Disorder with hotspot mutation

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9. *Florey Institute of Neuroscience and Mental Health, Victoria, Australia*
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Objectives: To describe a far more severe, novel *SCN1A* phenotype of early-onset epileptic encephalopathy with profound impairment and movement disorder, associated with a recurrent hotspot mutation.

Methods: 7 children were identified. History, examination, MRI and video-EEG data were obtained.

Results: We identified 7 males (6-12 years) who presented at 8-12 weeks of age with hemiclonic (5) or generalized tonic clonic seizures (GTCS) in 2. All developed GTCS by 18 months and became intractable with status (6), myoclonic seizures (5), tonic seizures (4) and spasms (3). Development was clearly delayed by 8-16 weeks. Six children had regression or plateauing resulting in profound intellectual disability (ID) and were non-ambulant and nonverbal. All children developed a severe movement disorder (9 weeks-20 months) with choreoathetosis, dystonia and mini-myoclonus particularly in the orofacial area. EEGs developed background slowing and frequent multifocal discharges; neuroimaging was normal.

We found striking genetic homogeneity with 6/7 cases sharing the same hotspot mutation p.Thr226Met, proven to be *de novo* in 5. The seventh child had a *de novo* p.Pro1345Ser mutation.

Conclusions: We identify a novel *SCN1A* phenotype of profound early-onset epileptic encephalopathy associated with a hyperkinetic movement disorder. This new *SCN1A* phenotype can be distinguished from Dravet syndrome by earlier age of onset, profound ID and movement disorder. This is the first clear phenotype-genotype correlation for *SCN1A* that determines a severe prognosis for affected children.

Egorova N[1], Cumming T[1], Shirbin C[1], Werden E[1], Brodtmann A[1]

Cognitive control network connectivity in mild post-stroke depression

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Aim

Depression within the first year after stroke is typically observed in a third of patients. Previous studies showed that depression causes cognitive impairment and slows down stroke recovery, advising that early depression diagnosis and treatment could increase stroke survivors' chances of speedy recovery. Post-stroke depression has been associated with frontal lesions, and specifically lesions in the left dorsolateral prefrontal cortex (DLPFC), however due to the limitations of lesion-based diagnosis and the fact that depression is a network disorder, a reliable biomarker of post-stroke depression is still lacking. Several studies of depression in non-stroke populations successfully tapped into the cognitive control network (CCN) using the bilateral DLPFC as a seed and found that resting state connectivity within the network is reduced in even mildly depressed subjects, compared to healthy controls.

The goal of this study was to identify a resting state connectivity marker associated with depression in stroke patients with the purpose of assessing depression severity and predicting stroke recovery.

Methods

We analysed resting state fMRI data from 64 stroke patients, 20 of whom showed signs of mild to moderate depression assessed with the Patient Health Questionnaire (PHQ-9) at 3 months post-stroke. We also obtained patients' quality of life (AQOL-4) scores at 12 months post-stroke as a measure of stroke recovery.

Results

The results suggested that reduced connectivity between the left DLPFC and the right supramarginal gyrus differentiates depressed and non-depressed patients (MNI: +66, -24, 15; cluster corrected p_{FDR}=0.007, k=103), correlating with PHQ-9 (r=-0.52, p=0.00001) in all patients (controlling for age, gender, NIHSS). This resting state marker also predicted AQOL [Total score (r=0.4, p=0.04) and 'Relationships' subscale (r=0.5, p=0.01)] at 12 months in the depressed cohort.

Conclusion

These findings confirm an important role of the left DLPFC in mild post-stroke depression showing promise for depression diagnosis and monitoring stroke recovery.

Bagot KL[1,2], Braitberg G[3], Choi C[4], Vu M[1], Donnan GA[1], Dewey HM[5], Hand P[3,6], Bladin C[1,5], Cadilhac DA[1,2]

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Strokes, TIAs, mimics: a comparison of Emergency Department and discharge diagnosis coding

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6. Victorian Stroke Clinical Network, Melbourne, Vic., Australia

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Aim

There are potentially cost, quality of care and quality of life implications (e.g., extended length of stay, inappropriate investigations, poorer patient outcomes) for discrepancies between admission and discharge diagnoses. However, few data are available regarding the agreement between Emergency Department (ED) and final diagnosis for patients presenting with stroke/stroke-like symptoms. The aim of this study was to compare the diagnosis of patients presenting to ED with the final diagnosis.

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Methods

Medical records for a 12 month period (between 2010 and 2014) in seven regional Victorian hospitals were reviewed. Patients allocated one or more of 16 International Statistical Classification of Diseases and Related Health Problems, Australian Modification 10th revision (ICD-10) codes related to stroke or stroke-like symptoms in either Emergency or at Discharge were included: recognised stroke (I619, I620, I621, I629, I639, I64), TIA (G459) or stroke symptoms - disorientation (R410), loss of consciousness (S0600, S0601), visual field defects (H534), other visual disturbances (H538), dysphagia (R13), dysphasia and aphasia (R470), other specified disorders of brain (G938), and dysarthria and anarthria (R471).¶

Results

Of 2776 patient records identified, 1005 had an ED and final diagnosis code recorded. While there was only 36% exact concordance between ED and discharge coding, there was 72% agreement at the stroke prefix level (i.e., I codes) or TIA code (i.e., G459). Specifically, 62% of TIAs and 85% of strokes diagnosed at the ED were concordant with the discharge diagnosis. A final diagnosis of stroke was allocated for 87 of the 271 (32%) patients receiving an ED TIA diagnosis.

¶

Conclusion

In regional Victoria, approximately one-third of TIAs diagnosed in the ED are subsequently diagnosed as stroke. This limits the provision of time-critical stroke therapies (e.g., thrombolysis) and further education may be warranted. Predictors of discrepancies shall be identified.

Bagot KL[1,2], Moloczij N[3], Moss K[1], Vu M[1], Donnan GA[1], Dewey HM[4], Bladin C[1,4], Cadilhac DA[1,2]

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Sustaining the use of a new stroke telemedicine service: barriers and facilitators identified after implementation

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4. Eastern Health Clinical School, Monash University, Box Hill, Vic., Australia

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Aim

The success of stroke telemedicine programs, including increased access to thrombolysis, is typically determined using quantitative methods, providing little detail on how success was achieved. Developing strategies to address barriers and emphasise facilitators is essential for successful implementation. However, what remains unknown is whether barriers and facilitators change after implementation. The aim of the study was to identify factors for sustaining a new stroke telemedicine service.

¶

Methods

A qualitative study using a pre-post design was conducted. Purposive sampling identified regional and metropolitan clinicians involved in the telemedicine service: pre-implementation (n=24) and 6-12 months post-implementation (n=25). Individual, semi-structured interviews were conducted (October 2010-December 2012. Recordings were transcribed and inductive thematic analysis was performed (10% double-coded independently) within NVivo.¶

Results

Similar themes were identified at post-implementation as were revealed at pre-implementation: perceptions of telemedicine systems and technology, organisational and cultural environment, processes of clinical care and benefits of utilisation. The close connection between thrombolysis and telemedicine was consistently reported pre-and post-implementation; that is, negative perceptions held about tPA were extended to telemedicine. There was variation in the sub-themes with additional barriers and facilitators identified. Clinicians' concerns around trust and confidence in each other as well as the technology were only reported prior to experiencing telemedicine. However, sustaining a telemedicine service requires ongoing education to address rotating staff and infrequent use. Fewer direct patient-related benefits and more clinician-related benefits emerged after experiencing the telemedicine service.

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Conclusion

Sustainable telemedicine practices require ongoing evaluation of telemedicine services beyond the preliminary pilot stage to ensure identification of both persistent and emerging barriers. By addressing these, the sustainability of the service can be improved.

Diagnostic Adequacy of Non-targeted Liver Biopsies in Radiology-A Retrospective Audit

(Paterson, G., Milligan, L., Lim R.L., Goodwin, M., Smith, J.)

Background: There was an anecdotally observed increase in liver biopsy samples obtained under ultrasound guidance in radiology that were insufficient for histology and diagnosis, and thus an audit of non-targeted liver biopsies was undertaken in 2015. A review of the literature found that diagnostic samples from ultrasound guided biopsy were reportedly diagnostic in 98-99% of cases (Rocket et al, Howlett et al).

The aims of the audit were

1. To determine percentage of diagnostic versus non-diagnostic samples, and how often repeat biopsies were required.
2. To investigate possible reasons for poor biopsy samples, including biopsy equipment, number of passes obtained, and by evaluating associations with operator experience. Additionally, complications post-biopsy were also recorded.

Methods: Information was obtained by searching the Radiology Information System (RIS) to identify the number of non-targeted liver biopsies performed in the radiology department over a 6 month period. In a 6 month period, it was feasible that 100 non-targeted liver biopsies would be audited. Sample size n=100.

Patient demographics (age, sex, past medical history, indication for biopsy) were obtained by searching Scanned Medical Records. No new information was recorded, and thus patient consent was not required, other than consent for the liver biopsy procedure which is required in standard clinical care. Austin HREC approval was obtained prior to commencing the audit.

Other information recorded included type of biopsy equipment utilised, blood tests (INR, platelets), histology report, inpatient/outpatient status, years of experience of doctor performing biopsy (1^{st}-5^{th} year registrar/consultant), and complications post-biopsy.

Results: Results of the audit found that of 100 non-targeted liver biopsies performed in radiology between February-August 2015, a diagnosis was made in 99% of samples.

80% of biopsies were collected with one pass, thus reducing risk of possible complications post-biopsy. Additional passes (maximum of 3 passes) were obtained where the 1^{st} pass was noted to have provided insufficient tissue, or was fragmented. Complication rate was low, where mild pain was the most common complication (17%).

Conclusion: In a 6 month audit of non-targeted liver biopsies performed, Austin radiology obtained 99% diagnosis, with results comparable to the literature. Results confirmed that Austin radiology is providing a valuable biopsy service to our patients, with low complication risk.

Sarah Jesudason, [1], Wesley NG, [1], Kunthi Pathmaraj, [1], S.T Lee,[1]

Chromobacterium Violaceum Bacteraemia – A Case Report.

1. Department of Molecular Imaging and Therapy, Austin Health

Background/ Aim

Chromobacterium Violaceum (CBV) is a rare gram-negative bacillus that causes skin infections when isolated from soil and water in tropical and sub-tropical regions after contact with stagnant water or soil. If untreated, it can progress to septicaemia with lesions to the skin, lymph nodes, liver, lung, spleen and brain leading to multi-organ failure[1]. We present such a case, studied with FDG PET imaging.

Method

An ^{18}F- FDG PET scan was performed on a 28 year old experiencing symptoms of sore throat, fever and weight loss. The patient was treated with antibiotics, however went into septic shock a few days later.
A CT scan of the chest demonstrated necrotic cervical lymph nodes and cavitating lung lesions. A PET/CT scan was requested for further characterisation the CT findings.
Eighty-two minutes after the intravenous administration of 252MBq of ^{18}F- FDG, emission tomographic images of the body were acquired from vertex to toes. A low dose CT (120kVp, 50 mAs) was performed for purposes of attenuation correction and PET/CT registration.

Results

Abnormal FDG activity was seen in the necrotic cervical node extending deep to the sternocleidomastoid muscle and also in the cavitating lung lesions.
Innumerable FDG-avid subcutaneous nodules could be seen throughout bilateral lower limbs, and on the anterior abdominal wall.
Further FDG uptake was noted all along the lower skeleton, consistent with osteomyelitis.

Discussion/ Conclusion

PET/CT findings were suggestive of extensive CBV infection, as well as osteomyelitis of the lower skeleton. Bone infection is not known to be a common complication of CBV bacteraemia, but in this case, the patient did develop osteomyelitis

The diagnosis of osteomyelitis by the PET/CT scan, forced a change in treatment regime from short-term antibiotics to long-term antibiotics. A few days after the treatment commenced, the patient's white blood cells count decreased and the patient was discharged.

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Jessica Welch, Wesley Ng, Kunthi Pathmaraj, Salvatore Berlangieri, Andrew Scott

Does Metformin contribute to poor quality FDG-PET brain images?

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Abstract

The demand for FDG-PET to investigate the presence and characterise the type of dementia, has greatly increased over the past few years. Concurrent diabetes can result in a high blood glucose level (BGL) that can lead to poor quality images and potentially decrease the confidence in reporting the study. Whilst a high BGL can contribute to loss of quality in a PET image, it has been noted that some images are poor despite a BGL within the normal range.

Aim

To determine if Metformin has an effect on FDG PET Brain image quality, despite a normal BGL.

Method

We retrospectively analysed 18 patients with Non Insulin Dependent Diabetes Mellitus (NIDDM) on Metformin based drugs, presenting for the investigation of dementia with FDG PET imaging. The images were analysed by two experienced reviewers who were blinded to the patient's BGL status. All scans were assessed qualitatively and rated as good, fair or poor quality.

Results

FDG-PET imaging when performed on non-diabetic patients with a BGL <7 mmol/L, produced good diagnostic quality images consistently. In this cohort of NIDDM patients, visual analysis of the images showed that only 11% of the images were of good quality, 62% were of fair quality and 27% were of poor quality. Patients who had a BGL in the normal range (<7 mmol/L) accounted for 73% of these studies and it was found that 7% were good quality, 61% fair quality and 23% poor quality.

Conclusion

The best chances of achieving optimal quality FDG PET scans is when the BGL is <7mmol/L in non-diabetic patients. However, when a patient is medicated with Metformin based drugs, the quality of the FDG PET scan shows degradation of varying degrees regardless of a normal BGL.

Wesley Ng,[1], Jessica Welch,[1], Kunthi Pathmaraj,[1], Andrew Scott,[1]

Implementation of modulated low dose CT for PET/CT scans to reduce radiation dose to patient

1. Department of Molecular Imaging and Therapy, Austin Health

BACKGROUND

Low dose CT (ldCT) is employed in current PET/CT scanners, but poses an additional radiation burden to patients, who are already receiving a radioactive injection for the PET scan. The quest to reduce radiation dose to the patient is always paramount. We have successfully implemented CT dose modulation to reduce radiation dose during a PET/CT scan, whilst maintaining an acceptable quality diagnostic PET image.

AIM

To implement the DOSE RIGHT INDEX (DRI) of the Philips Ingenuity PET/CT scanners to facilitate CT dose modulation. The aim of this study was to determine the appropriate DRI for different Body Mass Indices (BMI) that will deliver an overall reduction in radiation dose to the patient.

METHOD

Scan lengths for the PET/CT scan varies depending on disease site. The Dose Length Product (DLP) was used as a measure to indicate radiation dose delivered by the CT component. Our practice with ldCT is to tailor the mAs depending on BMI. The DLP received with ldCT was used as a reference point for each patient. We then chose a DRI, as high as possible, whilst ensuring a lower DLP compared to what the patient would have been received using the ldCT. A region of interest was drawn within the abdominal aorta at the level of the kidneys, for all patients. The Hounsfield Unit values and Standard Deviation (SD) values were recorded, as the SD values are an indication of the noise. For different DRI, the SD was plotted against the BMI.

RESULTS

Table 1 demonstrates the appropriate DRI for varying BMI and patient arm position.

	Ingenuity TF128 PET/CT Dose Right Index		
BMI Range	ARMS UP	ARMS DOWN	% reduction in DLP
< 22	13	13	25
22 - 25	12	13	26.3
25.1 - 30	11	12	15
30.1 - 40	10	11	21.5
> 40	9	10	26.8

Table 1.

CONCLUSION

The radiation dose delivered to patients using dose modulation protocol was compared to that with the original non-modulated ldCT protocol. We found on average, a 20% decrease in radiation dose to the patients and up to 45% in some cases with no degradation of image quality. In some cases, better image quality has been observed.

Pedersen M, [1], **Omidvarnia A**,[1,] **Jackson G.D**, [1,2,]

Adjusted Local Connectivity (ALC) for subject-level fMRI analysis in focal epilepsy

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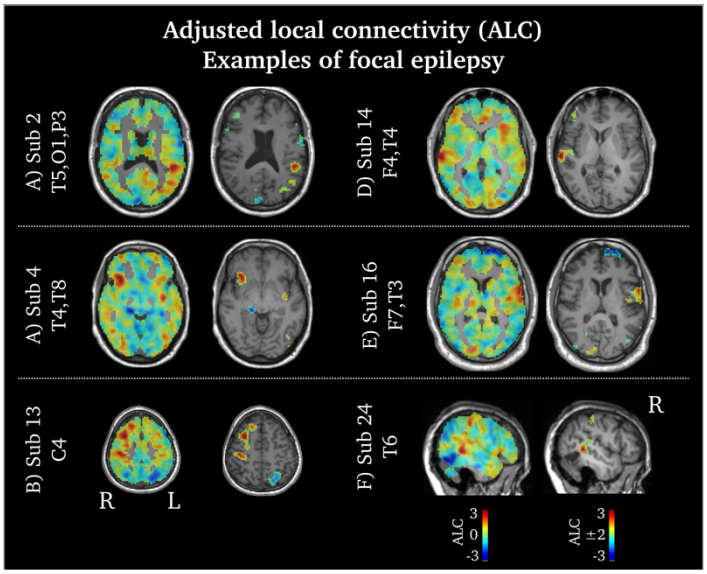
2. Department of Neurology, Austin Health, Melbourne, VIC, Australia.

Aim

Identifying potential targets for surgery constitutes a major clinical challenge in focal epilepsy; especially in cases where no visible epileptic lesion is seen on structural magnetic resonance imaging (MRI (1)). Thus, novel brain imaging tools are highly needed to provide confirmatory and/or exploratory hypotheses that may point towards a patient's seizure focus and/or surrounding brain networks. In an attempt to tackle this issue, we present a functional MRI (fMRI) tool called Adjusted Local Connectivity (ALC). ALC specifically targets brain network abnormalities in focal epilepsy, on a single-subject level.

Methods

ALC is based on the assumption that by controlling for the variance of normal local fMRI connectivity, one can detect specific brain regions with abnormal function in patients with focal epilepsy. This is formally done by quantifying differences in Regional Homogeneity (local fMRI synchronicity within < 1cm^3 of cortex (2)) between a single patient with focal epilepsy and 25 healthy controls.



Results

A supervised machine learning approach (linear support vector machine) was used to validate ALC. In sum, focal epilepsy subjects (N=25) were classified from healthy control subjects (N=25) with 88% accuracy (44/50 subjects were correctly classified - $p < 0.001$). This finding suggests that ALC 'features' are distinctive between epilepsy and control subjects. Several focal epilepsy patients also displayed ALC deviations in brain areas proximate to their respective EEG abnormalities. See attached figure.

Conclusion

ALC is a computationally efficient tool that may provide confirmatory and/or exploratory hypotheses in patients with focal epilepsy.

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Regional association between cortical volumes and imaging tau pathology using 18F-AV1451 and 18F-THK5351.

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Background:

Post mortem studies on Alzheimer's disease (AD) have shown that the stereotypical pattern and density of tau deposition is strongly associated with cortical loss. The development on new PET ligand specific to tau now allow *in vivo* investigation of this association.

Methods:

As part of the Australian Imaging, Biomarker and Lifestyle study, sixty-one participants underwent Tau and Ab imaging with 18F-AV1451 and 18F-Florbetapir (53-HC, 6-MCI, 1-AD) and forty-three others were imaging with 18F-THK5351 and 18F-Flutemetamol (22-HC, 15-MCI, 6-AD), all participants received a MRI scan. Three tau masks corresponding to different braak stagings were contructed: Mesial-temporal (*Me*), temporoparietal (*Te*) and the Rest (*R*) of the neocortex. Tau and Ab PET scans were quantified using CapAIBL®. Tau tracer retention was measured in the three masks and normalised with three standard reference regions: the cerebellar cortex, the pons and the whole cerebellum. A threslod was established for each mask and tau tracer. Cortical volumes was measured in the three masks using CurAIBL®. Cortical volumes were adjusted for age and intra-cranian volume.

Results:

From the three standard reference regions and for both tau tracers, the Pons SUVR normalisation yielded the highest correlations with local cortical volumes in all three regions. Neocortical Flute and Florbetapir SUVR were significantly associated with respectivelly THK-5351 and AV1451 SUVRPons in all *MeTeR* regions ($r>0.43$, $p<0.0005$). THK-5351 and AV1451 SUVRPons estimated in *Me* were only associated with the cortical volumes of *Me* ($r<-0.26$,$p=0.04$). THK-5351 SUVRPons, estimated in *Te* or *R*, and AV1451 SUVRPons, estimated in *R*, significantly correlated with the cortical volumes of all regions of interest ($r<-0.43$,$p=0.003$) while AV1451 SUVRPons, estimated in *Te*, was significanlty associated only with cortical volumes of *Te* and *R* ($r<-0.27$,$p=0.03$). Categorically, studies with a "high" tracer retension in the *Me* or *R* regions had a significantly lower volumes ($p<0.03$) in the same inverstigated regions, while studies with a "high" tracer retension in *Te* had a significantly lower cortical volumes in all regions of interest ($p<0.04$).

Conclusions:

These preliminarly results showed that tracer retension in the *Me* region was only associated with the cortical volumes of *Me* strengthening the hypothesis that tau deposition in this region is just part of the ageing process. However, tracer retension in the *Te* region was associated with cortical volumes in all estimated regions suggesting the Tau needs to spread in the *Te* region to observe more severe cortical damage.

Effects of MAPT over brain grey matter atrophy in the AIBL cohort

Vincent Dore, Tenielle Porter, Pierrick Bourgeat, Victor L. Villemagne, Simon M Laws and the AIBL Research Group

Background

Recent studies have shown that the microtubule-associated protein tau (*MAPT*) gene, which is involved with several neurodegenerative diseases, is implicated in increasing the risk of developing Alzheimer's disease. This study aims to investigate the effect of the *MAPT* allele and its interaction with β-amyloid (Aβ), on cortical thickness, hippocampal volume, and rates of atrophy.

Methods

As part of the Australian Imaging, Biomarker and Lifestyle (AIBL) study of ageing, 286 HC, 58 MCI and 36 AD underwent MRI and Aβ PET scans (either PiB or flutemetamol). HC received follow-up scans every 18 months for up to 6 years. Aβ scans were scaled and normalised using CapAIBL®. At baseline, participants were classified as having either high or low Aβ burden using a threshold equivalent to 1.4 SUVR (~16.5 centiloids). In addition to *APOE* genotyping, *MAPT* H1/H2 status was determined through genotyping of the single nucleotide polymorphism, rs1800547. Hippocampal volumes and cortical thickness were measured with CurAIBL® in regions susceptible to AD neurodegeneration including frontal, medial inferior temporal, latero-temporal, precuneus/posterior cingulate cortex.

Results

There was no significant differences in the demographics between the H1 homozygotes and H2 carriers, although among the HC, MMSE score was lower in H2 carriers.

In the HC subgroup, the rates of atrophy were significantly associated with *MAPT* status in the caudate middle frontal gyri, the supra marginal gyri and in the temporal lobe when correcting for Aβ status. Aβ was associated with significantly faster rates of atrophy in all regions. There was no significant effect of the interaction between *MAPT* and Aβ on the rates of atrophy even though the F-value ($F>3.3$) was high in the hippocampus.

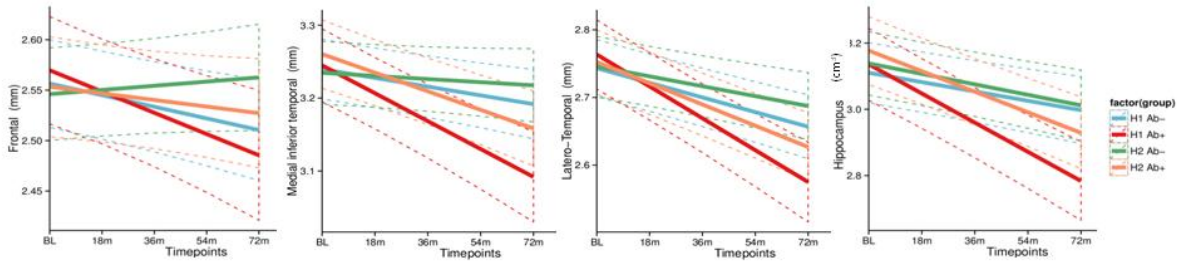
Among the MCI, the cortical thickness difference at baseline between H1 and H2 was significant only in the medial inferior temporal. No association was found in the AD group.

Conclusions

Both *MAPT* and high Aβ had an independent but additive association with rates of cortical atrophy in HC subjects. These findings also suggest trials that use grey matter as outcome

measures for assessment of treatment response in Alzheimer's disease may be improved by genetic stratification of the participants.

Figure 1: *Cortical thickness and hippocampal volumes as a function of time for the 4 different healthy control subgroups.*



Engineering Anti-Lewis-Y Hu3S193 Antibodies with Improved Therapeutic Ratio for Radioimmunotherapy of Epithelial Cancers

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Aims: The aim of the study was to explore Fc mutations of a humanized anti-Lewis-Y antibody (IgG1) hu3S193 as a strategy to improve therapeutic ratios for therapeutic payload delivery.

Methods: Four hu3S193 variants (I253A, H310A, H435A and I253A/H310A) were generated via site-directed mutagenesis and radiolabelled with diagnostic isotopes iodine-125 or indium-111. Biodistribution studies in Lewis-Y positive tumour-bearing mice were used to calculate the dose in tumours and organs for therapeutic isotopes (^{131}I, ^{90}Y and ^{177}Lu).

Results: ^{111}In-labelled I253A and H435A showed similar slow kinetics ($t_{1/2}\beta$, 63.2 h and 62.2 h respectively) and a maximum tumour uptake of 33.11 ± 4.05 and 33.69 ± 3.77 percentage injected dose per gram (%ID/g) respectively. ^{111}In-labelled I253A/H310A cleared fastest ($t_{1/2}\beta$, 9.1 h) with the lowest maximum tumour uptake (23.72 ± 0.85 %ID/g). The highest increase in tumour-to-blood area under the curve (AUC) ratio was observed with the metal labelled mutants (^{90}Y and ^{177}Lu). ^{177}Lu-CHX-A" DTPA-hu3S193 I253A/H310A (6:1) showed highest tumour-to-blood AUC ratio compared to wild-type (3:1) and other variants, and doubling of calculated dose to tumour based on red marrow dose constraints.

Conclusions: These results suggest that hu3S193 Fc can be engineered with improved therapeutic ratios for ^{90}Y- and ^{177}Lu-based therapy, with the best candidate being hu3S193 I253A/H310A for ^{177}Lu-based therapy.

Synthesis of fluorine-18 agents for PET imaging of hypoxic tissue in tumours

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Background: The presence of hypoxia in tumours is a negative prognostic factor since those tumours are more resistant to chemo- and radiotherapy than normoxic tumours. Imaging of tumour hypoxia has proven to be of importance for therapy planning, particularly in head and neck cancer. Since the currently used imaging agent F-18 FMISO has several shortcomings, development of novel imaging agents is needed.

Aim: [^{18}F]SO5O1[1] showed promising uptake in hypoxic SK-RC-52 tumours implanted into BALB/c nude mice using positron emission tomography. However, as it utilised a halogen exchange radiolabelling method it had a non-decay corrected RCY of 2.5%. The aim of this project was to develop novel imaging agents for tumor hypoxia based on SO501 with higher radiolabellng yields.

Methods: Using SO5O1 as a lead compound and incorporating a propargyl group allowed click chemistry to be used as the method of radiolabelling, increasing the non-decay corrected RCY to 25% (EOS). To alter the hydrophilicity of the lead compound various length peg linking groups were investigated, in addition to this the ethyl group was substituted with an iso-propyl group so mechanistic studies on the mode of retention could be undertaken

Results: A series of 5 precursors were synthesised and radiolabelled with fluorine-18 via a 1,3 huisgen cycloadditon using [^{18}F]fluoroethyl azide. To date 4 of the radiotracers have been tested using SK-RC-52 xenograph models. Initial analysis of in-vivo small animal PET/MR data showed that [^{18}F]LC-1-41 had uptake in hypoxic tumours cell.

Conclusion: [^{18}F]LC-1-41 is the most promising radiotracer synthesised with a non-decay corrected radiolabelling yield of 25%.

References: [1]Laurens, E. Synthesis and biological analysis of novel Fluorine-18 positron emission tomography (PET) imaging agents for hypoxic tissues in tumours. School of Chemistry, The University of Melbourne. 2012 PhD.

Investigation of novel Oncrasin-1 analogues for use in imaging kRAS mutant cancers

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Background: Mutations of kras can lead to constitutive activation of the kras pathway and result in aggressive and drug resistant cancers. Mutant kras is therefore a promising target for drug and radiotracer development. Oncrasin-1 analogues have shown selective toxicity against kRAS mutant cell lines[1-3].

Aims: Previous work utilizing small molecule drugs show that the radiolabeled analogues show potential for use as radiotracers. Novel radiolabeled Oncrasin-1 derivatives are being investigated as radiotracers for diagnosis, stratification, staging and monitoring of kRAS mutant cancers.

Methods: A number of structural variations have been investigated. In an attempt to further optimise the lead structure, a number of structural variations are being tested in combination. A number of known and novel fluorinated analogues of the parent compound have been synthesized and characterized. Potency testing of these compounds is being undertaken to find the compound with the highest activity specifically in mutant cell lines to be developed as a radiotracer across a wide range of cancer phenotypes. In addition to potency testing, cell cycle analysis and protein profiling is being carried out to further probe the target of Oncrasin-1 derivatives.

Results: Testing of known Oncrasin-1 analogues in new cell lines has provided results concordant with previous work in terms of relative potencies of previously characterized analogues. This testing is ongoing with further testing of other known compounds and novel compounds.

Conclusion: This work will be used to establish the best candidate for radiolabeling with [^{18}F] and imaging of the proposed radiotracer.

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Development of a Molecular Imaging Probe for Imaging Tissue Transglutaminase 2

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Background: Overexpression of tissue transglutaminase 2 (TG2) is observed in many diseases such as arthritis, fibrosis, celiac disease and cancer. In most cancers, TG2 overexpression is a negative prognostic factor due to chemoresistance and increased invasiveness of these tumors. Noninvasive imaging of TG2 using molecular imaging techniques could help identify patients that can benefit from treatment with TG2 inhibitors.

Aim: The aim of this project was to radiolabel the TG2 selective Hitomi peptide with the PET radionuclides ^{68}Ga and ^{18}F, and to investigate the in vivo properties of these novel radiotracers in mouse models of breast cancer.

Methods: The native "Hitomi" peptide as well as N-terminally modified versions of the Hitomi peptide were purchased from Mimotopes. Modifications modified at the N-terminus with DOTA, 4-pentynoic acid and 5-azidopentanoic acid groups for attachment of radiolabels. The native peptide was radiolabelled with ^{18}F-succinimidyl fluorobenzoate (SFB) at the N-terminus and the DOTA peptide was radiolabelled with ^{68}Ga. The 4-pentynoic acid peptide was radiolabelled with^{18}F 2-fluoroethyl azide using copper (I) catalysed click chemistry. The 5-azidopentanoic acid peptide was labelled with ^{18}F-fluorobenzoylated DBCO by employing copper free click chemistry. Radiotracers were investigated in vivo using TG2 overexpressing MDA-MB-231 tumours and TG2 deficient MCF-7 tumours, grown in Balb/c nude mice.

Results: ^{68}Ga labelling of the DOTA peptide required high concentrations of peptide at 60°C. At higher temperatures less peptide was required however, a significant amount of decomposition was observed. In vivo, the ^{68}Ga labelled peptide showed no uptake in MDA-MB-231 tumors. ^{18}F-SFB labelling of the native peptide was highly pH dependent and produced a significant number of unwanted by-products, thus reducing the overall radiolabelling yield. Copper catalysed click chemistry between 2-fluoroethyl azide and the pentynoic acid peptide resulted in a product that was difficult to separate from the copper (I) catalyst. The best results were obtained when labelling the 5-azidopentanoic acid peptide with ^{18}F- fluorobenzoylated DBCO. This reaction was independent of pH and gave quantitative yields of a single product at room temperature after 20 min of incubation. Uptake of this radiotracer was observed in TG2 overexpressing MDA-MB-231 tumours, whereas no tumour uptake was observed in MCF-7 tumors.

Conclusion: Copper free click chemistry between ^{18}F-fluorobenzoylated DBCO and a 5-azidopentanoic acid modified peptide was found to be the best strategy for labelling a TG2 selective peptide, and is a promising molecular imaging strategy for identifying TG2 expression in-vivo.

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Kinetic Analysis of ^{11}C-Choline PET Uptakes in the Prostates of Patients Undergoing Neoadjuvant Docetaxel Chemotherapy

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Aim

An open-label single arm trial was conducted in men receiving neoadjuvant docetaxel chemotherapy (NDC) prior to radical prostatectomy. ^{11}C-Choline PET imaging was performed to assess the correlation between known prognostic factors and metabolic response to NDC. This study aimed to evaluate the temporal dynamics of ^{11}C-Choline uptakes in prostate and validate the correlations between kinetic and semi-quantitative parameters.

Methods

^{11}C-Choline PET studies of pelvis in 10 patients prior to (387±67 MBq) and after (371±35 MBq) after NDC were included for analysis. The 60-min list-mode data were sorted into 22 dynamic sinogram frames which were corrected and reconstructed using RAMLA3D. Choline uptakes in prostate were measured semi-quantitatively using SUV. SUV ratios (SUVR) in prostate tissues were also calculated using the SUVs in gluteal muscle which represented non-specific uptakes of ^{11}C-Choline. Parametric maps of net influx constant (K_i) derived using the two tissue compartmental reversible model and the non-displaceable binding potential (BP_{nd}) derived using the Logan reference model were generated for kinetic analysis.

Results

SUV, K_i and BP_{nd} in prostate tumours were significantly greater than those in normal prostate tissues ($p<0.001$). In prostate tumours, mean SUV_{max} peaked at 30-40 min post-injection (4.30±1.11); mean K_i and BP_{nd} were found to be 0.19±0.12 min^{-1} and 4.23±2.37, respectively. In normal prostate tissues, mean SUV_{max} at 30-40 min post-injection was 2.63±0.51; mean K_i and BP_{nd} were 0.10±0.04 min^{-1} and 1.76±0.95, respectively. Mean SUVR in sextants at 30-40 min post-injection showed greatest correlation with BP_{nd} (r=0.997), while mean SUV_{max} in 60-min showed moderate correlation with K_i (r=0.558).

Conclusion

The BP_{nd} parametric maps have potential for providing quantitative assessment as well as optimal visual interpretation of ^{11}C-Choline kinetics in prostate. The close correlation between SUVR and BP_{nd} peaking at 30-40 min post-injection indicates that the ^{11}C-Choline prostate imaging protocol can utilize a shorter acquisition time window without compromising image quality.

Sylvia J. Gong[1], Graeme J. O'Keefe[1]

Information-based Implementation of Radiation Management and Assessment of Radiation Protection in Molecular Imaging and Therapy

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Aim

In compliance with the key aspects of the statutory and regulatory requirements enacted by the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) in protecting patients, workers, and the public against hazards of ionising radiation, the aims of this study were to develop an information-based system framework in supporting the implementation of radiation safety management, as well as the assessment of radiation protection in the Department of Molecular Imaging and Therapy of Austin Health.

Methods

The information system design incorporated the configuring and maintenance of multiple databases with user-friendly interfaces. The database layouts included: library of international guidelines, national regulations, institutional policies and departmental procedures of radiation safety and precaution; registration of departmental radiation sources and monitoring apparatus; update of optimised dose levels corresponding to diagnostic imaging procedures; log of reported radiation incidents; record keeping of occupational radiation exposure dose history; map of area and radioactive waste dose rates, etc. Application modules were also developed to perform the data analysis, risk notification and periodic reporting.

Results

The relational database and application modules were successfully integrated using FileMaker Pro™. The main functions included the timely notification of dose exceedences; charting of occupational radiation doses of individuals and critical groups along time; in-advance schedule of source licensing, apparatus servicing and compliance testing; data sorting for patient internal dose assessment; reporting of compliance test, area survey, and radiation experiment results; and summarizing radiation management activities in a defined period, etc. The training and quiz module in radiation safety is under construction.

Conclusion

The system is useful to facilitate and enhance the information sharing and efficient communication of radiation risks and envisaged protective measures; and to potentially expedite assessment and audit of radiation events for recommending correction actions.

High yield radiolabeling of DOTA-TATE and PSMA with ^{68}Ga using the new MultiSyn radiosynthesizer

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Background: The high clinical impact of PET with ^{68}Ga-conjugated peptides including [^{68}Ga]DOTA-TATE for targeting somatostatin receptors in neuroendocrine tumors and more recently [^{68}Ga]PSMA for targeting prostate-specific membrane antigen in prostate cancer has led to the need for efficient and reliable automation strategies for labeling with radio-metals. Although the synthesis procedures are relatively straightforward, the issues for routine use of ^{68}Ga for peptide radiolabeling applications can be automation reliability, large volume of generator eluate, low pH, and potential metal ion impurities including ^{68}Ge breakthrough.

Aims: In this study, we evaluate the efficiency and reliability of [^{68}Ga]DOTA-TATE and [^{68}Ga]PSMA radiolabeling using a commercially available MultiSyn (iPHASE Technologies) automated radiosynthesizer.

Methods: The MultiSyn uses a disposable cassette and reagent set. The prepared peptide is loaded directly into the reactor manually whereas all other reagents are pre-loaded into vials/syringes and installed onto the cassette during preparation. ^{68}Ga is automatically eluted from the generator (ITG) with 4mL 0.05M HCl (no pre-purification) and reacted with the peptide. The reaction mixture is then passed through a Phenomenex Strata-X SPE tube, the tube washed with saline and the radiolabeled peptide eluted with 1mL ethanol and reformulated in saline (10% ethanol) before passing through a sterilizing filter.

Results: The average radiochemical yield decay corrected and uncorrected at end of synthesis for [^{68}Ga]DOTA-TATE was 94.3% and 72.3% respectively and for [^{68}Ga]PSMA was 96.9% and 79.0% respectively. Total synthesis time was 26min for [^{68}Ga]DOTA-TATE and 18min for [^{68}Ga]PSMA.

Conclusion: The MultiSyn radiosynthesizer fully automated the synthesis of both [^{68}Ga]DOTA-TATE and [^{68}Ga]PSMA with high reliability and high radiochemical yield. In the future, the MultiSyn will also be investigated for radiolabeling of other relevant positron emitters, including ^{64}Cu, ^{89}Zr, ^{86}Y and ^{177}Lu for complexation with bifunctional chelators conjugated to peptides.

Uptake and metabolism of 16β-[^{18}F]fluoro-5α-dihydrotestosterone in castration resistant prostate cancer

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Background: The increased interest in therapies directed at androgen receptors (ARs) in metastatic lesions has sparked the development of PET tracers that can noninvasively image AR status. The ^{18}F labeled 16β-[^{18}F]fluoro-5α-dihydrotestosterone (^{18}F-FDHT) analog has been identified as the most promising PET tracer for the imaging of ARs.

Aim: In this study, we synthesized ^{18}F-FDHT and studied its uptake and metabolism in vivo in patients suffering from castration resistant prostate cancer.

Methods: We choose a FlexLab radiosynthesizer (IPHASE Technologies), which has been proven reliable for the radiolabeling of other complex molecules.
Imaging: Patients were injected with a maximum of 9 mCi of F18-FDHT and imaged using the Phillips TF128 PET/CT scanner. One hour post injection, a 25-40 min whole body scan was acquired.
Intravenous blood sampling (~10 mL) was performed at 5, 10 and 30 min post injection. To 1.5 mL of plasma, 1.5 mL of acetonitrile was added to precipitate proteins and the supernatant injected into a Shimadzu HPLC system using a semi-preparative reversed phase HPLC column. The Perkin Elmer Radiomatic 150TR Flow Scintillation Analyzer was used to detect radioactive compounds.

Results: ^{18}F-FDHT was produced in 90 min, radiochemical yields were 18-23%, radiochemical purity was >98% and specific activity was > 55.5 GBq/µmol (1.5 Ci/µmol).
At 5 min post injection, intact F-18 FDHT in plasma was measured at 60-45%, which dropped to 12-8% at 30 min post injection. In vivo, AR positive lesions were detected in 2 out of 3 patients suffering from castration resistant prostate cancer.

Conclusion: The radiochemical yields of ^{18}F-FDHT using the FlexLab synthesizer was highly reliable (18-23%). This method is now validated at our site and is used to routinely produce ^{18}F-FDHT. Although F-18 FDHT metabolizes quickly in vivo the radiotracer can be used to identify AR positive lesions in patients.

Minimising radiation exposure of PET radiopharmacists following implementation of Tema µDDS-A automatic dose dispensing system and optimising work practices

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Background Increasing production of PET radiopharmaceuticals can potentially cause increases in radiation exposure to staff if work practices are not reviewed. There has been an observed increase in finger dose to the radiopharmacist due primarily to the increased handling of manually dispensed FDG doses. It was for this reason that an automatic dose dispensing system was installed for the dispensing of FDG. The µDDS-A Automatic Dose Dispensing System from Tema Sinergie allows safe and precise dispensing of radiopharmaceuticals into shielded syringes or vials. Installed into a shielded laminar flow BSCII, the µDDS-A offers operator safety whilst preserving pharmaceutical quality and traceability. Results of measured radiation exposure prior to and following the installation of the µDDS-A are presented.

Aim To optimise the work practices and minimise radiation exposure of the PET radiopharmacist involved with FDG production.

Method Radiation measurements have been performed using real time (calibrated AGEIS ED2-D) and passive (TLD) dosimeters. Measurements included a radiation survey of the ambient levels in the radiopharmacy and personal monitoring of the radiopharmacists. Levels have been compared pre and post optimisation.

Results The determination of the yearly projected radiation dose to the radiopharmacist for FDG production was performed utilising real time monitoring methods. For whole body exposure this was approximately 4.1 mSv per year and a dose of 221 mSv per year to the hands. The radiation dose burden from all duties was recorded using TLD's and was found to be 4.5 mSv and 321 mSv for whole body and hand radiation doses respectively. Since the implementation of an automatic radiopharmaceutical dose dispenser, radiation exposure recorded to the hands by TLD measurements have fallen by 39%. Further optimisation has seen the ambient radiation levels fall by 15%.

Conclusion It has been shown that by reviewing work practices that a significant decrease to radiation exposure can be achieved for the PET radiopharmacist enabling exposure rates to remain well below the radiation dose constraints required by law. Continued review of optimisation ensures that radiation exposure is kept as low as reasonably achievable.

Observed interference effects of reagent water in critical HPLC analysis

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Background Interfering impurity peaks were observed in a gradient HPLC analysis and the quality of reagent water used was suspected to be the cause.

Aim To investigate the effects of different grade reagent water in HPLC mobile phase formulations and the effects of mobile phase degradation with time in laboratory conditions. Different sources of water for injection (WFI) for interfering UV impurities were also investigated as WFI is commonly used in final product formulation.

Method Two sources of reagent water were used to make up the mobile phases for the gradient HPLC and multiple samples of different sources of WFI were analyzed. The experiment was repeated at 24 hours and 5 days. Different batches of reagent water and WFI were also used to eliminate batch variation. All analysis was performed with UV/Vis wavelength at 300nm as this is our HPLC method under investigation. Experiment conditions: Column XBridge C18 2.5µm, 3.0 x 50mm, flow at 0.85 mL/min, mobile phase A: acetonitrile/water (5/95), mobile phase B: acetonitrile/water (90/10). Gradient 100% A to 100% B in 8.6 minutes hold at 100% B for 3 minutes 100% A for 3.3 minutes. All analysis was performed with LC solution software.

Results Impurity peaks were observed in mobile phase formulations using Baxter WFI which interfered with chemical purity determinations. The same impurity peaks were not observed in experiments utilizing ultrapure water from the Milli-Q Plus system. In addition investigation of different brands of WFI resulted in different UV impurity peaks being observed. Impurities were observed to increase in the mobile phase with time.

Conclusion Our recommendation is that fresh mobile phase (<24 hours) with Type I ultrapure reagent water should be considered if interfering UV peaks is an issue for quantitative analysis.

A versatile GMP compliant semi-automated system for filling open or closed vials and syringes

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Objectives To develop a versatile GMP grade vial filling system with the capability to fill both closed vials and open vials.
The process would need to be performed in a Grade A laminar flow environment, be operator and product protective, be simple to perform and as contingency have ability for manual override should unforseen circumstances arise.

Method Construction of new clean room dispensing laboratories, together with the acquisition of new hot cells, gave the capability of producing higher activities of FDG as well as offering operator safety.
The Austin Hospital Centre for PET is not a commercial facility but supplies outside institutions with FDG doses on a regular basis. From 4-6 vials of FDG are dispensed daily so a vial filling system with flexibility was required to meet our needs. A fully automated system was overkill for our requirements and too expensive.
A collaboration with Tema Sinergie to develop a suitable system resulted in the utilisation of their µDDS-A Automatic Dose Dispensing System combined with a modified version of their crimping station from their fully automated vial dispensing unit DDS-VIALS. Simultaneously a versatile Dispensing hot cell was developed to house the system resulting in the FLEX, multi-purpose GMP grade, shielded isolator.
Present regulations in Australia allow for closed vial filling but the system developed gives the flexibility for open vial filling should the regulations change.

Results Dispensing accuracy is 2-10% depending on the concentration of the radiopharmaceutical being dispensed and labels can be printed of the dispensed product. Everything is controlled via PC touch screen control. Filling operations can be performed as an automated procedure or can be overridden manually. A full audit trail of procedures is recorded and operator radiation exposure is minimal.

Conclusion A GMP compliant system for filling vials was developed. It has the versatility to fill either closed or open vials in a Grade A air isolator environment with the added capability to fill shielded syringes.

Quality Control Method Validation for ^{68}Ga-DOTA-TATE

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Background The demand for scintigraphy of neuroendocrine tumors using radiolabelled somatostatin analogs is increasing. Several ^{68}Ga-labelled somatostatin analogs have been utilized with [DOTA^{0}, Tyr^{3},Thr^{8}]-octreotide (DOTA-TATE) becoming the most popular in Australia.
Recently official Pharmacopoeia monographs have become available in the Ph. Eur 2014 for ^{68}Ga-Gallium Chloride Solution for radiolabelling and ^{68}Ga-DOTA-TOC.

Aim This presentation reports on TLC and HPLC methods being adopted at Austin Health for the quality control of ^{68}Ga-DOTA-TATE and their validation against the system suitability tests of the Ph. Eur. 2014.

Method Two TLC methods and one isocratic HPLC method was investigated. The TLC systems both utilized ITLC-SG glass-fibre backed strips, system 1 solvent was 0.1M sodium citrate and system 2 solvent was 50:50 methanol:0.1M ammonium actetate. The HPLC method was performed on a Shimadzu Prominence system equipped with a radioactive detector and UV-detector set at 220 nm wavelength. The chromatography was performed on a reverse-phase C18 5 µm column (75mm x 4.6mm) with the mobile phase of 25% acetonitrile in 0.1% TFA in water.
The radiolabelling of the ^{68}Ga-DOTA-TATE was performed on an in-house built semi-automated system and the ^{68}Ga(III) was eluted from a ITG ^{68}Ge/^{68}Ga generator.

Conclusion Analytical chromatographic methods have been successfully developed and validated for the quality control of ^{68}Ga-DOTA-TATE. However, the pharmacopoeial system suitability tests are confusing and in their current guise non-reproducible. This presentation discusses suggested adjustments required for validation.

Quality control validation of 16β-[^{18}F]fluoro-5α-dihydrotestosterone produced with the FlexLab radiosynthesiser

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Background The ^{18}F labelled 16β-[^{18}F]fluoro-5α-dihydrotestosterone (^{18}F-FDHT) analog has been identified as a promising PET tracer for imaging the androgen receptor. The complex synthesis was performed using a FlexLab radiosynthesizer (iPHASE Technologies), which has proven to be reliable for the radiolabelling of other complex molecules. A fully automated and reliable synthesis for ^{18}F-FDHT was developed with overall radiochemical yields of 18-23% (decay corrected).

Aim In this study the ^{18}F-FDHT automated production method was validated for use in human studies.

Method Validation was performed with the usual physiochemical and biological testing which included endotoxin, sterility, residual solvents, radionuclidic identity and pH. Radiochemical purity was performed using a Shimadzu Prominence HPLC system. The stationary phase was a Phenomenex Gemini NX C18, 5µ RP column, 150 x 4.6 mm. Acetonitrile/water (55:45) was used as the mobile phase at a flow rate of 1.0 mL/min. Specific activity was measured at UV 220 nm wavelength. Stability testing was observed for 5 hours.

Result ^{18}F-FDHT was produced with a radiochemical purity >98% and a specific activity > 55.5 GBq/µmol (1.5 Ci/µmol). The final product passed all physiochemical tests as well as endotoxin and sterility tests. The product is stable for at least 5 hours.

Conclusion The fully automated production of ^{18}F-FDHT using the FlexLab radiosynthesizer was successfully validated for use in human studies.

A practical evaluation of effectiveness of commonly used syringe shields for PET dose dispensing

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Background Extremity doses from handling unsealed radioactive sources are a major concern to nuclear medicine staff. Automated and semi-automated syringe dispensers for dispensing FDG doses result in a significant reduction in exposure. However it is not practicable to use the dispenser system for research compounds and it is estimated that this was now contributing around 70% of extremity doses.
Thus a review of PET dose dispensing practices was undertaken.

Method Two experienced operators manually dispensed 20 syringes of PET radiopharmaceutical each, 10 syringes without a syringe shield and 10 with. The syringe shield used was 85 mm tungsten shield designed for PET radiopharmaceuticals.
The activity dispensed was 370 MBq, a common dose for research. The operators were timed and the dispensed activities recorded. Exposure measurements were recorded using the instadose™ dosimeter worn around the wrist of the dominant hand. In addition, 10 doses were dispensed using an alternate 30 mm syringe shield available in nuclear medicine departments for SPECT radiopharmaceutical dispensing. The premise for this was to evaluate whether the lighter, easier to handle shield would afford any protection.

Results The same extremity exposure and dispensing time is shown by both operators when dispensing with unshielded syringes.
Operator A's exposure was 20% less when dispensing using a PET syringe shield, however dispensing time increased threefold. Operator B's exposure rate only decreased slightly when dispensing with PET shielded syringes, probably due to the syringe being removed from the shield when removing the air bubble because of difficulty with visualisation through the syringe shield lead glass. However the easier air removal procedure resulted in only doubling the unshielded syringe dispensing time. Dispensing with the lighter SPECT syringe shield yielded no time advantage over using the PET syringe shield. Additionally the 30 mm syringe shield does not seem to provide enough attenuation for 511 keV photons to provide a benefit to radiation finger dose.

Conclusion Dispensing PET radiopharmaceuticals using PET syringe shields can lead to a significant reduction in hand exposure. However there is a significant increase in dispensing time due to the awkwardness of handling a heavy shield and difficulties with visualisation through the lead glass.
Using a lighter, easier to handle SPECT syringe shield offers no net benefit to radiation finger dose when compared to an unshielded syringe.
Decreasing exposure time is not as effective as shielding. Further investigation is warranted.

The Implementation of Clinical Decision Support Systems to Support Medical Students Diagnostic Reasoning Skills

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ABSTRACT

Background: A Clinical Decision Support System (CDSS) is a computer system that helps physicians to make decisions and is typically used in either the diagnostic process or to support clinical management. CDSSs synthesize information based on patient data and use the information to generate a prediction. Prior research demonstrates that using a CDSS to assist physicians' diagnostic and treatment processes improved both the effectiveness and efficiency of patient care[1]. However, the application of CDSSs in medical education is still limited[2]. The use of CDSSs to support patient diagnosis is of particular interest in the field of medical education and it is our intention to investigate the potential benefits of CDSSs for the development of medical students' clinical reasoning skills. We will do so by embedding a CDSS within a purpose designed and built learning tool. The learning tool, which will take the form of a virtual patient presentation, will allow students to systematically work though an unfamiliar case, gathering and evaluating relevant information so as to formulate an appropriate diagnosis.
Objective: We propose to implement a CDSS-based learning and teaching tool to support the development of problem-solving and decision-making skills in medical students.
Materials and Methods: Students will use this tool to explore one or more common clinical presentations, assessing patient histories, selecting and evaluating appropriate investigations and integrating these findings to arrive at a suitable diagnosis with support from the learning system. We designed the system with three supporting models; domain, tutoring, and learner models. The domain model receives the level of student understanding and misconception from the learner model, matches the information to select a new scenario with appropriate features and level of difficulty. The domain model presents a three-stage scenario. At each stage, the student selects a set of combination of patient history, physical examination, and investigation options. The domain model processes the selections and provides the student provide with a list of potential diagnoses. The learner model monitors and records how students select information and formulate their hypotheses. The learner model transfers input information to the tutoring model. The tutoring model treats the information as an unknown instance and uses the CDSS system to predict the instance with the student's diagnostic hypotheses. The tutoring model interprets the prediction to find a correlation between patient information and diagnostic hypotheses. The tutoring model generates appropriate feedback and sends it to the domain model. The domain model uses this feedback to inform the learning path and provide feedback on decision making and progress to the student.
Expected outcome: The CDSS component of the tool is designed to support students' diagnostic processes and to provide targeted feedback as they work through a case. Our research will assess the effectiveness of this feedback and whether the tool, and the appropriate use of a CDSS more generally, can influence or enhance the development of students' decision-making skills.

Keywords: clinical decision support systems, clinical reasoning, virtual patient, medical education, machine learning.

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"Well, That's a Bit Surprising" - Students' Reactions to, and Interactions with Personalized Feedback Reports for Multiple-Choice Tests.

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Introduction:
Feedback on performance is a key learning and teaching tool, yet we know comparatively little about its role in students' prospective learning behaviour. This study adds to our understanding by analysing students' reactions to, and interactions with on-screen feedback and their perceptions of how it might direct their future study behaviour.

Methods:
The study involved 21 second year MD students who sat a non-compulsory multiple-choice test. Participants were invited to complete a Modified Motivated Strategies for Learning and Regulatory Focus questionnaire, designed to measure student motivation and learning approached, two weeks before and six weeks after the test. Feedback reports were provided two weeks after the test. Participants were observed viewing these reports on-screen and were encouraged to explain their thoughts and actions aloud. On-screen actions and verbal comments were recorded using screen-capture software.

Audio recordings were transcribed and screen-capture videos were coded into a series of time-based events. Survey and screen-capture data were analysed in Minitab, using T-tests. Audio transcripts were subjected to thematic analysis using NVIVO.

Results:
Most students described the feedback as useful, and spent an average of 13 minutes reviewing their reports. Approximately 1/3 of their time was spent on orientation material, with the rest reviewing results. Survey results suggested students were motivated to self-monitor and seek opportunities for learning over extending previous knowledge. Analysis of audio transcripts revealed four major themes: interpretation of content (cognition), emotional responses to feedback, intended behaviour, and impressions of testing and feedback. Students responded most strongly to feedback items comparing their performance to their peers (normative feedback). Negative emotional reactions to performance and lower than expected performance was often associated with intended changes to study habits. Few students outlined specific future learning goals or strategies.

Conclusion:
Emotion appears to play an important role in how students respond to feedback, with negative perceptions of performance more likely to elicit intended changes in study behaviour. Students value normative feedback but it appears to drive general rather than specific learning intentions or behaviours. Further development of feedback reports should focus on providing students with clearer guidance for future learning.

AGED CARE NURSE PRACTITIONER-LED OUTREACH MODEL REDUCES HOSPITAL REPRESENTATION FOR FRAIL COMMUNITY-DWELLING ELDERLY

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Introduction. Multimorbid, frail community-dwelling elderly are at greater risk of hospitalisation and mortality. Many are also vulnerable to social isolation, with reduced ability to access primary and specialist healthcare. The Older Persons' Complex Care (OPCC) is a multidisciplinary team model composed of geriatrician, aged care nurse practitioner, nurse and occupational therapist, conceived to deliver timely responsive acute care and case management in response to needs identified on review of existing hospital community programs.

Aims. To review patient characteristics and outcomes (including need for hospital presentations, Emergency Department presentations avoided/bypassed) for clients treated under OPCC.

Methods. Prospective audit of all clients seen under OPCC over a six-month period. LACE Score was used to predict risk of planned readmission or death. Number of hospital presentations were compared for six months prior to and following OPCC referral.

Results. 97 consecutive client referrals with six-month follow-up were reviewed. The median age was 84 years (range 61-98). Most clients (92.3%) had medium- or high-range LACE score (average LACE = 11.2±4.5, (corresponding to ~17% probability of death or hospital admission within 30 days). The average number of hospital presentations in prior to OPCC was 2.1±1.9 vs 0.9±1.4 during/following OPCC. 51.2% of hospital presentations under OPCC were planned, with 34.8% directly to wards, bypassing the Emergency Department. Six-month mortality was high, consistent with the frail nature of OPCC clients (22.4%).

Conclusion. A multidisciplinary team with expertise in geriatric medicine can reduce hospitalisation and avoid unnecessary Emergency Department presentation for frail community-dwelling elderly.

Valente G[1,2], Lynch E[1,2], Brown N[1], Wallis M[1], Delatycki M[1], Cotter M[1], Ramchand J[1], Farouque O[1], Hare D[1], Hawkes E[1], Gan H[1], Sutherland M[1], Kerr F[1], Murphy B[1], Gaff C[2] and the Melbourne Genomic Health Alliance[2]

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Genomic sequencing for Austin Health patients through the Melbourne Genomics Health Alliance

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1.Austin Health, Heidelberg, Victoria, Australia;
2.Melbourne Genomics Health Alliance, Parkville, Victoria, Australia

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Background

As genomic testing becomes increasingly available and affordable, it will inevitably form an important part of patient care. However, there are many challenges related to how best to implement this new technology both in Victoria and worldwide. The Melbourne Genomics Health Alliance has been established with a vision to integrate genomic medicine into everyday healthcare. Austin Health is one of 10 leading Victorian healthcare and research organisations participating in the Alliance.

Aim

Genomic sequencing allows for relatively rapid analysis of all genes in the genome in a single test and therefore can produce a much more rapid diagnosis. This project aims to transition genomic medicine into everyday healthcare by tackling the associated challenges from several different angles including: assessing the value of genomic testing in practice, establishing the best procedures and infrastructure, upskilling the workforce and ensuring appropriate access to quality genomic information.

Methods

Over the next four years, Melbourne Genomics will provide genomic sequencing to around 2,000 Victorian hospital patients with specific genetic conditions who will be enrolled under disease “Flagships”. Austin patients are eligible for each of the Flagships if specific recruitment criteria are met.

Results

Recruitment for this project is currently underway, under six disease Flagships: dilated cardiomyopathy, immunological disorders, congenital deafness, lymphoma, solid tumours and children with complex medical needs. Austin Health is the primary site of patient recruitment for the dilated cardiomyopathy disease Flagship. Approximately 180 Austin patients will access genomic sequencing through these current Flagships. Five further disease Flagships will be announced at the end of 2016.

Conclusion

Clinicians who would like more information about Melbourne Genomics, or have patients that may be suitable for recruitment, should contact Austin Health’s Melbourne Genomics Genetic Counsellor, Giulia Valente on giulia.valente@austin.org.au. Through this project Victoria has become a world leader in using genomics in healthcare.

Androgens act via the Androgen Receptor (AR) in progenitor cells residing within the bone marrow to reduce fat mass in male mice.

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Testosterone negatively regulates fat mass in males, however the mechanism by which testosterone exerts these effects are poorly understood. We and others have shown that deletion of the target for testosterone action, the androgen receptor (AR), in mice results in a phenotype that mimics the three key clinical aspects of hypogonadism in human males, that is increased fat mass, and decreased bone and muscle mass. We now show that replacement of the AR gene specifically in progenitor cells (PCs) residing in the bone marrow of Global-ARKO mice (PC-AR Gene Replacements), completely attenuates their increased fat mass, resetting subcutaneous and peri-renal visceral fat depots to below the normal levels seen in wild type (WT) littermates by 12 wks of age ($P<0.001$ *vs* WT & Global-ARKO, n=11-18/grp). The marked decrease in subcutaneous and visceral fat mass in PC-AR Gene Replacements is associated with a shift in the distribution of adipocyte cross-sectional area with more, smaller adipocytes than WT and Global-ARKOs ($P<0.05$ *vs* WT & Global-ARKO, n=4/grp, 4 fields counted/section), suggestive of a healthier metabolic profile. Euglycaemic/hyperinsulinaemic clamp studies in the PC-AR Gene replacement mice demonstrate higher glucose infusion rates compared to WT mice ($P<0.01$ vs WT, n=3-5/grp) indicating an increase in whole-body insulin sensitivity with increased glucose disposal into various tissues in the PC-AR Gene Replacements. We have previously shown that replacement of the AR in bone marrow PCs of Global-ARKOs restores trabecular and cortical bone to WT levels, while skeletal muscle mass is unaffected. This increase in bone in PC-AR Gene Replacements is associated with increased *Runx2* expression, a key osteoblast differentiation factor, compared to Global-ARKOs ($P<0.05$, n=10/grp). Taken together, our data support an action for testosterone *via* the AR in bone marrow PCs to divert their differentiation away from the adipocyte lineage towards the bone lineage, thereby reducing fat accumulation.

Contributing factors to increased mortality in men undergoing long-term androgen deprivation therapy.

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Background:
A 3 year course of androgen deprivation therapy (ADT) is an effective treatment for high risk localized prostate cancer; however is associated with adverse cardio-metabolic risk. Cardiovascular disease is the leading cause of death in men with prostate cancer. We aimed to evaluate whether baseline cardiovascular risk factors could predict mortality in men undergoing long-term ADT.

Methods:
We conducted a prospective cohort study of men with prostate cancer newly commencing ADT referred to a dedicated ADT Clinic at a tertiary referral hospital (Austin Health, Victoria) between March 2007 and December 2012. Death was ascertained by hospital medical record review. Kaplan-Meier survival analyses, Mantel-Cox log rank test to assess predictors, and Wilcoxon signed rank test were used. Median [interquartile range] are presented.

Results:
Of the 353 men, 106 had data for analysis at 4 – 5 years (60 had not reached 4 years, 9 did not have a visit within this window, 93 lost to follow up, 37 discharged, 48 deceased). At baseline, 64% had hypertension, 60% hypercholesterolemia, 83% overweight/obesity, 22% diabetes mellitus, 25% ischaemic heart disease, and 25% had smoking history. None of these cardiovascular risk factors predicted mortality after 4 years. The only predictor of death was increasing age ($p<0.0001$).

83 had ceased ADT at 4 years (median duration on ADT 3.0 years [2.8, 3.0], off ADT 16.7 months [13.3, 26.2]. Waist circumference significantly increased by 3cm ($p=0.005$). Blood pressure was lowered ($p=0.011$) as was total cholesterol, LDL and triglycerides (all $p<0.001$), HOMA2-IR ($p=0.84$) and HbA1c remained stable (0.077).

Conclusions:
Older men with prostate cancer commencing ADT have a significant cardiovascular risk burden which can despite increasing central adiposity, be mitigated with proactive management. Although baseline cardiovascular risk burden did not predict medium-term mortality, further study is required to analyse whether adequately controlling these risk factors impacts on mortality.

Lack of improvement in fat mass following cessation of androgen deprivation therapy: A 4 year case-control study.

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Background
Loss of muscle mass and gain in fat mass occurs in men undergoing androgen deprivation therapy(ADT) for prostate cancer. Whether body composition improves after cessation of ADT is not known.

Methods
We conducted a prospective case-control study over 4 years (2 years on ADT, 2 years off ADT) involving 34 men newly commencing ADT and 29 age- and radiotherapy-matched prostate cancer controls. Serum sex steroid levels were measured and body composition was assessed using dual x-ray absorptiometry. To determine differences between groups over time, a clustered linear regression model was performed which accounted for baseline values.

Results
We report preliminary results for 10 men in the ADT group and 8 controls. All patients recovered total testosterone levels to a normal range (median 15.4 nmol/L) by two years post therapy. Compared with controls, the ADT group gained the majority of fat mass in the first 12 months of ADT. At 4 years (2 years after ADT cessation), there was no recovery in gained fat mass with between group difference +4331g [2106,6556], p=0.002. Lean mass decreased throughout duration of ADT but improved after cessation. At 4 years, lean mass in the ADT group compared with controls was not significantly different from baseline.

Conclusion
These preliminary findings indicate that, fat mass once gained, does not improve despite recovery of testosterone levels. Whether the recovery of lean mass mitigates some of the deleterious effects of persistent adiposity requires further study. These results emphasise the importance of mitigating fat gain in the early period after commencement of ADT to minimise cardiovascular morbidity and mortality.

Word count 300

Sexual and racial dimorphism in bone microarchitecture requires adjustment of the region of interest for skeleton dimensions

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Introduction Bone size, shape, and micro-architecture vary point by point around and along the length of a bone, especially at metaphyses, irregularly designed ends of long bones. Image acquisition using HR-pQCT is achieved by scanning fixed region of interest (ROI) without considering bone length. Given the heterogeneity in structure, sex and racial differences may be a consequence of measuring different regions rather than true differences in bone. To quantify sexual and racial differences in bone microarchitecture we examined effects of placement of the ROI to ensure anatomical identity was maintained by sex and race.

Methods In 77 women (40 Asian and 37 Caucasian) and 85 men (37Asian and 48 Caucasian), age range 22-52 years, the distal part of non-dominant radius was scanned using HR-pQCT. Images were analysed slice by slice using StrAx 1.0. Total vBMD and porosity of total and compact cortex were assessed using the standard-fixed method (110 slices) versus a region of 4.3-6.2% of the radius length before and after adjustment for total cross sectional area (TCSA) of the ROIs.

Results The standard-fixed method produced either no differences in porosity or higher porosity in males than females. After adjusting for bone length to ensure the same anatomical location, differences in porosity either disappeared or reversed. However, when the standard-fixed or adjusted ROI was adjusted by total CSA, the same result was found; females had higher porosity than males in both races and there is no racial differences in men and women.

Conclusion Differences in the relative to position of the ROI has biologically significant effects on cortical porosity which may result in erroneous reporting of age, sex and racial differences in this trait. Adjustment for Total CSA is sufficient to correct for anatomical variation in the ROI in persons with differences in radius length.

THE INFLUENCE OF PHYSICAL ACTIVITY AND LEAN MASS ON VOLUMETRIC BONE DENSITY AT THE TIBIA TWO YEARS AFTER STROKE

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Objectives: Accelerated bone loss associated with immobility and muscle atrophy contributes to increased fracture risk of paretic limbs. The aim of this study was to observe changes in magnitude of the side-to-side difference (STS-diff) in volumetric bone mineral density (vBMD) between paretic and non-paretic legs from early after stroke and its relationships to physical activity and lean mass.

Methods: Prospective observational study. Participants unable to ambulate were recruited within week of first stroke, and assessed 6-monthly for two years. Primary outcome: vBMD at bilateral distal tibiae, derived using high-resolution peripheral quantitative computed tomography (HR-pQCT); analysed by generalised estimating equation, controlling for age and stroke severity (National Institutes of Health Stroke Scale, NIHSS). Secondary outcomes: physical activity (accelerometer recorded proportion of time standing, and number of transitions between lying, sitting and standing), serum markers of bone resorption (carboxyterminal crosslinked telopeptide of type 1 collagen, CTX) and formation (N-terminal propeptide of type 1 procollagen), dual energy X-ray absorptiometry (DXA) derived lean mass.

Results: 16 participants aged 65.3±10.2 years, NIHSS 12.8±5.4 (n=7 females). Between baseline and two years, the STS-diff in vBMD increased (p=0.01) from 1.0% (95%CI -1.3,2.4) to 2.9% (-1.6, 9.0); a monthly change of 0.17% (95%CI 0.04, 0.30). STS-diff in lean mass increased monthly by 0.09% (95%CI 0.01, 0.17; p=0.03), from -2.35% (-3.97, 1.40) to 0.69% (-2.43,4.02). Between baseline and two-years, proportion of time standing increased (p<0.01) from 1.22% (0.27, 4.8) to 23.46% (15.33, 32.67) and transitions from 58.5 per day (33, 75) to 71 (58, 108). STS-diff in vBMD was not associated with STS-diff in lean mass or physical activity. Proportion of time standing was inversely associated with CTX (-2.86, 95% CI -5.2, -0.6; p=0.01).

Conclusion: The magnitude of the difference in vBMD between paretic and non-paretic legs increased within two years of stroke. Increasing time standing may reduce bone resorption after stroke.

Functional MRI changes in Type 1 Diabetes with and without Renal Hyperfiltration

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Introduction

We aimed to determine if functional MRI is able to detect change in renal function in patients with type 1 Diabetes (T1DM). We hypothesized that compared to controls, patients with T1DM have: (i)a decrease in intra-renal oxygenation as measured by blood oxygen level dependent (BOLD) imaging, represented by an increased medullary to cortical R2* (MCR), and (ii)changes in diffusion tensor imaging (DTI) metrics, fractional anisotropy (FA) and apparent diffusion coefficient (ADC), representing renal parenchymal water motion.

Methods

32 patients with T1DM and 10 healthy controls underwent 3 Tesla MRI in a prospective study. Hyperfiltration was defined as a measured Glomerular Filtration Rate (mGFR)≥120mls/ min/1.73m^2 determined by ^{99m}Tc-DTPA. Based on intra and inter-reader concordances from two blinded readers (R1 and R2), we performed analyses on BOLD data for both readers and DTI data for R1 alone. MCR, FA and ADC values between: (i)T1DM versus Controls (ii)T1DM with hyperfiltration versus those without (stage1+Diabetic Kidney Disease (DKD)) were analysed using Mann-Whitney tests.

Results (Table 1)

There were no significant differences between T1DM and controls, except for medullary FA (p=0.03). Lower medullary FA in the stage1+DKD group compared to hyperfiltration did not reach statistical significance(p=0.4). T1DM with hyperfiltration had a significantly higher cADC compared to those with stage1+DKD(p=0.0007).No differences were found between hyperfiltration and stage1+DKD for BOLD-derived parameters.

Table 1: Functional MRI changes in patients with T1DM, with and without hyperfiltration and controls

	T1DM N=32	Controls N=10	T1DM mGFR$^+$ < 120mls/min N=22	T1DM mGFR$^+$ ≥120mls/min N=10
mGFR$^+$ (mls/min/1.73m^2)	105 (78,121)	NA	94(70-105)	124(121-129)
R1 MCR	1.45 (1.38, 1.56)	1.44 (1.35, 1.61)	1.46(1.37, 1.56)	1.45(1.41, 1.48)
R2 MCR	1.37 (1.20, 1.48)	1.41 (1.16, 1.54)	1.38(1.29, 1.50)	1.29(1.27, 1.46)
Cortical FA	0.151 (0.141,0.171)	0.163 (0.145,0.169)	0.151 (0.141, 0.162)	0.158 (0.144, 0.189)
Medullary FA	0.386 ** (0.356,0.435)	0.446 ** (0.395, 0.471)	0.377 (0.337,0.431)	0.399 (0.365, 0.441)
Cortical ADC (10^{-3}mm^2/s)	2.503 (2.324,2.638)	2.441 (24.13,2.484)	2.454** (2.275,2.526)	2.661** (2.592,2.687)
Medullary ADC (10^{-3}mm^2/s)	2.306 (2.204,2.530)	2.239 (2.114, 2.437)	2.276 (2.160, 2.497)	2.425 (2.341, 2.692)

$^+$Measured Glomerular Filtration Rate (mGFR) based on Tc-99m-DTPA nuclear medicine GFR with Brochner-Mortensen correction. R1= Reader 1, R2= Reader 2, MCR=medullary-cortical R2*, FA=fractional anisotropy ADC= apparent diffusion coefficient
Results expressed as Median (IQR). Comparison analysis with Mann-Whitney test**.** **p -value <0.05 is considered significant

Conclusion:

There were no differences in functional MRI parameters between T1DM and controls apart from a lower mFA in T1DM.This finding, together with the lower cADC in the stage1+DKD group may potentially reflect disruption of medullary tubular architecture in progressive DKD. These findings should be interpreted with caution given the small patient population. Further studies in a larger cohort may demonstrate differences between different degrees of DKD using functional MRI.

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ACE2-AAV gene therapy improves plasma glucose and pancreatic islet function in diabetic mice with NAFLD

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Aim
Diabetes is one of the commonest diseases in man. Despite the availability of a range of drugs to manage the condition, there is no therapy to improve the dysfunctional islet cells. Angiotensin II peptide of the classic renin angiotensin system (RAS) has been implicated in the pathological changes associated with islet cell dysfunction. Angiotensin converting enzyme 2 (ACE2) of the 'alternate RAS' degrades angiotensin II to beneficial peptide, angiotensin-(1-7). We therefore sought to determine the potential of ACE2 therapy on dysfunctional islet cell population and insulin production in a diabetic mouse model with fatty liver disease.

Methods
C57BL/6 mice were rendered diabetic by two consecutive daily injections of streptozotocin (STZ) after 15 weeks of high fat (20%) high cholesterol (2%) (HFHC) diet. Pancreas- and liver-specific ACE2-AAV vector or control vector carrying human serum albumin (HSA) were injected intraperitoneally into mice 15 weeks post-STZ injection and the animals were sacrificed 10 weeks post-ACE2 or HSA treatment. Fasting plasma glucose and insulin levels were determined using plasma glucose analyser and ALPCO mouse insulin ELISA, respectively. Insulin immunohistochemistry and double immunofluorescence to co-localize ACE2 and insulin proteins were performed on pancreatic tissue sections.

Results
Fasting plasma glucose levels were significantly reduced ($p<0.05$) in the ACE2 treated group compared with the control vector treated group. ACE2 therapy tended to increase fasting insulin levels ($p=0.08$) in comparison with the HSA-AAV group. Immunohistochemical quantification revealed increased pancreatic insulin levels ($p<0.05$) in ACE2 treated mice compared with HSA-AAV injected mice.

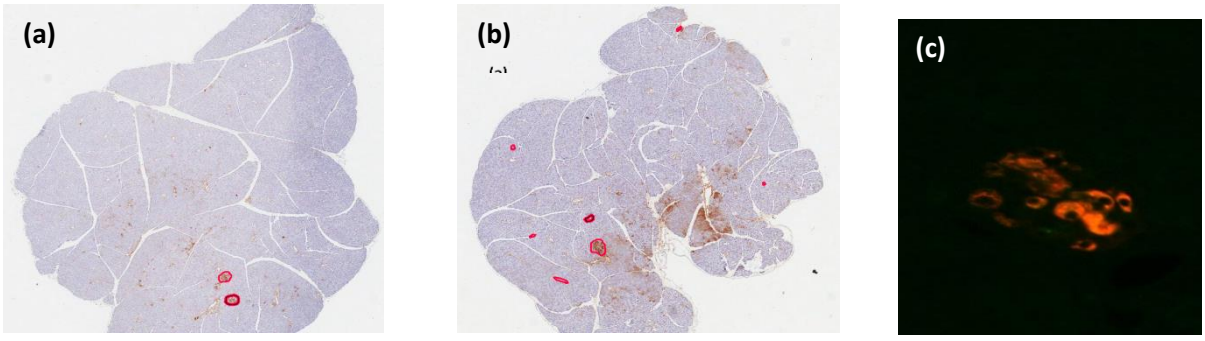

Figure 1. Immunohistochemistry revealed increased insulin staining (red circles) in islets from ACE2-AAV treated (b) when compared with HSA-AAV (a) treated mice. ACE2 protein is co-localized with insulin protein (merged-orange) (c).

Conclusion
In summary, ACE2 therapy improves pancreatic insulin levels and reduces plasma glucose levels in diabetes. We therefore conclude that ACE2 therapy has potential to improve diabetic pancreas.

Changes in insulin requirement and glycaemic control during the third trimester in women with type 1 diabetes on insulin pump therapy.

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2. Mercy Hospital for Women, Melbourne, VIC

Background:

Increase in insulin requirements across gestation occurs in maternal Type 1 diabetes (T1DM), predominantly secondary to increased bolus insulin(1). However, towards end of gestation, some women on multiple daily injections have a fall in insulin requirements potentially related to altered placental function or foetal draw(2).

Aim:

To examine changes in insulin requirements in maternal T1DM patients on Insulin Pump Therapy.

Methods:

We analysed data in pregnant women with T1DM who received antenatal care at Mercy Health, 2010-2016. Weekly averages of total, basal, and bolus insulin, carbohydrate intake, blood glucose (BGLs), and episodes of BGL <3.9mmol/L were recorded in the 1st(T1), 2nd and the 3rd(T3) trimester at 29,31,33,35,36,37 weeks. T3 time-points were classified as week(s) prior (1, 2-3, 5 and 7 weeks) to delivery to account for variable gestations. Differences were analysed by repeated measures ANOVA.

Results:

Seventeen patients' pump data have been analysed. Gestation at delivery: 36.7±1.3 weeks, booking BMI 24.2±8kg/m^2. There was increased total insulin between 7 and 5 weeks pre-delivery (55.05±14.86 vs 62.26±17.1 units; p=0.01), no change thereafter. Carbohydrate intake remained constant with no difference in basal insulin (35.43±18.3 vs 31.9±19.5units;p=0.11) and bolus insulin (38.8±18.6 vs 33.1±18.9units p=0.19); weeks 1 vs 7. Reduced average BGL occurred before delivery (7.4±1.2mmol/L vs 8.4±1.7; p=0.03; weeks 1 vs 5). The percentage of BGL <3.9mmol/L was greater towards the end of gestation (9.2% vs 4.8%; p=0.036; week 1 vs 5). 10 of 17 patients showed some degree of decline in total insulin in the final gestational week (66.77±18.52 vs 63.01±17.94 units;p=0.003;weeks2 or 3 vs 1) translating to an average 6% insulin reduction (0.7 –14.3%).

Conclusion:

T3 is a dynamic time of change of insulin requirements and glycaemic control, seemingly unrelated to change in carbohydrate intake. Better characterisation of these parameters could assist in the management of maternal T1DM.

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Pilot Study: The impact of substantial pre-conception weight loss in obese women and on glucose control at 26-28 weeks gestation

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Background: In Australia, 1 in 3 women of reproductive age are obese, but no pre-pregnancy weight loss interventions have been shown to reduce the risk of obesity-related pregnancy complications for both mother *and* child. The HAPO study observed that small changes in maternal glucose at 26-28 weeks gestation are associated with significant changes in the rate of adverse pregnancy outcomes.

Aim: To determine if substantial pre-conception weight loss (10-15% body weight) in obese (BMI >30kg/m2) women reduces fasting glucose at 26-28 weeks gestation by ≥10% compared with modest (≤3%) weight loss.

Method: 78 women were randomised to either a lifestyle program expecting modest weight loss (MWL; ≤3% body weight; n=38), or a modified VLED program expecting substantial weight loss (SWL; 10-15% body weight; n=40). Attrition over the 12-week program was 20% (MWL 10/38 (25%), SWL 6/40 (15%)). Only completers were considered in the preliminary analysis. Subjects were followed for 12 months and if pregnancy occurred, maternal plasma glucose was measured at 26-28 weeks gestation. Of the 24 subjects who were >6 months post-intervention, 10 were pregnant and had completed 28 weeks gestation.

Results: Weight loss in the MWL (n=28) and SWL (n=34) groups was 2.1% and 13.1% respectively. Mean reduction in plasma glucose after12 weeks was 1.24% (SE 1.40) in MWL and 9.12% (SE 1.83) in SWL group. Of those who achieved pregnancy (MWL= 3, SWL=7), mean decrease in plasma glucose between the start of the weight loss program and 26-28 week gestation was 1.85% (SE 1.83) and 11.51% (SE 3.17) in the MWL and SWL groups respectively.

Conclusion: This pilot data suggests that, in obese women, pre-conception weight loss may result in a decrease in fasting plasma glucose which is maintained into pregnancy. The reduction in plasma glucose is greater when substantial pre-pregnancy weight loss is achieved.

Impact of substantial weight loss on thyroid function in obese women planning pregnancy

Meilun Ly, Sarah Price, Elif I. Ekinci
Department of Endocrinology, Austin Health, University of Melbourne

Background: Maternal obesity is associated with significant maternal and neonatal complications. To address this, weight-loss must begin pre-conception.

Hypothetically: substantial weight-loss could be accompanied by changes in thyroid function. Given thyroid hormones are essential for early fetal neurodevelopment, it is imperative to understand these changes. The impact of both modest and substantial weight-loss on thyroid function has been poorly described. Furthermore, there are no prospective studies evaluating the effects of weight-loss on thyroid hormones in the context of pre-pregnancy care.

Objective: To investigate the impact of substantial weight-loss on thyroid function in obese women planning pregnancy.
Method: Obese pre-pregnant women aged 18-38 years were randomized to substantial weight-loss (VLED diet) or modest weight-loss (lifestyle advice based on current Australian guidelines) for 12 weeks. Fasting blood samples were collected at baseline and 12 weeks for measurement of thyroid function (fT3, fT4 and TSH). In a subset of 11 women who fell pregnant after the intervention, a third blood sample was collected at 12 weeks gestation for analysis. All samples from the pregnant subgroup were further tested for rT3 levels.

Results: 48 women (mean age: 33.78 ± 3.28, mean parity: 0.75±1.13, mean BMI: 36.84 ± 6.36kg/m^2 and mean weight 98.94 ± 18.67kg) were randomized as above. Total body weight-loss in the substantial and modest weight-loss arms were 13.87 ± 4.22kg and 2.55 ± 2.03kg respectively. There were no statistically significant differences in the levels of serum fT3, fT4 or TSH between those with modest weight-loss and those with substantial weight- loss at baseline, week 0 and 12 weeks gestation.

Conclusions: In conclusion, substantial preconception weight loss was not associated with statistically significant changes in serum levels of TSH, fT3 or rT3 when compared to moderate weight loss. Reassuringly, substantial pre-pregnancy weight-loss does not significantly alter maternal thyroid function.

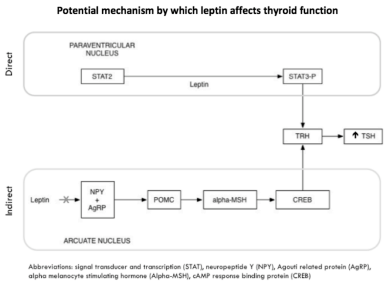


Figure 1.

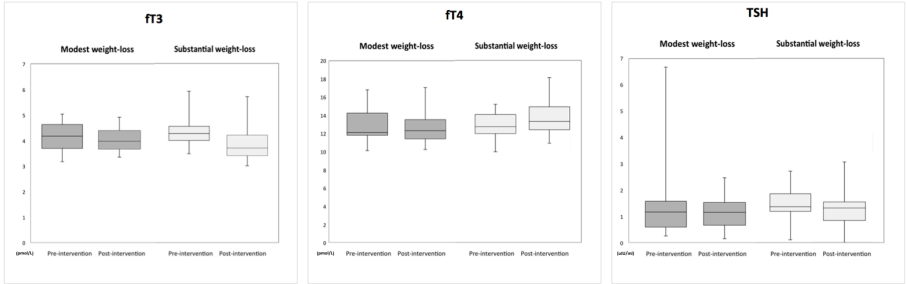


Figure 2.

The effect of habitual dietary salt intake on endothelial microparticle levels in Type Two Diabetes Mellitus

Liu D[1], Baqar S[1,2], Lincz LF[3], Kong YW[1], Jerums G[1,2] and Ekinci EI[1,2]

[1] Department of Medicine Austin Health, The University of Melbourne, Faculty of Medicine, Dentistry and Health Sciences, Victoria, Australia.
[2] Department of Endocrinology, Austin Health, Victoria, Australia.
[3] Hunter Haematology Research Group, Calvary Mater Hospital, Newcastle, NSW, Australia

Background
Low dietary salt intake has been associated with higher mortality risk in individuals with Type Two Diabetes Mellitus (T2DM). Microparticles (MP) are membrane vesicles released during cellular activation, death and damage. Endothelial MP are accepted surrogate markers of endothelial dysfunction. The effect of salt intake on endothelial MP in individuals with T2DM has not been explored.

Aim
To investigate the effect of habitual dietary salt intake on endothelial MP levels in T2DM. We hypothesised lower habitual dietary salt intake to be associated with higher endothelial MP levels compared to higher habitual dietary salt intake.

Methods
Eighty-one patients attending Austin Health diabetes clinics were recruited in a prospective cross-sectional study. Habitual dietary salt intake was estimated using the mean of two out of three corrected 24-hour urinary sodium excretion measurements. Flow cytometry characterised and quantified endothelial MP isolated from peripheral blood samples. Seven participants were excluded due to pre-analytical processing differences. Thus seventy-four participants were included for final analysis. Corrected 24-hour urinary sodium excretion was correlated continuously with endothelial MP levels using Spearman rank correlation analyses. A P value <0.05 was considered statistically significant.

Results
A trend towards higher CD36+/CD235a+ erythrocyte MP levels were observed in patients with lower habitual sodium excretion ($\rho=-0.23$, $P=0.05$). There were no significant correlations between 24-hour urinary sodium excretion and total CD31+/CD42b-: $\rho=-0.17$, $P=0.14$; CD31+/CD42b-/Annexin V+: $\rho=-0.14$, $P=0.24$; CD54+/CD105+: $\rho=-0.08$, $P=0.50$; CD105+/CD62e+: $\rho=-0.07$, $P=0.54$; total CD105+: $\rho=-0.17$, $P=0.15$.

Conclusion
CD36+ MP are accepted biomarkers of T2DM and atherosclerotic plaque instability. We found a trend towards higher CD36+/CD235a+ erythrocyte MP levels and lower 24-hour urinary sodium excretion. These findings question the rigorous population-wide salt restriction guidelines in individuals with T2DM, however validation with larger interventional studies is required.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: *Victorian Spinal Cord Service (VSCS) Discharge Review Clinic (DRC) – Review*
Service Area: *VSCS/Spinal Community Integration Service (SCIS)*
Project Team Members: *Leanne Rees (Physiotherapist), Ruth Stewart (Occupational Therapist), Sue Dickson (Community Spinal Liaison Nurse), Trisha Dodds (Community Spinal Liaison Nurse), Raewyn Buchanan (Community Spinal Liaison Nurse), Belinda Rickard (Spinal Community Service Manager)*

What did your project set out to achieve?
The aim of this review was to see if the traditional format of the VSCS DRC sufficiently met the needs of the client given the presence of the SCIS – a multi disciplinary team supporting Victorians with a newly acquired spinal cord injury in the community for the first 12 months post inpatient rehabilitation. Analysis of attendance data found that utilisation rate was approximately 50% ,and a file audit revealed that clients weren't attending at the pre determined intervals of 1 month, 3 months and 6 months post discharge.

How were consumers involved?
A survey was sent to previous and current SCIS clients. Feedback received included: 'lack of formality in structure and purpose', 'appreciated seeing consultant and team', and 'opportunity to have issues addressed'. Additionally, whilst not captured in the survey, many clients reported that 10.30am (start time of the clinic) was a difficult time to attend due to morning routines, especially when living regionally, factoring in travel time, and relying on care.

How has the patient experience been improved?
The DRC now operates in the afternoon. This provides more time for the clients to get ready and attend the clinic on time. The DRC remains multidisciplinary, however an appointment is provided for 4 weeks post discharge and then on an as needs basis. This will free up appointment times for clients when they are urgently needed. A formal check in point has been created at the VSCS Community Services Office, and SCIS Liaisons encourage the client to pre-identify any issues that can be addressed at the clinic, creating more purpose and good utilisation of resources. This may include the presence of a staff member that is usually not involved at the DRC, e.g. Leisure Specialist, Exercise Physiologist, or Vocational Rehabilitation Consultant.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: We can individualise consumer care and reduce anxiety by using the recourses of a large public hospital.

Ward/Dept/Service Area*: Radiology, Clinical Education Unit and Victorian Respiratory Support Service (Community Ventilation).*

Project Team Members' Names & Roles*: Nicole Hosking (NUM - Radiology), Julie Preston (Clinical Education Coordinator - Radiology), Jane Warneke (Clinical Support Nurse - 5 West).*

What did your project set out to achieve? We wanted to increase radiology nurses' knowledge and skill of a ventilator used by a consumer when he comes to radiology for regular 3 monthly invasive procedures. This consumer depends upon this ventilator to breathe, however it is rarely seen in radiology. We also wanted to provide a positive experience by reducing his, his family and his carers' anxiety every time he comes to radiology.

How were consumers involved? Radiology, Clinical Education Unit and the Victorian Respiratory Support Service (Community Ventilation) liaised directly with the consumer, his family and carer to develop a specialised plan. His individual preferences and the complexities of his ventilator were included in the radiology nursing education and competency assessment strategy.

How has the patient experience been improved?

The consumer, his family and his carers are now more confident in the radiology nurses knowledge and skill associated with his ventilator and are less anxious when be comes to radiology for his regular invasive procedures.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: *Reducing Restrictive Interventions (RRI)*
Ward/Dept/Service Area: *Mental Health CSU – State-wide Child Impatient Unit*
Project Team Members' Names & Roles: *Adam Blake (ANUM), Keith Griffin (Grade 2 Advanced), Jane Negus (Acting NUM)*

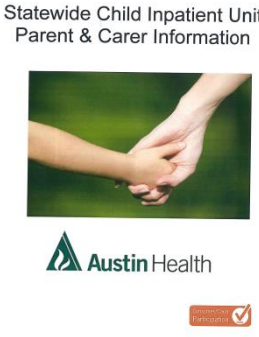
What did your project set out to achieve?

The aim of this project was to reduce the use of restrictive interventions within the child unit. Various strategies were implemented as part of this project to achieve this aim. This included;

- Involvement of parents/carers in development of a parents/carer handbook which informs parents/carers what to expect on the unit, and importantly detailing strategies employed on the child unit to aid in reduction of restrictive practice.
- Changes to the physical layout of the unit, resulting in 3 designated spaces to aid in the reduction of restrictive interventions,
- Education/training for all staff regarding trauma informed care.

How were consumers involved?

Consumer Care and Advisory Group (CCAG) were heavily involved in this project. Initial feedback was sought via a voluntary survey from past consumers (parents/carers). Following this, RRI project team members consulted with CCAG in the form of face-to-face meetings to further inform this project.



How has the patient experience been improved?

There has been a marked decrease in the amount of restrictive interventions since the implementation of the RRI project.

Restraint data demonstrates that prior to implementation of the project, approximately 42% of children admitted to the child unit were restrained. Post implementation of the project, this has been reduced to 21% of children admitted to the child unit being restrained.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: Peer Support at Austin Child and Adolescent Mental Health
Department: Austin Health - Child and Adolescent Mental Health Service (CAMHS)
Project Team Members' Names & Roles: The Austin CAMHS Super Hornets, Mr Pat O'Leary (CAMHS Manager) and Dr Joanne Sais (CAMHS Clinical Psychologist)

What did your project set out to achieve?
The Super Hornets is a youth advisory group comprising a dynamic and enthusiastic group of young people, who have each had a journey through CAMHS. Through this lived experience they bring wisdom, encouragement and hope to clients of this child and adolescent mental health service. The aim of this project is for the Super Hornets to provide weekly Peer Support to inpatients within the child and adolescent inpatient units of the service. Peer Support is the process of providing help by sharing knowledge, experience, and emotional or social support. Peer Support workers aim to deliver support to inpatients on the unit by: (1) enabling inpatients to talk about their experiences, (2) providing young people with a sense of hope regarding recovery, (3) helping clients feel valued as individuals, (4) enhancing staff awareness of youth issues, and (5) increasing client awareness of services available to them and opportunities for participation.

How were consumers involved?
The Super Hornets group comprises former clients of the service who have each had a lived experience. Therefore, the Super Hornets' past 'consumer' lived experience is used to promote recovery by engaging current clients. As recipients, clients of the service can choose to be involved in Peer Support through discussion to explore areas of concern, or alternatively by taking part in joint ward activities.

"*Knowing that they could get through it gave me hope…*" (Anonymous, 2015)

How has the patient experience been improved?
Questionnaires are made available to inpatients to review the Peer Support role. Feedback from this process is considered and ideas explored with the Super Hornets. The aim of this process is to improve the client experience and the delivery of Peer Support. Qualitative feedback from this questionnaire suggests the program is well received and it reinforces the empowering message that "*things can get better*" (Anonymous, 2015).

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: ***Patients as Teachers:*** ***Training Doctors and Nurses in Supported Conversation Skills***
Ward/Dept/Service Area: ***Speech Pathology Department***
Project Team Members' Names & Roles: ***Emma Burns, Senior Speech Pathologist , Austin Health Merrilyn Diverall and Dr. Rob Weller (Rehabilitation Medicine Training Victoria).***

What did your project set out to achieve (the aim)?

People with communication disability frequently encounter barriers to successful participation in conversations regarding their health which can make time in hospital even more stressful and challenging. Our project set out to improve the skills and confidence of medical and nursing staff to communicate with people with communication disability.

How were consumers involved?

Six people with *aphasia* (a communication disability often caused by a stroke) were employed to co-facilitate a one-day communication skills workshop. Sixteen doctors and nurses attended the workshop through Rehabilitation Medicine Training Victoria to learn the skills of supported conversation (SCA™). Part one involved direct training from a speech pathologist to teach the use of tools and strategies like gesture, drawing, pictures and key words to support people with aphasia to feel respected and participate in conversation more successfully. Part two was an interactive conversation session that provided the doctors and nurses with an opportunity to learn directly from the people with aphasia and practice the communication strategies they had learnt. Part two was developed in collaboration with the co-facilitators with aphasia. The co-facilitators met with a speech pathologist prior to the training to reflect on their experience of living with a communication disability and what accessing health care was like. All the facilitators prepared information, materials and key messages to convey to the healthcare staff in the interactive conversation sessions.

How has the patient experience been improved?

The doctors and nurses reflected on the value of the training and learning directly from people with communication disability. They reported an improvement in their skills and confidence communicating with people with aphasia after the training. Self perceived skills improved from an average 3.6/10 to 7.4/10 and confidence improved from 3.6/10 to 7.4/10.

Feedback from participants stated that the *training was* ***"very practical, with useful tips good to practice with real patients"*** and it ***"built confidence in a practical way for a very common situation"*** Overall ***"communication is the main ingredient in healthcare. All staff who work with patients with aphasia need to attend this workshop"***

After the workshop the co-facilitators participated in a debriefing session with a speech pathologist. All facilitators reflected on the value of meeting the doctors/nurses and teaching them about aphasia. They described feeling empowered to improve the patient experience of other people with aphasia. The key messages they had for the doctors and nurses were ***"Talk directly to me – not to my husband/partner", "Everyone's aphasia is different – treat us as individuals" "go slow, don't rush me"*** *and* ***" Living with aphasia is tiring, be patient with me"***

Based on the success of this program, the Speech Pathology department plans to employ people with communication disabilities in a wider roll out of supported conversation training opportunities to other staff across Austin Health.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: Reviewing the Health Independence Program (HIP) Central Phone Number Voice Message and Options
Ward/Dept/Service Area: Health Independence Program
Project Team Members' Names & Roles*:* Phuong Phan (Team Leader Community Rehabilitation Services), Jo Bombos (Administration Manager)

What did your project set out to achieve?
Our central phone number is often the first point of contact our consumers have with 17 of our HIP teams. We wanted to re-record a voice messaging service that is clear and engaging to the caller, and directs them to the correct team straight away.

How were consumers involved?
Consumers provided us with feedback that the old voice message was too long, not engaging and needed to be more natural and cheerful. They also fed back that the options provided made it difficult to know which number to press for which team. We workshopped with a consumer the message scripts and options and tested some case scenarios. From this we were able to develop new messages and a better flow of options to press. We then recorded the new messages with 4 different voices from team, and played them to consumers for feedback. The consumers overwhelmingly chose a favourite voice, which is now the voice that is heard when they call our central number.

How has the patient experience been improved?
When calling the central HIP number to access one of our 17 teams, consumers are now hearing a warm, inviting and engaging message with options that are clear to direct them to the correct team. Some comments regarding the new voice message are "the voice is very smooth", "I know which option to press now", "it's great that there is always a real person at the end of the phone".

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: **A New Social Aphasia Support Group*: Transition of the Austin Aphasia Integration Program into the Community***

Ward/Dept/Service Area: ***Rehabilitation Services, Health Independence Program***

Project Team Members' Names & Roles: ***Emma Burns and Lauren Kovesy (Speech Pathology), Sharon Bard and Birgitte Thoelen (Community Integration and Leisure) and Phuong Phan (Team Leader)***

What did your project set out to achieve (the aim)?

Our program set out to support people living with aphasia (a communication disability_) to build social relationships, communication confidence, and help them to establish a social support network in the community. 12 people with chronic aphasia participated in a speech pathologist-led multidisciplinary group program at Royal Talbot. The program commenced with an eight week intensive group made of conversation, technology, music, art and leisure activities followed by a four week transition and integration program. During the program the group members identified that they wanted to continue to meet once the program finished. Therefore, the staff involved helped them to source a new location, visit the new facility as a group and coordinate a time that would suit all members to meet in future.

How were consumers involved?

The group members and their families were involved in shaping the group program in several ways, they participated in:

• Individual interviews at the start and end of the program to discuss their goals and expectations of the group, give feedback on the value of the program and make suggestions for improvement;

• Facilitated focus group discussions regarding what parts they enjoyed, and their perceived value of meeting as a group; and

• Collaborative group discussion and problem solving to consolidate the groups desire to meet outside Royal Talbot and to establish how the group might run.

How has the patient experience been improved?

All group members and their family members reflected on the value of participating in the group program. The group members achieved the majority of the goals they set in the group and have started exploring new activities in the community. The focus groups revealed that the group members enjoyed the variety of activities that helped their communication, including conversation, games, art, quizzes , and singing. They also learnt about activities and services they could try in the community. They particularly enjoyed doing these activities with other people with aphasia, because they "***understand what it feels like***". They enjoyed "***learning about aphasia together***", learning that "***everyone's aphasia is different***", and valued the "***fellowship of being able to share each others problems***". They reflected that the group helped them ***"to feel positive about the future."***

Upon completion of the program the group members, with assistance from the Speech Pathology and Community Integration and Leisure department have started their own social aphasia support group at a local community centre. The first meeting of the new Aphasia Support Group will be held at the Stroke HUB in Kew on the 9th of September. Based on the success of this years program, the Health Independence Program plans to run another 12 week aphasia integration group program in 2017.

"He doesn't seem as frustrated since the group started. I don't think he realized there was other people like him out there. He loves to look back over the photos and share them with others."

- Feedback from a carer August 2016

Austin Health

CONSUMER ENGAGEMENT AWARD

***Title of Project**: Patient Centred Care Education*

***Departments**: Centre for Patient Experience & Clinical Education Unit*

***Project Team:** Patient Centred Care Toolkit working group & Robert LoPresti – Director Clinical Education Unit, Kimberly Haines – Allied Health Clinical Education Lead, Renee Chmielewski – Consumer Engagement Manager, Bernadette Vandenberg – Consumer Experience and Engagement Officer.*

Aim

Following the endorsement of the Austin Health Patient Centred Care Principles, a working group was established to create easily accessible tools to enable staff to improve the patients' experience. The Patient Centred Care Learning Package includes patient stories and staff tips. Staff then make a pledge to improve their care. Staff pledges becomes an objective for their annual Performance Review (PRD). The tools in the kit support staff to meet their pledge. Tools include policies, guidelines, links to training videos, most current research and patient stories. This resource aims to enhance all Austin Health patients' experiences.

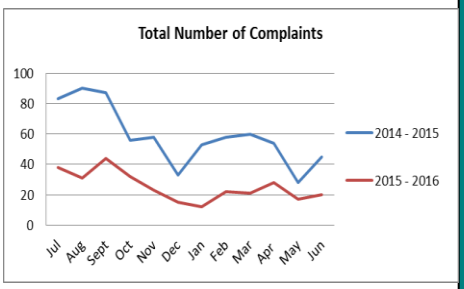
A consumer representative was an active member of the working group. Past patients provided stories for inclusion in the tool kit and tell their stories in the learning package. These are some of their statements :

Avril (Patient) – "*If you really want to work at this hospital, you've got to genuinely care for the people you are looking after*.'

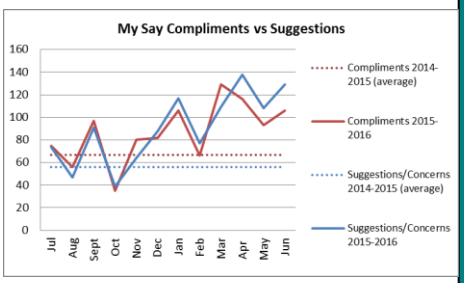
Kathy (Consumer Representative) - " *You can make the difference between a good and a bad patient experience*."

Outcomes

The Patient Centred Care Toolkit has been viewed 1,420 times between 'Go Live' in 1 October 2015 and 30 June 2016. 112 pledges have been made by staff between 25 May and 31 July 2016. Three phased evaluation of the package will be implemented focusing on review of the tool itself, monitoring of staff pledges and integration of pledges into the PRD cycle.



Pledge: '*I will ensure I give all patients the time they need to explain what they want from their admission. Help explain procedures and alleviate their fears, empower patients to take control of their care, and give the necessary support for their goals to be achieved*.'



Number of complaints and compliments are monitored for impact to consumers.

Austin Health

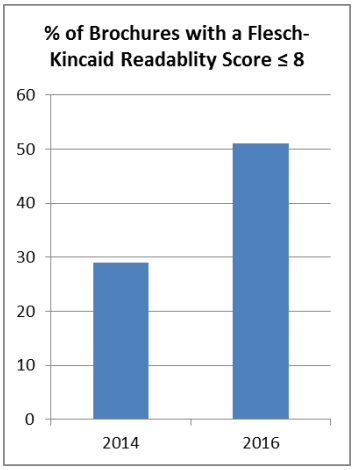
CONSUMER ENGAGEMENT AWARD

***Title of Project**: Plain English Coaching.*
***Service Area**: Information for Consumer Committee*
***Project Team** : Helen Robertson, Kathy Oswin, Shauna Poole, Maria Maggio De Leo, Norma Ward, Emily Lynch, Bernadette Vandenberg*

Project Aim:
Patients frequently say "*When I am feeling sick – less is more on a brochure*". The Information for Consumer Committee aimed to make Austin Health's patient information brochures more understandable, with a Flesch-Kincaid readability score between 6 and 8.

How were consumers involved?
An audit of 100 Austin Health brochures identified concerns with the level of readability of the brochures. Two Consumer Representative members of the Information for Consumers Committee together with the staff developed the expectations for patient information brochures. Plain English Coaching was created; including plain English theory sessions, workshops and resources. A consumer assisted with the development of the resources and co-presents the theory and workshop sessions.

Outcomes:



Staff evaluation:

'These sessions were very well run, validated the importance of health literacy, with good practical stuff. Thanks.'

"Loved the exercises and activities, all the tips were very useful – Thank you'

Austin Health

CONSUMER ENGAGEMENT AWARD

Title: **Partnering with patients to contribute to student feedback**
Service Area: **Spinal Rehabilitation, Physiotherapy**
Project Team Members: **Spinal Rehab Facility patients, Mel Kotze (PT)**

What did your project set out to achieve?

Develop a collaborative model for student assessment where patients contribute to feedback in order to:

- Increase the patient voice when working with students
- Improve patient and student communication
- Reduce patient frustration related to receiving treatment from a student
- Teach students about patient-centred care

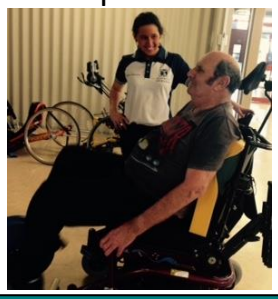
How were consumers involved?

Patients worked with physiotherapy staff to develop the model. They tested it with students during their 2015 placements and contributed to the evaluation of the model.

Patients who agree to work with students give structured feedback at the half way and end of student placements. They rate four aspects of the student's performance:

1. Ability to communicate
2. Ability to ensure patient safety
3. Ability to deliver appropriate information
4. Whether the student is addressing the patient's goals

Patients choose whether to give feedback directly to students themselves or via supervising physiotherapist



How has the patient experience been improved?

The collaborative model improved communication between patients and students, reduced patient frustration and provided useful feedback to students. All patients involved said they felt comfortable providing positive and negative feedback and most thought it helped the students to learn.

"Giving feedback to students is a great idea. It helped me and the student to think more about my goals" (Patient)

"I learned it's important to have a more open conversation with patients about how they prefer to learn and to keep this conversation going throughout your sessions" (Student)

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: 'The Cottage Garden Project'
Ward/Dept/Service Area: Epping Dialysis Unit
Project Team Members' Names & Roles:
Katina Aspridis, Nurse Unit Manager; Chris Hogan, Ward Clerk

What did your project set out to achieve (the aim)?
Create a Cottage Garden to provide a common area for all that would:

- optimise patient/staff relationships
- acknowledge patients are the 'subject matter experts'
- empower patients
- encourage patients' ownership of the Cottage Garden.

How were consumers involved? (ie: focus group, working party, steering committee member, surveyed, interviewed, etc)


Courtyard 'Before' - 2010

Steven Wells presented the Garden Project idea to the NUM group in July 2010. EDU patients and staff were surveyed about implementing the project in the EDU courtyard space in October 2010.
Staff kicked off the project with a $5 donation each, and Bunnings also made a donation.
Patients donated vegie plants and skills!

How has the patient experience been improved?

The new Cottage Garden has:

- increased patient (and staff!) satisfaction
- helped to humanise the Dialysis experience
- enhanced the patient/nurse relationship
- begun to provide vegetables and herbs
- made a garden space for all to enjoy.


Courtyard 'After' – 2016

Our patients say: "… A lovely area to relax in before and after Dialysis."

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project:	**After Hours Spinal Gym**
Service Area:	**Spinal Rehabilitation**
Team Members:	Mark McDonald (PT), Mel Gregory (PT), Bryn Fittall (EP), Michelle Marriner (OT), Brynn Lewin (OT)

***Aim*:** To gain approval to open the spinal therapy gym on the weekend for the patients to exercise when staff are not present

Consumers expressed their reasons for wanting an after hours gym:

1. To provide more opportunity for spinal inpatients to exercise
2. To open the spinal therapy gym on the weekend
3. To make the exercise equipment more available
4. To allow the patients to exercise in the gym using the equipment *without any staff in attendance*

They also said:

- Their weekends are miserable without anything to do
- They feel worse Monday because they've been sedentary all weekend

Since its inception on 28th May the after hours gym has been open on 12 Saturdays with over 70 recorded attendances.

How has the patient experience been improved?

Consumer quotes

'It gives me something to do on the weekends.'
'I have the freedom to exercise when I want.'
'It helps me *mentally*.'

Recently consumers asked for the gym to be open on Sundays. The After Hours spinal gym is **now open on Saturdays and Sundays**.

Austin Health

CONSUMER ENGAGEMENT AWARD

***Title of Project* :"Bringing simulation to life":** Volunteer Simulated Patient Program
Ward/Dept/Area: Simulation Centre, Clinical Education Unit (CEU), Austin Health
Project Team Members' Names & Roles: Robyn Purcell (Simulation Educator), Kimberley Haines (Allied Health Education Lead CEU), Robert LoPresti (Director CEU)

What did your project set out to achieve (the aim)?

The Volunteer Simulated Patient Program was initiated to engage **volunteers** to simulate (act out) being a **patient** or a **family member** with the aim of working with us in simulation education for Austin Health staff and healthcare students.
Simulation in education is a representation of the real world to achieve educational goals through experiential learning. It replicates clinical situations in a controlled environment and provides a powerful learning opportunity for learners to develop skills in areas such as clinical care and **communication**.

How were consumers involved?

With the assistance of the Consumer Experience & Engagement Officer, two volunteers were recruited and trained. This process included i) an interview to gauge suitability to the role and to fully explain the process ii) attendance at a half-day training and orientation program (which included sessions on how to: role play, provide effective feedback and to focus on patient centred care) and iii) coaching and support by education staff before, during and after the individual Simulation activities.

How has the patient experience been improved?

The Volunteer Simulated Patients add value to our education sessions by providing a consumer or "real person" perspective to our scenarios. It is an excellent way of teaching learners to communicate effectively, gain an understanding of the patient and family perspective and develop advanced interpersonal skills, such as difficult conversations where the opportunity in the clinical environment might be limited. The flow on effect is that it ***improves the safety and quality of healthcare delivery for our patients.***

Learner feedback : *"The volunteers give excellent feedback, particularly around your communication and bedside manner."*

Volunteer feedback: *"Thanks so much for your kind words and encouragement. You were so friendly and relaxed and that made my task so much easier. It was a great learning experience for me and I look forward to working with you again."*

Austin Health

CONSUMER ENGAGEMENT AWARD

Improving access to care for Austin Health Home Enteral Nutrition (HEN) patients

Department: Nutrition and Dietetics
Personnel: Caitlyn Green (Project Coordinator), Kate Hamilton (Project Officer), Tobi Erickson (HEN Dietitian), Dr Rhys Vaughan (Dept of Gastroenterology), Leonie Pearce (Manager, Nutrition & Dietetics)

What did your project set out to achieve?

This project aimed to develop a standardised care pathway to streamline and improve access to care for patients with gastrostomy tubes. Preliminary data showed that patients on the Home Enteral Nutrition (HEN) program experienced prolonged waits in the Emergency Department and were subject to a complex and fragmented system when seeking assistance with management of their feeding tube.

How were consumers involved?

Consumers were involved at all stages of this project. A baseline consumer survey was conducted and this indicated that 27% of patients on the HEN program were dissatisfied with the service they received when complications arose with their feeding tube. A consumer representative was recruited as a member of the project steering committee and attended regular meetings, where they provided feedback on the care pathway and newly developed education materials. Consumer involvement enabled us to ensure that the instructions provided to patients were clear and easy to follow. A post implementation survey was sent to all users of the new pathway to determine if the patient experience was improved.

How has the patient experience been improved?

A standardised multi-disciplinary care pathway has been developed for the management of Austin Health patients with gastrostomy tubes. A fortnightly HEN clinic has been established, which is staffed by advanced practice dietitians who are credentialed to care for and replace balloon gastrostomy tubes. This clinic serves as a single point of contact for patients, where their care is streamlined and co-ordinated. The credentialed dietitians also provide a 5 day a week phone service to troubleshoot and enable timely access to care should complications arise. Consumer feedback regarding the newly implemented service model has been overwhelmingly positive – with 100% consumers reporting satisfaction with the new model and reporting that the clinic meets all of their needs.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: *People 's preferences for ongoing exercise programs.*
Ward/Dept/Service Area: *Health Independence Program (HIP) Rehabilitation Services/ Physiotherapy team.*
Project Team Members' Names & Roles: *Jannette Blennerhassett, Tom Cooper and Ali Logan. Physiotherapists.*

What did your project set out to achieve (the aim)?
Although exercise can promote recovery and wellbeing, people can find it challenging to stick with an ongoing exercise program. Our aim was to see if asking consumers about their preferences and possible barriers to exercise could help to design exercise programs during community rehabilitation.

How were consumers involved?
Physiotherapists asked 41 consumers about their preferences (e.g. level of supervision, venue, type of exercise and social support) and potential barriers (e.g. safety concerns, costs, access) for exercise programmes. The process promoted a two-way conversation about suitable exercise options and ways to overcome perceived barriers. In particular, it helped clarify wishes, and address areas of concern and knowledge gaps.

How has the patient experience been improved?
All consumers considered the structured interview was valuable as it promoted active involvement and decision making in their care. This may have encouraged consumers to exercise for their recovery and well-being.

For the 13 physios, the project highlighted the value of listening to the person's choices and concerns, and to collaborate when designing an exercise program. These reflections should promote consumer engagement by physiotherapists during community rehabilitation. In addition, the structured questionnaire is available for ongoing use to help partner with consumers when suggesting suitable exercise programs.

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: Cognitive Dementia and Memory Service (CDAMS) Information Session
Ward/Dept/Service Area: HIP CDAMS
Project Team Members' Names & Roles: CDAMS Team

What did your project set out to achieve)?

CDAMS Information Sessions are run 4 times a year to provide support and education to people caring for someone diagnosed with dementia. The participants were consumers who had been through CDAMS. Presenters were from Neuropsychologist, Alzheimer's Australia Victoria and Commonwealth Carers Respite Centre

How were consumers involved?

Evaluations were filled in by the participants to identify if the needs were being met by the session; looking at the content , structure as well as to compare their pre and post session understanding of disease process, supports and services discussed.

Feedback on the whole was positive, some changes to the format were made in response to ***'what if I can't manage to keep him at home?'*** by the addition of a presentation by Aged Care Assessment Service.

Something which was unexpected was ***"I wish I had had this opportunity then"*** from those who had experienced caring for someone with Dementia previously . From this is was decided to expand the access to include all Austin Health consumers. This was achieved through communication across Austin Health , including HIP and other Aged Care Clinics and Wards to advise, describe, and invite them to include this in their plan of care for suitable patients and their families.

How has the patient experience been improved?

60 participants attended the Information Sessions across 2015. In each of there were consumers who were referred from services other than CDAMS. ***" The chance to talk to someone who just knows what it's like, was wonderful"***

Austin Health

CONSUMER ENGAGEMENT AWARD

Title of Project: *Model of Care (Nursing)*
Service Area: *Nursing*
Project Team Members' Names & Roles*: Models of Care Working Party, Nonie Rickard and Kath Baylie*

What did your project set out to achieve?
To provide patient centred environment which involved the patient and their carers in their care planning. To utilise the nurses, skills, knowledge and experience in the most patient centred, cost effective manner.

How were consumers involved?
8 consumers (patients and/or families) were interviewed about their experience of each ward prior to making any changes to the Nursing model of care: including communication, involvement in care, promptness in answering call bells, positive aspect of the nurses along with suggestions for improvement. A consumer representative completed the interviews to encourage open and honest feedback. The feedback was included in the ward education sessions to inform the changes in model of nursing care deliver.

Most patients were considerate of the demands on the nurses' time and acknowledged their workload was high. Although reported "*It is a waiting game*" when waiting for call bells to be answered.

How has the patient experience been improved?
Hybrid models of Allocation and/or Team Nursing have been implemented through the organisation with raised awareness and commitment to:

- Nurse Rounding
- Improved delegation and supervision of GNY and EN's
- Allocation of nurse buddies for meal breaks
- Bedside handover with patient and family involvement.

The following feedback was received after the changes were implemented:

"I am surprised they are always available, very good, always comfortable to ask for help, encourage to have a shower to help always cared for."