Research Week 2016
First in research means best in care
Welcome to Research Week 2016

This year promises to be exciting offering more workshops, seminars and presentations. We received an impressive 224 abstracts for consideration, the highest number ever and clearly our research collaborations extend beyond that of the local academic community, universities, and medical research institutes to hospitals and institutions internationally.

The diverse project topics reflect our place in the research arena as a representative of the health concerns of the community we serve. All areas and disciplines are research active and this shows in the breadth of the presentations – endocrine disorders, cancers, physiotherapy, neurological conditions, mental health, infection and immunity, aged care, surgery, anaesthesia and pain management, nutrition, nephrology, palliative care, genomics and more.

I welcome our allied health Honorary Research Fellows from La Trobe University, Drs Mary Whiteside, Karl Landorf and Michael Dillon, who have pulled together the “Article critique workshop” and I encourage all clinicians to consider this event in their Research Week calendar.

In addition, our colleagues over at the University of Melbourne School of Population and Global Health are crossing the road to explain the nuances of designing economic evaluation in clinical research. The Office for Research is conducting an information session at Royal Park Campus on conducting research at Melbourne Health.

Other workshops and sessions include:
- Research Symposium – sessions on Friday, Saturday and Monday
- Study design and basic epidemiological and statistical concepts (page 5)
- Data management and analysis (page 6)
- Feasibility in clinical trials workshop (page 6)
- Approaching trusts, foundations, corporates and the community for funding (page 7)
- The University of Melbourne (RMH) Scholarly Selective students presenting their projects (page 8)

I cannot forgo mentioning the return of The Great Debate and this year’s moot, “Research is good for your health” seems to have inspired respective panel members to defend their argument at the expense of ... themselves?

I would like to thank the efforts of those involved in reviewing abstracts and posters and the session chairs during Research Week. Your time and expertise is greatly appreciated. I would also like to thank the Research Week Committee for compiling an exciting program and for all the work that goes into making this event such a success.

Research Week is for you: to learn, to engage and to enjoy.
Thank you

Professor Ingrid Winship
Executive Director Research

Research Week Committee 2016
Professor Ingrid Winship (Chair)
Ms Angela Bragato
Dr Bruce Campbell
Ms Alex Gorelik
Ms Ishani Hewage

Ms Angela Magira
Associate Professor Andrea Maier
Dr Emma O’Brien
Professor Terry O’Brien
Dr Angela Watt
Thursday 16 June 2016

Opening plenary

1.00 – 1.45 pm, Charles La Trobe Lecture Theatre, Function Centre, RMH
(Lunch at 12.30 pm)

Opening:  Professor Ingrid Winship, Executive Director Research, Melbourne Health
Invited Speaker:  Professor Jonathan Kalman, Director of Cardiac Electrophysiology, The Royal Melbourne Hospital

Mechanisms of atrial arrhythmias – from the simple to the complex.
Implications for treatment and prevention

Friday 17 June 2016

Research symposium

CONCURRENT SESSIONS: 9.15 – 10.15 AM

Infection and Immunity

Seminar Room 1  Chair: Professor Joe Sasadeusz
1 Dustin Flanagan, Postdoctoral researcher, UoM
The role of Frizzled-7 in gastric tumourigenesis.
2 Elizabeth Aitken, Dept of Medicine (RMH), UoM
Adipose tissue and Plasmodium
3 James Fielding, Epidemiologist, MH
Effectiveness of seasonal influenza vaccine in Australia, 2015: an epidemiological, antigenic and phylogenetic assessment
4 Katie Dale, Epidemiologist, Victorian Tuberculosis Program
Recurrence of tuberculosis in a low-incidence setting without Directly Observed Treatment (DOT): Victoria, 2002-2014
5 Cathryn Haigh, Senior Research Fellow, UoM
Three-dimensional cultures of murine neurones demonstrate prion-induced plaque pathology and cell death

Cancer

Seminar Room 2  Chair: Professor Geoffrey Lindeman
6 Chia Sharpe, PhD Student, ACRF Translational Research Lab
Can emerging drug therapies be combined with immunotherapies to improve the treatment of CLL?
7 Edmond Kwan, Medical Oncology Fellow, RMH
Use & impact of bevacizumab in patients undergoing liver resection for metastatic colorectal cancer in routine clinical practice
8 Ashleigh Poh, Postgraduate Student (PhD), WEHI
Hck activity in myeloid cells promotes colorectal cancer progression
9 Kenneth Elder, Research Fellow, RWH & RMH
Treatment intensity differences in screen-detected and community-detected early stage breast cancer (ESBC)
10 Thenugaa Sritharan, Intern, Austin Health
Long-term post-operative health-related quality of life in low-grade glioma, meningioma and acoustic neuroma

Brain & Mind

Charles La Trobe Lecture Theatre  Chair: Professor Andrew Chanen
11 Sarah Farrand, Neuropsychiatry Registrar, RMH
Deep brain stimulation for severe treatment-resistant OCD: The initial Australian experience
12 Bridgette Semple, Research Fellow, UoM
Traumatic brain injury in paediatric mice results in sex-dependent social behaviour deficits and aberrant neuronal morphology
13 Pablo Casillas-Espinosa, PhD student, UoM
Anti-epileptogenic effects of the novel T-type calcium channel blocker Z944 in the post-status epilepticus model of temporal lobe epilepsy
14 Tomas Kalincik, Senior Research Fellow, UoM & RMH
Prediction of Individual Response to 10 Immunomodulatory Therapies in Multiple Sclerosis: A global observational cohort study
15 Nathaniel Lizak, Research Assoc & Med Student, RMH & UoM
Immunomodulatory therapy slows accumulation of disability in moderately advanced multiple sclerosis
CONCURRENT SESSIONS: 10.30 – 11.30 AM

Genetics
Seminar Room 1
Chair: Professor Ingrid Winship

16 Emma Nolan, PhD student, WEHI of Medical Research
   RANK ligand as a target for breast cancer prevention in BRCA1 mutation carriers

17 Dominica Zentner, Cardiologist, RMH
   Long-term impact of the Cardiacgenetics clinic: a retrospective audit of patient recall and compliance

18 Paul James, Clinical Geneticist, RMH
   The advent of gene panel testing: has it changed the outcome of mutation detection gene testing in a cardiac genetics clinic?

19 Gita Vita Soraya, PhD Student, Dept of Medicine (RMH), UoM
   Ultrasensitive interdigitated capacitance sensors for rapid and high-resolution HLA-B allele typing for applications in personalized medicine

20 Kevin Chow, Nephrologist, MH
   CCR2+ inflammatory monocyte derived dendritic cells contribute to early graft dysfunction of mhc mismatched islet transplants

Emergency & Critical Care
Seminar Room 2
Chair: Professor Andrew Kaye

21 Jonathan Knott, Director of Emergency Research, MH
   Clinical impact of a high-sensitivity troponin assay introduction on patients presenting to the Emergency Department

22 Neha Kaul, Neurosciences Dietitian, MH
   Improvements in nutrition therapy to critically ill patients at RMH; Results from the ‘International Nutrition Survey’

23 Mark Tacey, Biostatistician, MH
   Identification of frequent presenters to the Emergency Dept at Royal Melbourne Hospital and their associated risk factors

24 Camila Battistuzzo, Postdoc Fellow, Dept of Med (RMH), UoM
   Early decompression following cervical spinal cord injury: examining the process of care from accident scene to surgery in Australia and New Zealand

25 Teddy Wu, Stroke Research Fellow, Royal Melbourne Hospital
   The natural history of peri-haematoma oedema and impact on outcome after intracerebral haemorrhage - data derived from the Helsinki intracerebral haemorrhage study

General Medicine
Charles La Trobe Lecture Theatre
Chair: Professor David Russell

26 Andrea Maier, Professorial Fellow, MH
   Assessment of health status by molecular measures in middle-aged to old persons, ready for clinical use?

27 Asvini Subasinghe, Research fellow, MCRI
   Strong relationship between high sensitivity C-reactive protein and prehypertension in 16-25 year old Australian females

28 Spiros Fourlanos, Diabetes and Endocrinology, RMH
   Impact of overnight closed loop (OCL) at home compared to sensor augmented pump with low glucose suspend (SAP-LGS) improves time in target range in adults and reduces hypoglycaemia in adolescents

29 Emma Callegari, PhD Student, UoM, Dept of Medicine
   Associations between vitamin D status, other determinants of bone health and tibial pQCT variables in young Australian women: the Safe-D study

30 Robert Stolz, Scholarly Selective Student
   Use of cable-driven treadmill gait-trainers for patients post-stroke within an intensive inpatient neurorehabilitation program to improve mobility: a randomized controlled trial

Poster Viewing Session
See abstract numbers 40 – 187

Friday 17 June 2016
11:45am to 12:45pm
Function Centre, The Royal Melbourne Hospital
Friday 17 June 2016

The Great Debate 2016

Research is good for your health

The angelic and hallowed “Affirmative” team highlight the significant benefits of clinical research to our patients, our researchers, our institution, our famous Parkville precinct, our economy, our nation, the world, life as we know it!

Prof Jo Douglass –
A.Prof Louisa Ng –
Prof Dennis Velakoulis –

The prophets of doom, the “Negative” team, will be cautioning us against being too enthusiastic about research, pointing us to the dark side that lurks behind the happy façade that research presents to the world

~ Dr Dominica Zentner
~ A.Prof David Smallwood
~ Prof Andrew Roberts

Distinguished Judges
Dr Gareth Goodier
Professor Andrea Maier
Professor Kate Drummond
MC
Professor Ingrid Winship

Join us for this most auspicious event, the highlight of each year’s Research week, for some light-hearted banter with just a hint of sensibility and educational value

Charles La Trobe Lecture Theatre
Friday, 17 June 2016 – 1:00pm to 2:00pm

Saturday 18 June 2016

Research symposium

Surgical Research Forum

8.30 – 9.30 am, Ewing Lecture Theatre, Level 5, Clinical Sciences Building

Chair: Professor Andrew Kaye, Head of University Department of Surgery and Director of Department of Neurosurgery, The Royal Melbourne Hospital

31 Marie Parsons, PhD Candidate, WEHI of Medical Research
Genomics study to identify novel cancer genes predictive for prognosis and 5-FU benefit and utility in stage II/III colorectal cancer

32 Andrew Gogos, Neurosurgical Registrar and PhD Student, RMH, Dept of Surgery (RMH) and the WEHI
Genetic and pharmacological disruption of YAP signaling impairs glioma cell growth and differentiation.

33 Ruth Mitchell, Neurosurgery Registrar, RMH
The structure and function of the EGF Receptor in Glioblastoma Multiforme

34 Chenkai Ma, PhD student, RMH
A comprehensive meta-analysis shows circulating MIRNAS in gliomas as potential diagnostic biomarkers
Monday 20 June 2016

Study designs and basic epidemiological and statistical concepts

9.00 am – 12.00 pm, Seminar Room 1, Function Centre, RMH

Ms Alex Gorelik, Senior Statistician, Melbourne EpiCentre, Melbourne Health

This half day workshop will provide an overview of different study designs, confounders, randomisation process, and different options for sample size calculations/power analysis. Participants will also gain some theoretical knowledge regarding data collection and data management in research, available data sources, basic statistical concepts and the main statistical tests used in clinical research.

Registration
Register via EventBrite at: https://www.thermh.org.au/events/how-conduct-small-clinical-studies

Research symposium

1.00 pm – 2.00 pm, Seminar Room 2, Function Centre, RMH

Neuroscience Research

Chair: Professor Stephen Davis, Director of Neurosciences, The Royal Melbourne Hospital

35 Vilija Jokubaitis, Research Fellow, UoM, Pregnancy protects against long-term disability accrual in relapsing-remitting MS

36 Bruce Campbell, Neurologist, RMH, CT perfusion imaging profiles and response to endovascular reperfusion in pooled analysis of randomized trials of endovascular stent thrombectomy

37 Chris French, Neurologist, RMH, How do drugs cause seizures as side effects?

38 Ariel Dahan, Medical Intern, Ballarat Health Services, Can semiautomated imaging software allow junior medical and radiology staff to monitor multiple sclerosis disease progression as well as neuroradiologists?

39 Chris Lim, Hospital Medical Officer, MH, Risk factors for contact lens-related microbial keratitis in Singapore

Article critique workshop – developing your appraisal skills

2.00 pm – 4.00 pm, Seminar Room 1, Function and Convention Centre, RMH

Dr Michael Dillon, Honorary Research Fellow, The Royal Melbourne Hospital; Senior Lecturer in Prosthetics and Orthotics, La Trobe University

It is important that clinicians develop the critical appraisal skills necessary to identify sources of bias and thereby be able to identify the best available evidence to inform treatment practices. In this way, knowledgeable consumers of the peer reviewed literature can decide for themselves how good the evidence is and the extent to which they can depend on the conclusions which have been drawn.

What is the workshop about?
This workshop aims to further develop the ability of allied health clinicians to critically evaluate the peer reviewed literature and make informed decisions about the extent to which the conclusions should inform practice.

Queries?
Dr Michael Dillon, ph: 9479 5889, email: Michael.Dillon@mh.org.au

Registration
Register via EventBrite at: https://www.thermh.org.au/events/critical-appraisal-professional-literature-allied-health
Tuesday 21 June 2016

Data management & analysis using Microsoft Excel

9.00 am – 12.00 pm, Computer Lab, The RMH Library

Ms Alex Gorelik, Senior Statistician, Melbourne EpiCentre, Melbourne Health

This practical workshop will be dedicated to data management and analysis using Excel. Participants will learn how to manage data, how to use Excel formulas to create new variables and calculate basic statistics. They will also learn how to perform sample size calculations and basic statistical tests (e.g. t-test, chi2) in Excel. Participants will be given some useful tips and tricks.

Registration

Designing economic evaluation alongside clinical studies

1.00 pm – 2.00 pm, Charles La Trobe Lecture Theatre, Function Centre, RMH

Dr Kim Dalziel. Senior Research Fellow and McKenzie Fellow, Health Economics Group, Centre for Health Policy, Melbourne School of Population and Global Health, The University of Melbourne

This seminar will provide an overview of cost-effectiveness analysis and examples of economic evaluations that have been conducted of clinical studies. Practical information on methods for prospectively collecting costs and outcomes data through administrative data linkage and patient surveys will be provided. It will also explain the techniques used to analyse economic data and illustrate this through examples.

Content overview:

» An introduction to economic evaluation
» Methods to assess quality of life and input of clinical outcomes in cost-effectiveness analysis
» Collecting relevant cost data
» Extrapolation, modelling and capturing uncertainty
» Economic evaluation reporting standards

Registration
Registration is required for this session as places are limited.

Wednesday 22 June 2016

Feasibility best practice for commercially sponsored clinical trials

12.00 pm – 1.00 pm, Seminar Room 1, Function Centre, RMH

Mr Richard Verrelli, Clinical Research Manager, Office for Research, Melbourne Health

With resources at a premium and increasing expectations from sponsors with respect to patient accrual, it is vital that researchers and coordinators get the feasibility process right to ensure we set ourselves up for success.

This workshop aims to:

» explore the challenges and pitfalls of conducting feasibility review for sponsored clinical trials
» review the trends at an institutional-level
» provide guidance and specific tools to ensure that review is thorough, considered and objective rather than an arbitrary “guesstimate”

This session is targeted to study coordinators and investigators who have experience in conducting commercially sponsored research projects, or have aspirations to become involved in this area.

Registration
Approaching trusts, foundations, corporates and the community for funding

1.00 pm to 2.00 pm, Seminar Room 2, Function Centre, RMH

Presenters
Matthew Clayton, Foundation Manager, RMH Foundation
Alison Byrne, Senior Partnerships Manager, RMH Foundation
Gareth Scott, Community Relationships Manager, RMH Foundation

Putting together submissions to Trusts and Foundations is often a very different process, than applying to purely research related organisations such as the NHMRC. In this session the Royal Melbourne Hospital Foundation will go through the different ways to approach these organisations, with some tips, tricks and a look at different funding opportunities and how the RMH Foundation can assist with this process. This session will also look at how the Foundation works to seek support from Corporate and Community donors to also assist with research related activity.

Registration
Register via EventBrite at: https://www.thermh.org.au/events/how-apply-funding-trusts-and-foundations

“Ask the Office for Research” forum at Royal Park

2.00 pm – 3.00 pm, HEC Building 3, RMH Royal Park Campus

Panel
Angela Watt, Director Research Governance and Ethics
Richard Verrelli, Clinical Research Manager
Angela Magira, Manager – Office for Research
Ila Karve, ReX Research Support Officer
Angela Bragato & Jessica Savage, Assistant Managers Research Integrity & Ethics

» Are you part of a team running clinical research projects?
» Are you interested in conducting research at Melbourne Health but don’t know where to start?

The Office for Research invites you to an “Ask the Office for Research” forum. Members of the team and a couple of our valuable associates will provide an overview of their responsibilities and discuss some of the most frequently asked questions received concerning ethics, governance, costings and grant applications.

This session is highly recommended for all investigators and research coordinators who will be submitting for ethics and/or governance applications as well as those who may have general questions about conducting research at Melbourne Health.

Registration
Register via EventBrite at: https://www.thermh.org.au/events/ask-office-research
Thursday 23 June 2016

University of Melbourne (RMH) scholarly selective project presentations

8.55 am – 12.00 pm, Charles La Trobe Lecture Theatre, Function Centre, RMH

Chair: **Professor Terry O’Brien**, *James Stewart Professor of Medicine, Department of Medicine, The University of Melbourne*

1st Session – 9.00 am to 10.15 am

188 **Katherine Darch**, *Dermatology*
Investigating the correlation between ion channels and receptors that detect irritants, and itchy, inflammatory skin conditions.

189 **Oliver Stewart**, *Anaesthetics*
A randomised controlled trial comparing fibreoptic-guided tracheal intubation through two supraglottic devices: Ambu Auragain LMA and LMA Fastrach

190 **Wai Hoe Alex Yow**, *Psychiatry*
Non-clozapine antipsychotic combinations for treatment resistant schizophrenia: a Cochrane systematic review

191 **Benjamin Sutu**, *Music Therapy*
Exploring the use and uptake of non-pharmacological methods for chronic pain management: From a patient and clinician perspective

192 **Jessica Cassells**, *Gastroenterology*
Abnormal liver function tests develop despite treatment with a gluten free diet in coeliac disease

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**MORNING TEA: 10.15 – 10.45 AM**

2nd Session – 10.45 am to 11.45 am

193 **Yi Heng Yong**, *Respiratory and Sleep Disorders*
Validation of a low fidelity 3D printed model as a tool for bronchoscopy simulation

194 **Douglas Tjandra**, *Colorectal Medicine*
A prospective study of the role of colon capsule endoscopy in the assessment of mucosal healing Crohn’s disease

195 **Arthur Thevathasan**, *Neurology*
Haemorrhagic transformation is associated with post-stroke seizures after endovascular therapy

196 **Michael Ginevra**, *Neurology*
Effect of Antipsychotic Drugs on Cognition-Related Processes in Hippocampal microcircuits; an in silico study.

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**LUNCH: 12.30 – 1.00 PM**

Closing plenary

1.00 – 2.00 pm, Charles La Trobe Lecture Theatre, Function and Convention Centre, RMH

Chair: **Professor Ingrid Winship**, *Executive Director Research*

Plenary: **Dr Charlotte Slade**, *Clinical Immunologist, Royal Melbourne Hospital; PhD Student*
Genetic diagnosis and personalised therapies for Primary Immune Deficiencies

Final presentation for Research Week followed by the annual awarding of the Research Week prizes handed out by the Executive Officer of Melbourne Health, **Dr Gareth Goodier**. Prizes will be awarded for best oral and poster presentations as well as the winner of the **Cleveland Young Investigator Award 2016**.
Abstracts

**Plenary presentation**

**Charlotte Slade**

Genetic diagnosis and personalised therapies for Primary Immune Deficiencies

SLADE C (1,2,3), Fliegauf M (4), Ameratunga R (5), Sceri T (1,2), Grimbacher B (4), Bahlo M (1,2), Douglass J (3,6), Hodgkin P (1,2), Bryant V (1,2)

1. Walter and Eliza Hall Institute 2. Department of Medical Biology, The University of Melbourne 3. Department of Clinical Immunology and Allergy, Royal Melbourne Hospital 4. Center for Chronic Immunodeficiency, University Medical Center Freiburg and University of Freiburg, Germany 5. Department of Virology and Immunology, Auckland City Hospital, New Zealand 6. Department of Medicine, The University of Melbourne.

**Aim:** To identify novel genetic aetiologies of primary immunodeficiencies via whole-exome sequencing and functional validation of variants, and to translate novel pathogenic mechanisms into improved patient management.

**Background:** Common variable immunodeficiency (CVID) is the most common primary immunodeficiency (PID), affecting at least 1:56,000 Australians. CVID is characterised by hypogammaglobulinaemia and poor antigen responses. Despite lifelong immunoglobulin replacement, patients suffer from recurrent infections, and autoimmune and malignant complications that significantly reduce their quality of life and life expectancy. The genetic causes of CVID are largely unknown and must be better understood to enable identification of improved therapies.

**Methods:** We established the Primary Immunodeficiency Donorbank in Victoria (PIDDonors Victoria), recruiting a cohort of 118 PID patients and their relatives from Royal Melbourne and Royal Children's Hospitals. 61 patients were diagnosed with CVID, 17 with PIDs, and 45 were healthy relatives. 12 families had multiple affected individuals. Initially, 4 CVID families were selected for whole-exome sequencing. Sequencing data underwent an established filtering process in order to identify the most likely disease-causing variants. Sanger sequencing was performed to confirm segregation of genotype with clinical and immunological phenotypes in families. Functional validation of novel variants was performed using our gene discovery pipeline, including: in silico predictions to determine likely pathogenic variants; analysis of gene and protein expression in patient cells; and in vitro analysis of mutant protein function via flow cytometry and immunoprecipitation, to demonstrate a causal relationship between the candidate genotype and clinical phenotype.

**Results:** We identified a disease-causing mutation in each family with important diagnostic and therapeutic implications, namely (i) identification of 3 novel CVID mutations, including the first description of NFKB1-deficiency in CVID; (ii) genetic diagnosis for a pregnant woman with diminishing Ig levels, which directed initiation of immunoglobulin replacement screening for cancers, particularly in patients with NFKB1 and NFKB2 mutations, since defects in NFKB2 are associated with gastrointestinal cancers; (iv) targeted therapies: 3 patients from one family were found to carry a pathogenic CXCR4 mutation, leading to a rediagnosis of WHIM (warts, hypogammaglobulinaemia, infections and myelokathexis) despite not fulfilling all diagnostic criteria. This prompted human papilloma virus (HPV) vaccination given their specific susceptibility to HPV-associated cancers, and potential treatment with the small molecule CXCR4 antagonist,plerixafor.

**Conclusion:** Whole-exome sequencing of patients with CVID can lead to better outcomes for patients due to more accurate diagnosis, better patient management and targeted therapies.

**Infection and Immunity**

**1. Dustin Flanagan**

The role of Frizzled-7 in gastric tumourigenesis

FLANAGAN DJ (1), Phesse TJ (1), Ernst MRW (2), Vincan E (1)

(1) University of Melbourne and VDRL, VIC, Australia (2) Olivia Newton-John Cancer Research Institute, Australia

Gastric cancer (GC) is the fourth most common cancer internationally and the second most common cause of death with a poor 5-year survival rate due to the late stage of diagnosis. Gastric cancer can be divided pathologically into two broad groups, intestinal-type and diffuse-type, as classified by the Lauren system. Of the reported genes mutated in gastric cancer, multiple components of the Wnt signalling pathway are commonly found mutated in gastric cancer. Wnt signalling is activated when Wnt ligand binds to Frizzled receptors associated with Lrp5/6 co-receptors and inhibits the formation of a cytoplasmic β-catenin degradation complex. This allows cytoplasmic β-catenin to accumulate and translocate to the nucleus, enabling gene expression. As such, we sought to determine the role of the Wnt receptor, Frizzled-7 and transcription factor c-Myc in gastric tumourigenesis.

**Methods:** We have employed conditional genetic deletion to assess the role of Fz7 in two mechanism-independent mouse models of gastric cancer that share many similarities to human intestinal-type gastric cancer. In addition, human derived gastric cancer cell lines were transfected with retro-viral constructs to probe the mechanism of Fz7 dependent cancer cell growth. Tissue and cell samples were subject to various molecular and histological assays.

**Results:** The successful deletion of Fz7 from gastric tumours significantly reduced overall in vivo tumour burden. This was accompanied by significant reductions in cell proliferation, Wnt/β-catenin target gene expression and angiogenesis. We also demonstrated reductions in tumour burden and associated decreased Wnt/β-catenin signalling was due to disrupted β-catenin transport mediated via PKC, thus effecting transcription of β-catenin target genes crucial for cell growth and proliferation. In addition, the growth of human gastric cancer cells can be influenced by Fz7 deletion or acute over-expression of Myc, suggestive of a Fz7-Myc signalling axis in human gastric cancer growth.

**Conclusions:** Our results show that Frizzled-7 is critical for transmitting Wnt signals that provide cell growth and angiogenic instructions to gastric tumours. Furthermore, we demonstrate that c-Myc is also required for tumour development and that c-Myc requires Fz7 to impart proper tumour growth.

**2. Elizabeth Aitken**

Adipose tissue and Plasmodium

ELIZABETH AITKEN (1), Daniel Fernandez Ruiz (2), Gayle Davey (2), William Heath (2) and Stephen Rogerson (1)

1. Department of Medicine (RHH); P. Doherty Institute, University of Melbourne. 2. Department of Microbiology and Immunology, P. Doherty Institute, University of Melbourne

**Aim:** Describe the adipose tissue in Plasmodium spp. infection.

**Background:** Adipose tissue has changed from being viewed as an inert energy store to a tissue which plays an active role in the regulation of the immune response. We know the parasite is present in adipose tissue however we do not know if this is accompanied in any other changes in the tissue.

**Methods:** Here we investigate how adipose tissue changes in malaria by examining adipose tissue from C57BL/6 mice infected with P. berghei ANKA by microscopy. Results: Observations of stained adipose tissue from infected mice included congested capillaries and the presence of large numbers of parasites and leukocytes. In addition the microscopy suggests the presence of crown like structures (macrophages surrounding individual adipocytes) which could indicate adipocyte death. Analysis of adipocyte size showed no difference in average size of adipocytes in infected mice compared to uninfected mice.

**Conclusion:** The appearance of adipose tissue changes dramatically with infection and the presence of parasites and leukocytes in the adipose tissue of infected animals strongly suggests for the first time that adipose tissue may play a role in malaria.

**3. James Fielding**

Effectiveness of seasonal influenza vaccine in Australia, 2015: an epidemiological, antigenic and phylogenetic assessment

FIELDING J(1,2,3), Levy A(4,5), Chihver M(6), Deng Y(7), Regan A(5,8), Grant K(1), Stocks N(6), Sullivan S(3,6,7,9)

Communicable Disease Control Directorate, Western Australia Department of Health; 9. Department of Epidemiology, Fielding School of Public Health, University of California.

Aim: To estimate effectiveness of the 2015 inactivated seasonal influenza vaccine against specific influenza virus types, subtypes, lineages and clades.

Background: A record number of laboratory-confirmed influenza cases were notified in Australia in 2015, during which type A(H3) and type B Victoria and Yamagata lineages co-circulated.

Methods: Three sentinel general practitioner networks conduct surveillance for laboratory-confirmed influenza amongst patients presenting with influenza-like illness in Australia. Data from the networks were pooled to estimate vaccine effectiveness (VE) for seasonal trivalent influenza vaccine in Australia in 2015 using the case test-negative study design.

Results: There were 2,443 eligible patients included in the study, of which 857 (35%) were influenza-positive. Thirty-three and 19% of controls and cases respectively were reported as vaccinated. Adjusted VE against all influenza was 54% (95%CI: 42, 63). Antigenic characterisation data suggested good match between vaccine and circulating strains of A(H3), however VE for A(H3) was low at 44% (95% CI: 21, 60). Phylogenetic analysis indicated most circulating virologies were from clade strain, however the clade included in the trivalent vaccine (3C,3a). VE was higher against B/Yamagata lineage influenza (71%; 95% CI: 57, 80) than B/Victoria (42%, 95% CI: 13, 61), and in younger people.

Conclusions: Overall seasonal vaccine was protective against influenza infection in Australia in 2015. Higher VE against the B/Yamagata lineage included in the trivalent vaccine suggests that more widespread use of quadrivalent vaccine could have improved overall effectiveness of influenza vaccine. Genetic characterisation suggested lower VE against A(H3) influenza was due to clade mismatch of vaccine and circulating viruses.

4 Katie Dale

Reurrence of tuberculosis in a low-incidence setting without directly observed treatment (DOT): Victoria, 2002-2014

Dale, K.1, Glisan, M.2 Tay, E.3, Trevan, P.1, Denholm, J.1,4

1 Victorian Tuberculosis Program; 2 Mycobacterium Reference Laboratory, Victorian Infectious Diseases Reference Laboratory; 3, Department of Microbiology and Immunology, The University of Melbourne

Aim: We aimed to analyse the rate of tuberculosis (TB) recurrence in our Victoria, a setting where TB patients self administer their TB treatment daily with individually tailored adherence support from clinical nurse consultants. We aimed to differentiate, where possible, recurrent TB cases that were likely relapses versus reinfections, and provide transparency regarding the likely treatment adherence of those cases that had relapsed.

Background: Even after TB has been successfully treated it can recur. Patients may have recurrent TB of the same strain (relapse) or a new strain (reinfection). It has long been emphasised that treatment adherence plays an important role in preventing the risk of relapse, however several meta-analyses have revealed that directly observed treatment (DOT) does not provide a solution to treatment adherence when compared to self-administered treatment (SAT), and is no better at preventing relapse. There has been a resultant call for research into effective ways to administer TB treatment, to reduce the risk of TB relapse. Victoria, Australia, is an industrialised setting with low TB incidence and universal health care. Individually tailored adherence support for self-administered daily TB treatment is provided. DOT is the Department of Medicine (RMH), The University of Melbourne.

Aim: Our research aims to grow neuronal cultures in three-dimensional space and use these cultures to investigate the spread and toxicity of prions.

Methods: Three-dimensional neuronal cultures were able to be infected with our M1000 prion strain. Disease was induced within these cultures by a single 72-hour exposure to M1000 prion infected mouse brain homogenates used to treat control cultures. Cultures were imaged following incubation with fluorescent probes that detect caspase (death effector protein) activation weekly for three weeks following infection. The cultures showed progressive infection-associated activation of cell death pathways. Examination of the cultures displaying heightened caspase activation showed death was accompanied by development of thioflavin-T positive deposits of the prion protein replicating plaque formation. Further utility of these cultures was verified by incubation with a novel in house compound designed as an anti-prion therapeutic, which demonstrated the ability to prevent plaque formation.

Conclusion: Our data make evident that three-dimensional neuronal cultures can be used to recapitulate prion-disease pathology and can be applied to discovery of novel therapeutics for prevention of plaque formation or disassembly of existing plaques.

Cancer Research

6 Chia Sharpe

Can emerging drug therapies be combined with immunotherapies to improve the treatment of Chronic Lymphocytic Leukaemia?

SHARPE C (1,2), Davis J (1,2,3,4), Mason K (1,2), Koide R (1,2,3,4), Chua B (5), Jackson D (5), Neeson P (1,2,3), Tam C (6), Ritchie D (1,2,3,4,7)

1. ACRF Translational Research Laboratory, The Royal Melbourne Hospital; 2. Department of Medicine, University of Melbourne; 3. Haematology and Immunology Translational Research Laboratory, Peter MacCallum Cancer Centre; 4. Sir Peter MacCallum Department of Oncology, University of Melbourne; 5. Microbiology and Immunology Research, Peter Doherty Institute; 6. Peter MacCallum Cancer Centre; 7. Clinical Haematology and Bone Marrow Transplantation Service, The Royal Melbourne Hospital

Aim: This study sought to understand how emerging drug treatments such as Brutinib and Venetoclax affect the immune function of Chronic Lymphocytic Leukaemia.
Lymphocytic Leukaemia patients, and to investigate the feasibility of novel therapeutic combinations of these drugs with immunotherapies.

Background: Chronic Lymphocytic Leukaemia (CLL) is the most common leukaemia in the western world. It is most commonly a disease of the elderly, and is characterised by the accumulation of malignant B cells that induces profound impairment of the patient’s immune system. Recent advances in treatment have shifted the paradigm from chemotherapy based approaches to small molecule inhibitors that target specific CLL survival mechanisms, with reduced side effects. Consequently there has been significant interest in immunotherapeutic approaches that harness the patient’s own immune system to enhance tumour clearance.

Methods: Using flow cytometric analysis of primary samples collected from untreated CLL patients we investigated the combination of two immunostimulatory Toll Like Receptor (TLR) agonists with Ibrutinib and Venetoclax.

Results: We found that TLR agonists were able to rapidly induce an activated phenotype in CLL cells. Activated cells exhibited increased immunogenicity and T cell stimulatory capacity, however there was an accompanying increased pro-survival protein expression and resistance to Ibrutinib and Venetoclax induced apoptosis. Additionally treatment with Ibrutinib and Venetoclax resulted in a reduction in TLR expression on both leukemic cells and CD3-CD19- cells. Furthermore it was found that the level of activation induced by TLR agonists correlated with the expression of the TLR on CD3-CD19- cells and not the leukemic cells themselves indicating that TLR mediated activation in CLL leukemic cells may be modulated by the activation of other immune cell subsets.

Conclusion: This pilot study raised questions about the suitability of combining immunostimulatory therapies with small molecule inhibitors. Activated cells showed decreased susceptibility to small molecule inhibitor induced apoptosis. Additionally cells treated with small molecule inhibitors displayed decreased responsiveness to TLR agonists. Furthermore these results indicate that the effects TLR stimulation may be mediated by non-lymphocyte immune subsets, which warrants further investigation.

7 Edmond Kwan

Use and impact of bevacizumab in patients undergoing liver resection for metastatic colorectal cancer in routine clinical practice

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Aim: In Australian patients with resectable or potentially resectable colorectal cancer liver metastases: (1) to assess patterns of use of bevacizumab with perioperative chemotherapy and (2) to explore the impact of bevacizumab on clinical outcomes.

Background: In metastatic colorectal cancer (mCRC) patients with isolated liver metastases, surgical resection offers the greatest likelihood of cure. Whilst for mCRC patients treated with palliative intent the addition of bevacizumab to the chemotherapy backbone is of proven benefit, whether to use bevacizumab in the resectable or potentially resectable population is a clinical dilemma.

Methods: Consecutive patients who underwent resection of liver metastases were identified from a prospective Australian mCRC registry that captures comprehensive data on patient and tumor characteristics, including resectability, treatment and outcome. The use of bevacizumab in this setting was examined and the impact on outcomes was explored.

Results: From a total mCRC population of 1700 patients, 543 patients with liver-only mCRC were identified, of which 217 patients (40%) underwent liver resection. Median follow-up was 30.8 months.

Perioperative chemotherapy was administered to 185 patients (85.3%), with bevacizumab added to chemotherapy in 73 (39.5%) patients. There was a trend for bevacizumab treated patients to be younger (median age 60.4 vs 65.1 years, p = 0.07) and fitter (mean Charlson score 2.22 vs 2.64, p = 0.054). Patients that received bevacizumab with perioperative chemotherapy were considerably less likely to have disease regarded as resectable at diagnosis (39 of 73 (53.4%) vs 95 of 112 (84.8%), p = <=0.01). At 5 years, overall survival was similar for bevacizumab treated and non-treated patients (61.4% vs. 59.2%, HR 0.83, p=0.52). There were no deaths within 30 days of surgery in any patients.

Conclusions: Despite limited evidence to support the use of bevacizumab in patients with resectable or potentially resectable liver-only mCRC, clinicians are not infrequently utilising this approach, particularly in younger and fitter patients and those not considered to have resectable disease at diagnosis. The addition of bevacizumab did not appear to impact survival outcomes. A multivariate analysis is underway to better define the impact of bevacizumab on survival outcomes.

8 Ashleigh Poh

Hck activity in myeloid cells promotes colorectal cancer progression

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Introduction: Colorectal cancer is the third most commonly diagnosed cancer worldwide, and may develop sporadically or due to chronic colitis. Macrophages are a major component of the colorectal tumour microenvironment and have an activation spectrum that ranges from classically activated ‘inflammatory’ to alternatively-activated ‘pro-tumorigenic’ macrophages. Hematopoietic Cell Kinase (Hck) is a myeloid-specific Src family kinase that plays a major role in macrophage function, and its increased activation is associated with a poor prognosis in colorectal cancer. However, the role of Hck in solid malignancies remains unexplored.

Methods/Results: We investigated the expression pattern of HCK in matched biopsies from sporadic colorectal cancer patients and observed elevated HCK activity in more than half of tumours compared to unaffected colon. RNAseq analysis of the corresponding biopsies also revealed an expression signature enriched for genes associated with the differentiation of pro-tumorigenic alternatively-activated macrophages in HCK-high expressing tumours.

To functionally assess the role of Hck signaling in colorectal cancer, Hck mutant mice that express a constitutively active form of the kinase (HckCA) were subjected to a chemically-induced model of sporadic colorectal cancer. HckCA mice developed larger and more frequent tumours compared to wild-type (WT) animals, coinciding with a significant increase in tumour-associated alternatively-activated macrophages. Furthermore, reciprocal adoptive bone-marrow transfers between HckCA and WT mice showed enhanced tumour formation and alternative macrophage polarisation in HckCA—WT mice, while these parameters were reduced in WT—HckCA mice. The contribution of adaptive lymphocytes was also investigated in B- and T-cell deficient HckCA:Rag1KO compound mutants. Interestingly, Rag1KO animals were protected from tumorigenesis while HckCA:Rag1KO developed a tumour burden similar to wild-type littermates.

Finally, pharmacological inhibition of HCK activity suppressed alternative activation of tumor-associated macrophages and the growth of colorectal tumors.

Conclusions: High HCK levels predict poor survival of colorectal cancer patients and enhance the growth and progression of colorectal tumors. These observations correlate with the increased differentiation of “pro-tumorigenic” alternatively-activated macrophages independent of the presence of mature lymphocytes. Accordingly, pharmacological inhibition of Hck activity suppresses alternative macrophage activation and the growth of colorectal tumors, suggesting that HCK is a therapeutic target for solid malignancies.

9 Kenneth Elder

Treatment intensity differences in screen-detected and community-detected early stage breast cancer

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Title: Treatment intensity differences in screen-detected and community-detected early stage breast cancer (ESBC)

Aim: To investigate the difference in intensity of treatment recommended by a breast cancer MD&M based on method of detection and whether these differences could add to the current debate surrounding breast screening programs.

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Background: The value of population based mammographic screening has been questioned by those who believe that the reduction in mortality from earlier diagnosis is outweighed by harms including over diagnosis and overtreatment as well as harms of false positive recall for assessment. Intensity of treatment received is rarely mentioned in the debate. We hypothesised that screen-detected (SD) cancers would receive less extensive surgical treatment and less intense adjuvant therapies than community-detected (CD) cancers. If demonstrated, the extent of these differences would form an important component of the debate over the role of mammographic screening.

Methods: Retrospective analysis of a consecutive cohort of female patients aged 50-69 and managed for ESBC between 2007-2014 within a large metropolitan Breast Service in Melbourne, Australia, diagnosed either via a population screening program (SD) or clinically referred to the Service (CD). Data on patient characteristics, symptoms, tumour characteristics and treatment recommendations were derived from hospital records. This was cross referenced with data held centrally by the Victoria Cancer Registry (VCR) to ensure accuracy.

Results: 823 cases were suitable for analysis. Of those with invasive disease 68% (433/641) were SD. Mean tumour size was smaller in the SD group (1.50cm vs 2.69cm, p<0.0001) and nodal involvement was less common (21% vs 43%, p<0.0001). Compared to CD cases, SD cases received less extensive surgery (mastectomy 14% vs 32% (p<0.0001), axillary dissection 18% vs 40% (p<0.0001)), less intensive adjuvant radiotherapy (radiotherapy after wide excision 91% vs 95% (p=0.052), radiotherapy after mastectomy 96% vs 59% (p=0.0039)). Endocrine therapy was more common in SD cancers reflecting differences in receptor status (88% vs 74% (p<0.0001)), but chemotherapy was much less frequently used (33% vs 64% (p<0.0001)).

Conclusion: Women diagnosed with ESBC through a population based screening program are less likely to receive mastectomy and/or axillary dissection, less likely to be recommended to receive radiotherapy, and less likely to receive adjuvant chemotherapy. This difference in treatment intensity should be considered in the current debate surrounding mammographic screening.

Brain & Mind Research

10 Thenegaa Sritharan
Long-term post-operative health-related quality of life in low-grade glioma, meningioma and acoustic neuroma

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Aim: To understand the long-term determinants of health-related quality of life (HRQoL) in low-grade glioma (LGG), meningioma (M) and acoustic neuroma (AN) patients after neurosurgery, in a pilot five-year longitudinal observational study.

Background: Health-related quality of life (HRQoL) is a multidimensional concept that assesses the impact of an individual’s health status on their physical, mental and social life domains. It is increasingly used as a secondary outcome measure in neuro-oncology. However, long-term HRQoL in low-grade glioma, meningioma and acoustic neuroma is novel and warrants further research.

Methods: 481 adult outliers with histologically-confirmed brain tumour (LGG=80, M=141, AN=85, S=175) were surveyed during 2014-2015 from the Royal Melbourne and Melbourne Private Hospitals. HRQoL was assessed using the questionnaires EORTC QLQ-C30 and EORTC QLQ-BN20, along with a short medical history survey and Folstein’s Mini Mental State Exam (MMSE) was used to assess objective cognitive deficits.

Results: Preliminary results indicate brain tumour patients have considerable impairments in HRQoL compared to a normal reference population but less so than non-tumour spinal surgery patients. Overall, emotional, cognitive and social impairments are prominent compared to physical and role impairments. Demographic variables (relationship and employment status, ability to drive) significantly affect HRQoL in LGG patients (p<0.05), while meningioma patients have greater symptom burden than spinal patients in vision (p<0.01), communication (p<0.01) and potentially cognition and headaches. Similarly, acoustic neuroma patients have reduced psychosocial function (p<0.01) and hearing loss (p<0.05) perceive worse HRQoL.

Conclusion: Our results support previous findings of significant HRQoL impairment in primary brain tumour patients compared to normal. We also show that psychosocial factors and activity limitations may account for much of the variation in overall HRQoL in all three tumour types, highlighting the potential benefits of interventions during post-operative rehabilitation. Furthermore, the aim at the conclusion of this five-year pilot study will be the development of ‘risk profile criteria’ to categorise individuals at risk of poor HRQoL and to design effective interventions to improve overall quality of life.

11 Sarah Farrand
Deep brain stimulation for severe treatment-resistant OCD: The initial Australian experience

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Aim: To describe the outcomes of seven patients with treatment-resistant obsessive-compulsive disorder (OCD) treated with deep brain stimulation (DBS), the largest such cohort in Australia.

Background: OCD is a disabling psychiatric disorder characterised by persistent intrusive thoughts (obsessions) and repetitive behaviours (compulsions). Despite best available treatments, up to 10% of patients remain treatment-refractory. Deep brain stimulation can be of benefit in carefully selected patients with severe intractable OCD.

Methods: Patient with severe OCD were referred by their treating psychiatrist for assessment of their suitability for DBS. Following successful application to the Psychosurgery Review Board, patients proceeded to have DBS electrodes implanted in either the nucleus accumbens (NAC) or bed nucleus of stria terminals (BNST) bilaterally. Clinical assessment, cognitive assessment and symptom rating scales were undertaken pre- and post-operatively at regular intervals. Rating scales used included the Yale-Brown Obsessive Compulsive Scale (YBOCS), Obsessive Compulsive Inventory (OCI), Depression Anxiety Stress Scale (DASS), Social and Occupational Functioning Assessment Scale (SOFAS) and the Brief Psychiatric Rating Scale (BPRS).

Results: Seven patients underwent DBS surgery and were followed for a mean of 26 months (3-48). These patients were referred from across Australia (including NSW, TAS, VIC and SA). There were four females and three males, with a mean age of 46 years (37-59), and mean duration of OCD of 25 years (15-38). The time from first assessment to surgery was on average 16 months (9-25). All patients except one showed improvement on symptom severity rating scales, with three patients showing a full response (defined by 35% or more improvement in the YBOCS), two patients were classified as non-responders, and two patients have only early data, awaiting further follow-up to determine their response.

Conclusions: DBS was an effective treatment for OCD in these highly selected patients. The results of the Australian DBS patients are comparable with other leading research groups in the field, as well as having similar efficacy to ablative psychosurgery techniques such as capsulotomy and cingulotomy. DBS provides advantages over lesional psychosurgery but is much more expensive and requires significant ongoing research is required to better understand the neurobiological basis for OCD and how this can be manipulated with DBS to further improve the efficacy of this emerging treatment.

12 Bridgette Semple
Traumatic brain injury in paediatric mice results in sex-dependent social behaviour deficits and aberrant neuronal morphology

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Background: Chronic social behaviour problems after paediatric traumatic brain injury (PTBI) significantly contribute to poor quality of life for survivors, however the mechanisms underlying such deficits have not been elucidated. We hypothesise that interconnected brain regions
comprising the ‘social brain network’ undergo aberrant neuroplasticity changes during development following pTBI, to influence social functioning at adulthood.

**Aim:** To determine whether pTBI influences neuronal morphology in the medial prefrontal cortex (mPFC), a region involved in social cognition and behaviour, prior to the development of social problems, in a clinically-relevant mouse model.

**Methods:** Littermate male and female C57Bl/6 mice were subjected to a unilateral controlled cortical impact or sham-operation at age postnatal day 21, approximating TBI during early childhood. One cohort were euthanised at 3 weeks post-surgery for Golgi-Cox staining (n=5/group); a second cohort were maintained until 8 weeks post-surgery for the evaluation of psychosocial and neurocognitive function (n=8-10/group).

**Results:** Morphological analysis of layer III pyramidal neurons in the ipsilateral mPFC revealed a reduction in dendritic complexity at adolescence after pTBI in male mice compared to sham controls, including fewer branch nodes and ends, as well as reduced basal dendritic length. By adulthood, consistent with previous studies, male pTBI mice showed deficits in social and sociosexual behaviours. In contrast, mPFC neuroanatomy was unaffected by pTBI in female mice, which also showed a more limited profile of social dysfunction. pTBI mice exhibited robust hyperactivity across multiple paradigms, to a greater extent in males compared to females.

**Conclusions:** Together, our findings demonstrate changes in neuronal morphology, remote from the injury site, several weeks after pTBI in male mice, and associated with the subsequent emergence of social behaviour deficits. Sex is a determinant of both regional neuroplasticity and social outcomes after pTBI. It remains unclear whether these changes are an indirect, stress-related consequence of pTBI, or a direct result of aberrant connectivity of the social brain network.

### 13 Pablo Casillas-Espinosa

**Anti-epileptogenic effects of the novel T-type calcium channel blocker Z944 in the post-status epilepticus model of temporal lobe epilepsy**

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**Aim:** To investigate the anti-epileptogenic effects of a novel T-type Ca2+ channel antagonist, Z944, in the post-status epilepticus model of temporal lobe epilepsy (TLE).

**Background:** TLE is the most common form of epilepsy in adults that is refractory to medical treatment. Current therapeutic treatment is symptomatic, suppressing seizures, but has no disease modifying effect on epileptogenesis. Importantly, T-type Ca2+ channels have been strongly implicated in the pathogenesis of TLE.

**Methods:** 10-week old Wistar rats underwent surgery to implant EEG recording electrodes. Sham animals had i.p. saline injections and the post-SE animals were injected with KA i.p to induce SE. After 4h of SE, animals had 2 weeks of continuous video-EEG recordings. Blood was collected at the end of treatment. After 4 weeks of drug washout, the animals had 2 weeks of continuous video-EEG recordings to evaluate the anti-epileptogenic effects of the treatments. Sucrose preference test was done to evaluate for depressive like behaviour. One week after the last behavioural test, brain tissue was collected for molecular analysis.

**Results:** Post-SE + vehicle animals had the highest average number of seizures per day (0.77±0.09), followed by Post-SE + levetiracetam (0.53±0.076). Treatment with Z944 after SE greatly reduced the number of seizures per day (0.017±0.012) which was significantly different compared to vehicle and levetiracetam treated animals (p<.0001). Importantly, only two of the eight Post-SE + Z944 animals developed seizures, having only 1 during both weeks of recordings. Seizure duration and severity where not significantly different between the treatment groups. For the sucrose preference test, post-SE + vehicle showed reduced sucrose preference when compared to both shams (p < 0.05). In contrast, Post-SE animals treated with Z944 had a similar sucrose preference to shams.

**Conclusion:** The results provide evidence that treatment with Z944 has powerful anti-epileptogenic effects in the post-SE model of TLE. This is the first study to show a drug that has disease modifying effect in epileptogenesis, but also has epilepsy comorbidity modifier effects. Furthermore, the results presented here show encouraging positive pre-clinical evidence for disease-modifying effects of Z944 for acquired TLE that it may be possible to translate to a clinical trial.

### 14 Tomas Kalincik

**Prediction of individual response to 10 immunomodulatory therapies in multiple sclerosis: A global observational cohort study**

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**Objective:** We have evaluated a large number of predictors of individual response to 10 immunomodulatory therapies in multiple sclerosis. These predictors were compiled into predictive models applicable in clinical practice.

**Background:** Prediction of individual treatment response in multiple sclerosis is limited by variability in patients’ treatment response. A comprehensive predictive algorithm developed and validated in a large global cohort is likely to contribute to evidence-based individualised therapy.

**Design/Methods:** Longitudinal data from MSBase, a large global cohort study, were used to identify predictors of relapse incidence, disability progression and disability regression, using univariable survival models. The predictors comprised 51 demographic, clinical and paraclinical variables. Multivariable survival models were used to design individual predictive algorithms. Dimensionality of the models was controlled with principal component analysis. Accuracy of the predictive models was tested within a training cohort. External validation was established using a validation cohort.

**Results:** In the training cohort (n=7121), the most significant predictors of treatment response comprised: age (HR=0.98-1.00), previous relapse activity (HR=1.18-1.32), pyramidal relapses (HR=1.23-1.40), and previous therapy (HR=10^-7 - 10^-5) for future relapse hazard; age (HR=1.02-1.03), previous therapy (HR=10^-7 - 10^-6), secondary progressive disease (HR=2.25-2.86) and pyramidal or cerebellar relapses (HR=1.14-1.34) for disability progression hazard; and disability step (HR=1.27-1.44), disability trajectory (HR=1.27-4.93) and previous therapy (HR=10^-7 - 10^-6) for disability regression hazard. The predictors varied moderately among different therapies. Accuracy of the multivariable predictive algorithms reached up to 88% for a 4-year individual prediction. In the independent validation cohort (n=1794), the algorithms’ predictive accuracy reached 16-74%, depending on therapy and predicted outcome.

**Conclusions:** The newly developed predictive algorithms are capable of estimating individual relapse and disability outcomes over 4 years, including estimation of prediction error and robustness. Further refinement of the models and increase in the size of the training cohort are likely to enhance accuracy of this prediction.

### 15 Nathaniel Lizak

**Immunomodulatory therapy slows accumulation of disability in moderately advanced multiple sclerosis**

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**Aim:** To evaluate variability and predictability of disability trajectories in moderately advanced multiple sclerosis and their modifiability with immunomodulatory therapy. We hypothesised that individual disability trajectories are not homogenous and can be predicted based on demographic and clinical characteristics.

**Background:** Three large cohort studies have previously examined factors influencing disability accumulation in moderately advanced multiple sclerosis, but arrived to contradictory results. The effect of...
therapy during this disease stage remains unclear and is currently under debate. Methods: The epochs between Expanded Disability Status Scale (EDSS) steps 3-6, 4-6, and 6-6.5 were analysed. Patients with relapse-onset multiple sclerosis, six-month confirmed progression to the baseline EDSS step (3/4/6), and ≥12 months pre-baseline follow-up were identified in MSBase, a global observational multiple sclerosis cohort study. We used multivariable survival models to examine the impact of relapse rate and proportion of time treated with disease-modifying therapies (prior to and during each epoch), age and disease duration at baseline, on progression to the outcome EDSS step (6 or 6.5). Sensitivity analyses with varying outcome definitions and inclusion criteria were conducted.

Results: For the EDSS 3-6, 4-6, and 6-6.5 epochs, 1,560, 1,504, and 1,231 patients were identified, respectively. Disability trajectories showed large coefficients of variance pre-(0.92-1.11) and post-baseline (2.15-2.50), with no significant correlations. Probability of reaching the outcome EDSS step was not associated with pre-baseline variables, but was increased by higher relapse rates during each epoch (hazard ratios: 1.58-3.07; P≤0.001). Greater proportion of each epoch treated with higher-efficacy therapies was associated with lower risk of the outcome EDSS (hazard ratios: 0.72-0.91 per 25%; P≤0.02). These results were confirmed by two sensitivity analyses.

Conclusion: Disease progression during moderately advanced and advanced multiple sclerosis is highly variable and amnesic to prior disease activity. Lower relapse rates and greater persistence on higher-efficacy immunomodulatory therapy after reaching EDSS steps 3, 4, and 6 are associated with a decreased risk of accumulating further disability. These observations justify treatment with highly-effective immunomodulatory therapy even after moderately advanced and advanced disability has been attained. This has important implications for treatment availability in jurisdictions where patients with moderate and severe disability are restricted from accessing immunomodulatory therapies.

Genetic Research

16 Emma Nolan

RANK ligand as a target for breast cancer prevention in BRCA1 mutation carriers

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Background: Women who carry germline mutations in the tumour suppressor gene BRCA1 have a high lifetime risk of developing basal-like breast cancer, which is thought to arise in an aberrant luminal suppressor gene BRCA1 have a high lifetime risk of developing basal-like breast cancer. This study utilized preneoplastic histological tissues to investigate the role of RANK in the development of breast cancer.

Methods: We have investigated the role of the RANK pathway in the initiation and progression of BRCA1-associated basal-like breast cancers. We have utilized preneoplastic human breast tissue isolated from BRCA1-mutation carriers. Notably, RANK+ luminal progenitors isolated from BRCA1-mutation carriers following risk-reducing surgery, and in vivo studies were performed using Brca1-deficient mice.

Results: A novel subset of RANK+ luminal progenitors in histologically normal human breast epithelium from BRCA1-mutation carriers was identified. Notably, RANK+ luminal progenitors isolated from BRCA1-mutation carriers were more clonogenic and exhibited higher ALDH activity (a feature of BRCA1 tumours) than their RANK– counterparts. Expression profiling revealed that RANK+ luminal progenitors are highly mitotically active and bear a molecular signature closely aligned to that of basal-like breast cancer. Importantly, inhibition of RANKL signaling in 3D breast organoid assays using BRCA1-mutant preneoplastic tissue significantly attenuated cellular proliferation, while pharmacological inhibition of RANKL in vivo significantly delayed tumour onset in Brca1-deficient mice.

Conclusion: Our findings suggest that RANKL inhibition may be a promising novel strategy for breast cancer prevention in BRCA1 mutation carriers.

17 Dominica Zentner

Long-term impact of the Cardiogenetics clinic: a retrospective audit of patient recall and compliance

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Aim and Background: Risk assessment and screening advice are core elements of a multidisciplinary cardiogenetics clinic (CGC) but there is little information on long-term impact for families. A clinic audit of a CGC was undertaken to (1) determine recall and adherence to clinical advice provided and (2) review the role of genetic testing in previously assessed families.

Methods: Individuals attending the CGC between mid 2007 and end 2013 were eligible. A structured telephone review of consultants or the nominated family contact person by a single investigator was performed following a predetermined protocol.

Results: 204 individuals have undergone review. There have been relevant medical changes in 2 (0.9%) and 6 deaths (2.9%) in the families. Recall of advice was excellent in the majority. Adherence to medical advice was high for individuals advised to cease screening but much lower where ongoing screening was advised (40%); a further 20% reported inconsistent screening. In 70 cases review led to an invitation to attend clinic, including the option for further genetic testing.

Conclusion: A substantial part of the benefit of a CGC derives from accurate and personalised advice about screening and follow-up. This process of review has indicated that compliance to positive screening advice is low – potentially impacting on the effectiveness of the CGC model. These data provide a strong case for a program of ongoing review as a core CGC component although this has obvious resource implications. Determination of the role of genetic testing or utilisation of updated technology for previously seen families remains a challenge.

18 Paul James

The advent of gene panel testing: has it changed the outcome of mutation detection gene testing in a cardiac genetics clinic?

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Background: Genetic testing has moved from a candidate gene to a gene panel testing model. These data provide a strong case for a program of ongoing review as a core CGC component although this has obvious resource implications. Determination of the role of genetic testing or utilisation of updated technology for previously seen families remains a challenge.

Aims: To describe the pattern of mutation detection genetic testing results from a single centre cardiac genetic clinic (CGC).

Methods: Database interrogation of all genetic tests ordered by the cardiac genetic clinic. Collection was undertaken of demographic details and the outcome of genetic testing categorised as positive (mutation detection), negative (no mutation detection) or as a variant of uncertain significance (VUS).

Results: There were 420 mutation detection tests ordered by the clinic since inception to end 2015. Median age at testing was 38 years (26 – 51), gender spread 66% male to 33% female. Results were: positive mutation detection in 168 (40%) with no mutation identified in 157 (37.4%) and a variant of uncertain significance (VUS) in 93 (22.1%) (2 results from 2015 pending).

Conclusion: Transition to NGS has resulted in an increase in the number of mutation tests ordered over time. Though overall the rate of positive mutation detection has increased, the most striking change is the increased likelihood of finding a VUS. This highlights the challenges facing cardiac genetic testing and the importance of testing within a clinical context and with the input of a multidisciplinary clinic.
Conclusion: In this proof-of-concept study, we described an alternative reading. mismatched alleles (HLA-B*46:01:01, HLA-B*15:01) generated Vout differentiating the impedance of positive and negative samples. for detection, in which 100 Khz (n=3, p=0.0295) was optimal for treatment prior to detection produced optimal differentiation between found that adding a thin film of silicon-dioxide (SiO2) and plasma-critical in determining success of the LAMP-IDC platform. Firstly, we minutes. Upon hybridization, several parameters were found to be frequencies towards the sensors's inherent dielectric proper categories. This was performed using lock-in-amplifier based electrical impedance measurements, by analyzing effects of various external frequencies towards the sensors’s inherent dielectric properties. All hybridizations were at room temperature, for 20 minutes. Results: Our LAMP assay was capable of eliminating a majority of HLA-B alleles and amplify targets from crude blood samples within 20 minutes. Upon hybridization, several parameters were found to be critical in determining success of the LAMP-IDC platform. Firstly, we found that adding a thin film of silicon-dioxide (SiO2) and plasma-treatment prior to detection produced optimal differentiation between our positive and negative controls. Second was the applied frequency for detection, in which 100 Khz (n=3, p=0.0295) was optimal for differentiating the impedance of positive and negative samples. At 100 Khz, it was observed that positive controls and the 100% match HLA-B*15:02 ampcions generated output voltage (Vout) of 2 mV whilst mismatched alleles (HLA-B*46:01:01, HLA-B*15:01) generated Vout below 2 mV, suggesting 2mV as potential cutoff-value for positive reading. Conclusion: In this proof-of-concept study, we described an alternative method for detecting the HLA-B*15:02 allele using a combination of LAMP and IDC-biosensing. First-degree differentiation of HLA-B variants was possible isothermally within 20 minutes on blood samples, eliminating need for DNA extractions. Second degree differentiation of few base-pair mismatched HLA-B AMP ampcions on IDC-sensors was possible within 20 minutes with a constant cutoff value for positivity at 2 mV. The total assay time for HLA-B*15:02 detection is <1 hour, and the simplified protocol can be potentially miniaturized into a point-of-care device.

20 Kevin Chow

CCR2+ inflammatory monocyte derived dendritic cells contribute to early graft dysfunction of MHC mismatched islet transplants

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Aim: To determine the role of monocyte derived dendritic cells (moDCs) in mediating early graft dysfunction following allogeneic islet transplantation. Background: Islet transplantation can cure type 1 diabetes, but is limited by lack of donor organs and early graft dysfunction, such that many patients require multiple transplants to achieve insulin independence. moDCs arise during inflammation and allograft encounters where they can promote various innate and adaptive immune responses. Methods: To determine whether moDCs impair early graft function following allogeneic islet transplantation, we transplanted MHC-mismatched BALB/c (H-2d) islets into diabetic C57BL/6-CCR2.DTR recipients (H-2b), treated with either saline (control) or diphertheria toxin (DT) to deplete moDCs. Graft function was assessed by blood glucose (BG) measurement. Results: DT resulted in specific depletion of graft site moDCs post-transplant. Despite equivalent pre-transplant BG levels (27.0 +/- 1.3 vs 29.6 +/- 1.1 mM, ns), DT recipients achieved lower post-transplant BG levels and better rates of normoglycemia than control recipients (11.0 +/- 1.9 vs 19.1 +/- 1.4 mM, p = 0.004) at day 1 post-transplant in diabetic recipients. When a marginal donor dose of 200 islets were transplanted, DT-induced moDC depletion resulted in normoglycemia in 78% compared to 25% of control recipients (p = 0.03). As well as amelioration of graft dysfunction in the immediate peri-transplant period, prolonged DT administration (15 days post-transplant) resulted in improved graft survival (21 vs 11 days, p = 0.005).

Conclusion: moDCs impair early graft function post-allogeneic islet transplantation. moDC depletion may allow for improved early graft function, permit transplantation with lower islet masses, and enhance graft survival.
in the RMH ICU and since then there has been a significant amount of nutrition focused quality improvement undertaken.

Aims: 1. To evaluate improvements in nutrition delivery to patient in the RMH ICU over 8 years; 2. To compare nutrition practices at RMH to best practice guidelines.

Methods: This is a period prevalence multicentre survey, which has been undertaken in ICUs internationally every 12-18 months for the past 10 years. RMH has participated in four surveys these include 2007, 2011, 2013 and 2014. On each occasion 20 consecutive patients were recruited, who were mechanically ventilated within 48-hours of admission and remained in the ICU for a minimum of 72 hours. Data collection included demographics, severity of illness, route of nutrition, prescribed and received energy and protein, feeding interruptions and clinical outcomes.

Results: Over 150 sites participated in each survey. There has been on average a 20% improvement in energy delivery since the dietetics service was established in ICU. The RMH overall ranking has improved from 79-160 (50%) to 19-166 (12%). In the most recent survey in 2014, patients received a mean (range) of 73% of prescribed calories, compared to 57% (21%-95%) internationally. The mean (range) time to initiating nutrition support was 24 hours (0-108) compared to 27 hours (0-260) at sister sites and 38 hours (0-276) internationally. Enteral feeds were interrupted 33% of the time with the median [IQR] time of interruptions of 7.0 hours [3.0-10.0], 65% of this was related to fasting for procedures.

Conclusion: Nutrition delivery has significantly improved in the RMH ICU over the past 8 years, since the establishment of a dedicated dietetics service. Compared to sister sites and internationally RMH achieved good compliance with best practice guidelines. However in order be considered as international leaders, a greater focus on, decreasing fasting and quicker progression to feeding targets is needed.

23 Mark Tacey
Identification of frequent presenters to the Emergency Department at Royal Melbourne Hospital and their associated risk factors
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Aim: To develop a predictive model to identify frequent presenters to the Emergency Department (ED) at Royal Melbourne Hospital (RMH) sooner than they are currently identified.

Background: The RMH ED has recently established a multi-disciplinary committee to identify patients who are frequent presenters, who are then assigned an ED management plan with the aim of reducing the number of re-presentations. Previous studies have shown that the ED management plans are effective in reducing the number of re-presentations. However, patients will on occasion, have had over 10 presentations to the RMH ED prior to being identified by the committee and assigned an appropriate ED management plan. Therefore, this study sought to develop a predictive model that would enable the committee to consider a plan appropriate for these patients at an earlier time-point, thus potentially reducing the number of re-presentations.

Methods: A retrospective cohort study was undertaken of patients presenting to RMH ED between 1 July 2007 and 30 June 2011. In order to isolate patients with the potential to frequently present, the eligibility criterion was restricted to patients with at least 2 presentations over a 30-day period. Of these, 392 (3.5%) were found to be frequent presenters. Factors found to be independently associated with frequent presenters were being male (OR 1.49, 95%CI: 1.12-1.99), indigenous (OR 4.06, 95%CI: 1.47-11.21), having 4 or more ED presentations within 12 months (OR 13.68, 95%CI: 8.55-21.87) and several comorbidities including chronic pulmonary disease, fluid and electrolyte disorders and psychoses. The C-statistic of 0.775 indicated an excellent predictive performance of the model.

Conclusion: The high predictive performance of the developed model may provide a valuable extension to the identification process of patients suitable for RMH ED management plans, with further consideration required to determine how the predictive model may be integrated into the current process.

24 Camila Battistuzzo
Early decompression following cervical spinal cord injury: Examining the process of care from accident scene to surgery in Australia and New Zealand
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Background: Early decompression may improve neurological outcome after spinal cord injury (SCI), but is often difficult to achieve because of logistical issues.

Aims: The aims of this study were to determine (1) the time to decompression in cases of isolated cervical SCI in Australia and New Zealand and (2) where substantial delays occur as patients move from the accident scene to surgery.

Methods: Data were extracted from medical records of patients aged 15-70 years with C3-T1 traumatic SCI between 2010 and 2013 from each of the 8 participating surgical centres. Non-parametric data were compared using Mann-Whitney U test and significance was set at p < 0.05. Data are presented as median (IQR).

Results: A total of 192 patients were included. The median time from accident scene to decompression was 21h, with the fastest times associated with closed reduction (6h). A significant decrease in the time to decompression occurred from 2010 (31h) to 2013 (19h, p = 0.008). Patients undergoing pre-surgical hospital admission had a significantly lower time to decompression compared to patients undergoing pre-surgical hospital admission (12h vs. 26h, p < 0.0001).

Medical stabilisation and radiological investigation appeared not to influence the timing of surgery. The time taken to organise theatre following surgical hospital admission was a further factor delaying decompression (12.5h). There was an inverse relationship between the timing of decompression and the proportion of patients demonstrating substantial recovery (2-3 AIS grades).

Conclusions: In conclusion, the time of cervical spine decompression markedly improved over the study period. Very early decompression may promote neurological recovery. Direct admission to a surgical hospital, rapid organisation of theatre and where possible use of closed reduction, are likely to be effective strategies to reduce the time to decompression.

25 Teddy Wu
The natural history of peri-haematomal oedema and impact on outcome after intracerebral haemorrhage - data derived from the Helsinki Intracerebral Haemorrhage Study
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Aims: To demonstrate the natural history of peri-haematomal oedema and its association with outcome after intracerebral haemorrhage (ICH).

Background: Oedema is associated with outcome after ICH. We assessed the natural history after ICH undergoing surgical evacuation, lack of planimetric data, or baseline imaging performed >1 week from onset. We assessed the correlation
between oedema extension distance (EED) growth and time from ICH onset, creating an oedema growth trajectory model using all available scans. We identified clinical and imaging characteristics associated with more than expected EED growth. Association between high EED with mortality was assessed using logistic regression adjusting for known predictors of ICH outcome.

Results: From a series of 1013 consecutive patients, 861 were included. There was a strong inverse correlation between EED growth rate (cm/day) and time from onset (days): EED growth = 0.162 * days - 0.027. Baseline factors associated with larger than expected peak EED were older age (74 vs 69, p = 0.007), higher NIHSS (16 vs 9, p < 0.001) and lower GCS (13 vs 15, p < 0.001), larger ICH volume (33.5 vs 12.7, p < 0.001), larger initial EED (0.46 vs 0.31, p < 0.001) and higher glucose (7.7 vs 6.9 mmol/L, p = 0.001). Patients with larger than expected EED were more likely to have midline shift (58% vs 32%, p < 0.001), hemiation (14% vs 5%, p < 0.001), higher 3 month (51% vs 26%, p < 0.001) and 6 month (54% vs 28%, p < 0.001) mortality. In the logistic regression model higher than expected EED was associated with mortality at 6 months (OR 1.81 95% CI 1.12-2.92, p = 0.015) adjusted for age, male gender, warfarin use, NIHSS, GCS, ICH volume and ventricular extension.

Conclusion: Oedema growth can be readily monitored and is an important independent determinant of outcome after ICH. It is strongly correlated with time from stroke onset and is associated with larger haematoma volume. Oedema growth is an important treatment target for strategies to improve patient outcome.

General Medicine

26 Andrea Maier

Assessment of health status by molecular measures in middle-aged to old persons, ready for clinical use?

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Background: In addition to measures already used in clinical practice, molecular measures have been proposed to assess health status, but these have not yet been introduced into clinical practice.

 Aim: To test the association of functional capacity measures used in current practice and molecular measures with age and health status.

Methods: The cohort consisted of 178 middle-aged to old participants of the Leiden Longevity Study (range 42-82 years). We tested associations between functional capacity measures (physical tests: grip strength, 4-meter walk, chair stand test; cognitive tests: Stroop test, digit symbol substitution test and 15-picture learning test) with age and co-morbidity. The association between high sensitivity C-reactive protein (hs-CRP), numbers of senescent p16INK4a positive cells in the epidermis and dementia and putative immunosenescence (presence of CD57+ T cells).

Results: All functional capacity measures were associated with age. CRP and epidermal p16INK4a positivity also were associated with age, but with smaller estimates. Grip strength and the Stroop test were associated with cardiovascular or metabolic disease, as was epidermal p16INK4a positivity. All associations with cardiovascular or metabolic disease attenuated when adjusting for age.

Conclusion: In middle-aged to old persons, the molecular measures tested here were more weakly associated with age and health status than functional capacity measures. Whether these molecular measures associate more closely with health status in the elderly or in specific groups of patients needs to be explored.

27 Asvini Subasinghe

Strong relationship between high sensitivity C-reactive protein (hs-CRP) and prehypertension in 16-25 year old Australian females

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Aim: To investigate the association between obesity, high sensitivity C-reactive protein (hs-CRP) and prehypertension in females aged 16-25 years.

Background: The relationship between hs-CRP and prehypertension has never been documented in adolescent females in Australia.

Methods: Women aged 16-25 years living in Victoria were randomly recruited via targeted Facebook advertising for the Young Female Health Initiative (YFHI) and Safe-D studies. Socio-demographic information was collected via a web-based questionnaire. Anthropometric and blood pressure measurements were conducted by trained staff. Levels of inflammatory marker CRP were assessed by hs-CRP testing (Abbott Architect assay). Chi2 tests and multivariable logistic regression were used to determine associations between modifiable cardiovascular risk factors and prehypertension.

Results: Demographic data were collected from 639 females (mean ±SD age 22.3±3) and blood pressure data were available for 513 participants. Approximately 28% had prehypertension (≥120-139/80-89 mmHg) and 3% had morbid hypertension (≥140/90mmHg). Approximately 16% had a hs-CRP level > 5.0mg/L, (reference range: 1.0-3.0 mg/L). In multivariable analyses, females who were overweight (odds ratio (OR), 1.9 95% confidence interval (CI) 1.1–3.3, p = 0.02) or obese (OR, 6.0 95% CI 2.7–13.3, p < 0.001) were more likely to have prehypertension compared with those with a normal body mass index (BMI). Elevated hs-CRP levels (≥ 5 mg/L) also were associated with an increased odds of prehypertension (OR, 2.2 95% CI 1.2–4.0, p = 0.01).

Conclusion: The high prevalence of prehypertension is of concern in this sample of 16 to 25 year old Australian females. Positive associations were detected between hs-CRP, obesity and prehypertension, despite the absence of cardiovascular disease in this sample. There are currently no guidelines addressing the association between hs-CRP and cardiovascular risk in adolescents. Blood pressure lowering strategies directed at young Australian females should be developed to reduce their future risk of cardiovascular disease.

28 Spiros Fourlanos

Impact of overnight closed loop (OCL) at home compared to sensor augmented pump with low glucose suspend (SAP-LGS) improves time in target range in adults and reduces hypoglycaemia in adolescents

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Background: Insulin pumps combined with continuous glucose monitoring – sensor augmented pump with low glucose suspend (SAP-LGS) have emerged as the current best method to achieve excellent glycaemic control and to avoid hypoglycaemia. However, the holy grail for type 1 diabetes treatment and the next exciting development is the closed loop pump in which continuous glucose monitoring data guides insulin dosing through a algorithm in the pump.

Aim: In this study we aimed to compare glycaemia achieved with overnight closed loop (OCL) with that achieved with SAP-LGS.

Method: We conducted a randomised controlled cross-over study to evaluate the performance of OCL at home. Sixteen adults (Mean [SD] age 42.1 (9.6)y; HbA1c 7.3 (0.6)% with type 1 diabetes were assigned in random order
to OCL (proportional integral derivative with insulin feedback algorithm (Version 1.0); Medtronic, Northridge, CA) and SAP-LGS for 4 nights at home.

Results: Adults and adolescents had CL active for 90% of 00:00-8:00 AM. In adults time in target range (TTR) was 72-144 mg/dl (primary endpoint) was greater with OCL overnight and for the entire 24-hours. In adolescents, OCL decreased % time in the hypoglycaemic range overnight. Overall, the number of symptomatic hypoglycaemic episodes overnight was lower with OCL vs. Control (6 vs. 23; p=0.0016). OCL reduced glycaemic variability (sensor glucose SD) overnight.

Adolescents on SAP-LGS spent greater time in target range overnight than adults (64.4 vs 44.5%; p=0.003) and less during the day (43.9 vs 53.0%; p=0.04).

Conclusions: OCL improved time in target range overnight and the following day in adults. The main benefit of OCL in adolescents was nocturnal hypoglycaemia reduction. A CL system addressing day-time glycaemia may be more effective in improving time in target range in adolescents. Forthcoming trials will evaluate 24 hour closed loop therapy in a larger outpatient population for longer periods.

29  Emma Callegari

Associations between vitamin D status, other determinants of bone health and tibial pQCT variables in young Australian women: the Safe-D study

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Aim/Background: Vitamin D deficiency is associated with poor musculoskeletal health. However, data investigating the association of 25-hydroxyvitamin D (25OHD) levels with peripheral quantitative computed tomography (pQCT) parameters is limited in younger populations. The Safe-D study comprehensively assesses vitamin D status and a range of clinical, behavioural and lifestyle factors in young women, an understudied demographic. Here we investigated the association between vitamin D status and pQCT parameters.

Methods: Female participants aged 16-25 years living in Victoria, Australia, were recruited through Facebook advertising. Participants completed an extensive online health survey and attended a site visit. The 4% and 66% sites proximal to the distal end plate of the non-dominant tibia were scanned using pQCT (Stratec XCT-3000). DXA was used to measure areal bone mineral density (aBMD) at the lumbar spine (L1-L4), total hip and femoral neck. Serum 25OHD was measured using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Daily calcium intake was measured using the Dietary Questionnaire for Epidemiological Studies Version 2.

Results: Serum 25OHD levels and pQCT data were available for 406 participants. The mean (± SD) serum 25OHD concentration was 67.4 ± 26.9 nmol/L, with 28% vitamin D-deficient (25OHD <50 nmol/L). Forty-five (11%) participants had low BMD on DXA (Z-score < -2.0). Vitamin D deficiency was significantly associated with low aBMD at any skeletal site when compared to serum 25OHD levels above 50 nmol/L (17% of the vitamin D deficient group had low BMD compared to 9% in participants with adequate vitamin D levels, p = 0.027). By univariate analysis, 25OHD was associated with cortical volumetric BMD (β = -0.15, p = 0.003) and total bone cross-sectional area at the 66% site (β = 0.32, p = 0.004). The relationship between 25OHD trended towards significance with polar stress-strain index (SSI polar, β = -0.15, p = 0.058) and peristemel circumference (β = 0.02, p = 0.053). Cortical volumetric BMD and total bone cross-sectional area at the 66% site remained significant after adjustment for age, serum parathyroid hormone level, daily calcium intake, height, fat mass and physical activity (β = -0.17, p = 0.001 and β = 0.30, p = 0.045, respectively).

Conclusion: Vitamin D deficiency was significantly associated with low BMD, total bone cross-sectional area at the tibial shaft and cortical volumetric BMD. The biological significance of the findings requires further investigation. However, results suggest a positive association between vitamin D status and bone size and therefore bone strength. These studies should improve understanding of the determinants of bone health in young women.

30  Robert Stolz

Use of cable-driven treadmill gait-trainers for patients post-stroke within an intensive inpatient neurorehabilitation program to improve mobility: a randomized controlled trial

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Background: Physical disability from stroke commonly leads to disruptions in walking ability. In recent years, novel gait trainers that utilise cable drive systems that assist or resist lower limb movements during the gait cycle have been developed.

Aim: To determine if a cable driven gait trainer is more efficacious than usual practice in improving gait speed, endurance and balance and also quality of life and length of inpatient rehabilitation stay.

Methods: 32 rehabilitation inpatients will be randomised to intervention (cable-driven treadmill training replacing up to half of each of their daily land-based physiotherapy session) or control (usual physiotherapy program). Outcome measures include 10 metre walk test, 6 minute walk test (6MWT), Functional Independence Measure (FIM), Timed Up and Go (TUG), Step test and Euro-Quality of life EQ-5D. Measurement timepoints will be on admission, discharge and 4 weeks post discharge.

Results: This study is currently in progress and results will be presented at MH research week.

Conclusions: This study is currently in progress and results will be presented at MH research week.

Surgical Research Forum

31  Marie Parsons

Genomics study to identify novel cancer genes predictive for prognosis and 5-FU benefit and utility in stage II/III colorectal cancer

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Aim: To identify novel genes predictive and prognostic of 5-FU benefit in treatment of stage II/III Colorectal cancer (CRC)

Background: CRC is the third most common cancer worldwide, affecting over 15,000 individuals in Australia each year. While CRC is often detected at a stage where resection of the primary tumour is possible, 50% will relapse from metastatic disease. Current practice to determine clinical management is determined by the extent of cancer spread at diagnosis, tumour depth and lymph node stage. Adjuvant 5-fluorouracil (5-FU) based chemotherapy is offered to the majority of patients with stage III CRC, reducing recurrence by approximately 40% in stage III and a subset of high risk stage II CRC patients. This approach is suboptimal, resulting in the under treatment of stage II patients who relapse (approximately 20%). Contrarily, a large number of stage III patients are over treated with only 15% responding to 5-FU as a first line treatment. There is an urgent need to identify biomarkers of prognosis and predictive benefit from 5-FU treatment for stage II and III CRC to refine outcome prediction and use of current adjuvant therapy.

Materials and methods: A panel of 113 candidates CRC genes were identified as significantly mutated in whole genome and whole exome sequencing studies from 85 MSS cancers, 53 cell lines and 276 MSS colon cancers from the TCGA using the MutSigCV algorithm from the Broad Institute.74 CRC risk variants discovered in genome-wide association (GWA) studies were also included in this panel. Custom amplicon panels for target enrichment were designed using SureDesign (Agilent Technologies) for use with the HaloPlex™ target enrichment system. Sample libraries were prepared using the automated Bravo liquid handling platform followed by next-generation sequencing (NGS) on the Illumina Next-Seq 500.

Results: We have developed a novel and custom cancer gene panel and validated the panel design for use on fresh frozen and formalin-fixed paraffin-embedded tissue specimens. We evaluated this panel in 250 patients with stage II/III CRC who were treated with or without 5-FU chemotherapy resulting in successful generation of libraries for next
32 Andrew Gogos
Genetic and pharmacological disruption of YAP signaling impairs glioma cell growth and differentiation

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Aim: To explore the effects of inhibiting Yes-associated protein (YAP) on glioma growth and differentiation in vitro.

Methods: In vitro experiments were performed using the glioma cell lines U87, U118 and MU004, a Royal Melbourne Hospital glioma stem cell line. A doxycycline inducible shRNA knockdown model was developed. Cells were stably transfected with GFP expressing lentiviral shRNA. Two different YAP specific shRNAs were used and a scramble construct (ie. random non-targeting shRNA) was used as control. Cells were then sorted by flow cytometry for expression of the vector. After activation, proliferation was quantified using an MTT assay and cell morphology was assessed by light microscopy. Additionally, the above assays were utilized after the cells were treated with verteporfin, a YAP inhibitor. Experiments were completed in triplicate and means compared using Students t-test.

Results: Induction of YAP shRNA resulted in up to 61% reduction in glioma cell proliferation in all cell lines at 5 days (p < 0.01). The scramble shRNA had no significant effect. Morphologically, YAP shRNA cells were less numerous, larger, and had fewer and shorter processes. Treated cells never reached full confluence despite extended culture duration. After withdrawal of doxycycline from the culture media (to inactivate the shRNA), cells began proliferating again. Their morphology returned to normal and they reached full confluence. YAP inhibition with verteporfin resulted in up to 76% reduction in proliferation in all cell lines at 5 days (p < 0.01). Similar morphological changes were noted as above.

Conclusion: Pharmacological and genetic disruption of YAP signaling results in significantly impaired glioma cellular proliferation and altered morphology in vitro, suggesting YAP is a promising therapeutic target in glioma. Follow up experiments will test these findings in vivo using an orthotopic xenograft model.

33 Ruth Mitchell
The structure and function of the EGF receptor in glioblastoma multiforme

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The epidermal growth factor receptor (EGFR) gene is frequently mutated in glioblastoma multiforme (GBM), affecting almost 30% of all GBM patients. Furthermore, a constitutively activated form of the receptor, encoded by EGFRvIII, also occurs in a high proportion of high-grade glioma tumors, especially when the EGFR gene is amplified (Lau, Magill et al. 2014).

Current therapies for GBM are unsatisfactory. Standard therapy, comprising post-resection radiotherapy with alkylating chemotherapy followed by adjuvant chemotherapy, leads to a median survival of 14.6 months with a two-year survival of 26.5% (Stupp, Mason et al. 2005). Patients with favourable MGMT promoter methylation status have a two-year survival of 46%, with a median survival of 21.7 months (Hegi, Diserens et al. 2005).

Currently, some EGFR antagonists and inhibitors, including gefitinib, tarceva, erlotinib, and cetuximab, are approved for use in other human cancers (e.g. colon cancer). Unfortunately these targeted drugs have had a limited benefit in GBM (Lau, Magill et al. 2014). Purified full-length EGFR will be assembled into discoidal phospholipid bilayer membranes, termed nanodiscs, with the size of the nanodisc determined by the Membrane Structural Protein (MSP) (Nath, Atkins et al. 2007). In this format not only the structure of the EGFR, but the binding and action of selected antibody antagonists and EGFR kinase inhibitors will be investigated. The effects of these agents on the structure of nanodisc-EGFR will be investigated by electron microscopy.

We will present the cytostatic and cytotoxic effects of agents which target the EGFR in a gliosphere model in vitro, with a view to improving the killing of glioma cell in vivo. The effects of pair-wise combinations of antibodies, conjugated-antibodies (e.g. polyethyleneimine-polyethyleneglycol (PEI-PEG)–polyinosine/cytosine (polyc) conjugates (Abourbeh, Shir et al. 2012), kinase inhibitors and/or pro-apoptotic drugs on the survival of human gliospheres in vitro will be compared.

34 Chenkai Ma
A comprehensive meta analysis shows circulating mirnas in gliomas as potential diagnostic biomarkers

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Aim: To identify the diagnostic accuracy of differential expressed circulating miRNAs in gliomas and their biological function in tumour progression.

Background: Glioma is the most common malignant central nervous system tumour with rapid progression and metastasis, which require we identify some diagnostic tools for gliomas during the early stages. MicroRNAs (miRNAs) demonstrated their accurate predictive capacity in cancers and neurological diseases including gliomas. Despite that altered miRNAs are correlated with diagnosis and prognosis with gliomas from healthy controls, there is still a controversial issue.

Methods: PubMed, Medline and Cochrane database were searched for collecting studies which demonstrated single miRNA or miRNA panel derived from circulating blood were potential diagnostic biomarker for gliomas. The pooled diagnostic parameters were calculated by random effect models and the overall diagnostic performance of alter miRNAs was illustrated by the summary receiver operator characteristic (SROC) curves. The pooled sensitivity, specificity, positive likelihood ratio (PLR) and negative likelihood ratio (NLR) from each study were calculated by mixed model.

Results: Eleven studies involving 27 miRNAs from serum or plasma met our criteria and were included in this meta-analysis. Sixteen of 27 miRNAs were up regulated in the serum or plasma compared with the healthy controls, whilst 11 miRNAs were down expressed. The pooled PLR, NLR and DOR were 6.95 (95%CI, 4.82-10.00), 0.17 (95%CI, 0.10-0.21) and 47.41 (95%CI, 25.13-89.43), respectively. The pooled sensitivity, specificity and area under the curve (AUC) were 0.87 (95%CI, 0.82-0.91), 0.87 (95%CI, 0.82-0.91) and 0.93 (95%CI, 0.90-0.95), respectively, which demonstrated circulating miRNAs are capable of distinguishing glomas from healthy controls.

Conclusions: Collectively, this meta analysis demonstrated circulating (serum or plasma) miRNAs are promising diagnostic biomarkers for gliomas, which can distinguish gliomas from health controls with excellent performance. Circulating miRNAs have the potential to being the ideal biomarkers for liquid biopsy.
Neuroscience

35 Vilija Jokubaitis
Pregnancy protects against long-term disability accrual in relapsing-remitting MS
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Background: The long-term effects of pregnancy on the accumulation of disability in relapsing-remitting MS (RRMS) are poorly understood. Past studies report contradictory findings including: worsening of disability, no change, or benefit.

Objective: To determine the effect of pregnancy on 10-year EDSS outcomes in a relapsing-remitting cohort of women who initiated injectable disease-modifying therapy (DMT).

Methods: Using data obtained from MSBase, we identified females with RRMS followed for a minimum 10-years after initiating treatment with their first injectable DMT. Patients need only have remained on therapy for one day and were monitored on any approved DMT, or no therapy thereafter. Median EDSS score changes over a 10-year period were determined. Only patients with clinically significant EDSS score changes (according to a 3-step progression/regression paradigm), or those with no change in score were included in the analysis. All reported pregnancies, including those that were prematurely terminated, were included in median quartile regression analyses. All analyses were adjusted for age, disease duration, baseline EDSS, DMT use, annualised relapse rate, and location. Sensitivity analyses were further performed.

Results: We identified 1472 females meeting inclusion criteria. 241 pregnancies for 179 females were reported that resulted in live births, with a further 10 women reporting one or more aborted pregnancies. 108 (45%) of pregnancies were conceived whilst on therapy. Women spent an average 82% of the observation period on therapy. EDSS scores increased by a median 1.5 points (interquartile range 0, 2.5) at 10 years post-baseline. Pregnancies were independently associated with lower EDSS scores over the 10-year observation period ($\beta$-coefficient -0.46, 95% CI: -0.49 to -0.43, p=0.007). Comparing the proportion of the observation period spent pregnant to that spent on first-line therapy, we found on adjusted analysis, that even when taking in to account post-partum relapse spikes, pregnancy was 6x more therapeutically potent than DMT (95% CI: 6.6x-4.2x). Sensitivity analyses including only those women whose EDSS scores were subsequently confirmed (n=761) supported the above results.

Conclusion: Our study provides evidence of long-term benefit of pregnancy in women with relapsing-remitting MS, with a dose-response effect on disability accrual. Further we demonstrate that pregnancy is more effective in preventing disability accrual than first-line DMT.

36 Bruce Campbell
CT perfusion imaging profiles and response to endovascular reperfusion in pooled analysis of randomized trials of endovascular stent thrombectomy
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Background and purpose: The role of CT-perfusion imaging in selection of patients for endovascular thrombectomy has been controversial. We pooled data to investigate the association of CT-perfusion imaging profiles in 5 recent randomized trials of endovascular stent thrombectomy.

Methods: Patient-level imaging data from the MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME and REVASCAT trials were pooled (HERMES Collaboration). CT-perfusion data were uniformly reprocessed using RAPID software (IschernaView) as used in the EXTEND-IA and SWIFT PRIME trials. Irreversibly injured ischemic core was defined using a relative cerebral blood flow threshold<30% of normal brain. Tissue at risk of infarction (ischemic penumbra) was estimated using a Tmax threshold >6 seconds. The association between pre-treatment ischemic core and mismatch volumes and the 90 day modified Rankin scale (mRS) was examined by treatment status and reperfusion status. The number needed to treat (NNT) to achieve at least 1 unit improvement in the mRS with endovascular treatment versus control was calculated as a function of ischemic core volume as a continuous variable. A similar analysis was performed for the NNT to achieve an extra patient with independent outcome (mRS 0-2).

Results: The results will be presented at research week and are expected to include over 400 patients with pre-treatment CT-perfusion imaging.

Conclusions: This analysis will comprise the largest series examined to date with CT-perfusion imaging prior to endovascular therapy using current technology. The resulting insights into whether CT-perfusion parameters are prognostic, treatment effect modifying or both will be highly relevant to clinical practice.

37 Chris French
How do drugs cause seizures as side effects?
Chris French
RMH, University of Melbourne

Aim: To discover how two types of drugs, antipsychotics (haloperidol, "HAL" and clozapine, "CLZ") and a commonly used analgesic (tramadol, "TDL") could cause seizures in patients.

Background: Seizures are a serious side effect of antipsychotic drugs as well as the analgesic tramadol. The rate of seizures is dose-dependence, but can reach 9% in persons taking high-dose clozapine. Seizures can cause physical injury, as well as anxiety and impairment of social function.

Methods: Isolated rat CA1 hippocampal pyramidal neurons were voltage clamped in vitro, and relevant drugs were acutely applied via direct perfusion. Voltage clamp depolarisations were used to evoke voltage-dependent potassium channels. Greater than 50 neurons were recorded for the antipsychotic drug experiments, and n was 5-6 for tramadol experiments. A neural network model was constructed for complementary observations on an "in silico" model.

Results: Antipsychotic drugs and tramadol both strongly suppressed voltage-gated potassium currents. The IC50's for haloperidol and clozapine were 1.5 uM and 7.39 uM respectively. At likely therapeutic concentrations, 10 and 100 nM for HAL and CLZ respectively, a reduction in peak potassium currents of about 10% was observed. The inhibitory effect of the antipsychotic drugs was not blocked by a dopamine type 2 antagonist, L741,626. Likewise, an ERG class of channel blocker again did not change the potassium channel inhibition. It was therefore inferred that the effect of HAL and CLZ were not mediated through dopamine receptors or ERG channels. The computer network model developed "seizure-like" activity if potassium conductances were reduced in amplitude by proportions similar to those that might be observed thereapeutically. Tramadol also inhibited voltage gated postassium channels with an IC50 of 31 uM. Its effect was not inhibited by an opiate receptor blocker.

Conclusions: Inhibition of neuronal voltage-gated potassium channels was demonstrated at therapeutic concentrations of antipsychotic drugs and tramadol. These effects are likely to explain the seizures that occur as side effects of these drugs, as potassium currents have a strong suppressive effect on excitability in neurons. It is also possible that potassium channels may be therapeutic targets of these drugs.

38 Ariel Dahan
Can semiautomated imaging software allow junior medical and radiology staff to monitor multiple sclerosis disease progression as well as neuroradiologists?
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Aim: To assess whether a semiautomated software allow doctors in training to accurately interpret magnetic resonance imaging (MRI) studies in patients with multiple sclerosis (MS) for disease progression as effectively and efficiently as neuroradiologists.

Background: Optimizing MS management with disease-modifying drugs requires regular monitoring by neurologists in the community. As most demyelinating events are clinically silent, neuroimaging is the primary tool used to measure disease progression. MS follow-up can
Risk factors for contact lens-related microbial keratitis in Singapore

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Risk factors for contact lens-related microbial keratitis in Singapore and estimate their impact on disease load. Background: Patterns of contact lens prescribing, lens supply, wearer behaviour and environmental microbiota vary across different cultures and climates. These may impact on the risk of contact lens related microbial keratitis. It is therefore important to examine specific populations to determine specific risk factors associated with the use of contact lenses in these populations. This is the first study to measure the risk of all contact lens related microbial keratitis in Singapore.

Methods: Cases were contact lens wearers presenting to Singapore National Eye Centre with microbial keratitis between 2008 and 2010. Community contact lens wearers were recruited as controls. All wearers completed a previously validated questionnaire describing contact lens wear history, hygiene and compliance habits, and demographics. Risk factors significant in univariate analysis (P<0.2) were evaluated in a multivariate model.

Results: In all, 58 cases of microbial keratitis and 152 contemporaneous controls were identified. When controlling for other variables, Chinese had a 7 x lower risk compared with other races (95% CI: 2.3-21.3, P=0.001). Those aged between 25 and 44 years were at 3 x increased risk compared with younger wearers (95% CI: 1.1-9.6, P=0.04). Occasional overnight contact lens wear (less often than one night per week) was associated with a 4 x higher risk (95% CI: 1.2-15.4, P=0.03) compared with daily use. Not washing hands before handling was associated with a 13 x increased risk (95% CI: 1.9-84.8, P=0.008). Use of multipurpose solution A carried a 16 x higher risk compared with hydrogen peroxide (95% CI: 1.5-174.0, P=0.02). The combined PAR% for modifiable risk factors (occasional overnight wear, not washing of hands, and MPS A) was 82%.

Conclusion: Consistent with previous findings, independent risk factors for contact lens-related microbial keratitis include poor hand hygiene, occasional overnight wear, and type of lens care solution. Prolonged overnight or extended contact lens use was infrequent in this population.
Electroanatomical mapping was performed using a novel basket catheter with 64 electrodes and automated electrogram annotation. Bipolar activation maps were created and regional atrial conduction times calculated. Regional atrial conduction was correlated with the regional voltage map.

Results: In the 16 patients studied, 18 atrial flutter circuits were observed. Eleven (61%) had counterclockwise CTI dependent atrial flutter, 2 (11%) clockwise CTI dependent atrial flutter and one (6%) example of intra-isthmus re-entry. Two (11%) cases of upper loop re-entry were observed. Two (11%) circuits were consistent with left atrial flutter. Maps had a mean of 24202 ± 9939 points acquired in a mean of 21 ± 14 minutes. Activation maps showed marked regional variability in conduction velocity. Notably however, no patients demonstrated conduction slowing within the CTI and this correlated with this region having preserved voltage. Regions of slow conduction (SC) and conduction block (CB) were observed in the following regions: crista terminalis (SC 3; CB 6); septal RA at anatomic region of fossa ovalis (SC 6; CB 2); posterior RA (SC 1, CB 0) superior RA (SC 4, CB 0) and lateral RA (SC 1, CB 0). In all cases the region of SC with isochronal crowding corresponded to an arc or region of lower voltage. There was no fixed pattern to the regions of abnormal substrate demonstrated with marked variability observed even in patients with CTI dependent flutter. Conclusion: During MAT, there is a close correlation between regions of abnormal atrial substrate and regions of conduction slowing. There is considerable individual substrate variation even for an apparently stereotyped arrhythmia such as CTI.

42 Bhupesh Pathik

Can we always believe what we see? Entrainment remains important for diagnosis of atrial macro-reentry in the era of high density 3D mapping

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Introduction: Entrainment mapping is an established electrophysiological technique to identify arrhythmia mechanism as well as define components of the reentrant circuit. With the recent advent of high resolution 3D electroanatomical mapping that allows automated electrogram annotation and rapid acquisition of activation points, the ongoing utility of classical entrainment techniques to define reentrant circuits is uncertain. We sought to determine whether all apparent reentrant loops seen on high density 3D electroanatomical maps are active circuits when using entrainment mapping.

Methods: 16 patients with macro reentrant atrial tachycardia undergoing catheter ablation were studied. High density (HD) 3D electroanatomical mapping was performed using a novel basket catheter with 64 electrodes and automated electrogram annotation. Entrainment mapping was performed at multiple sites in the atria considered to be part of the active circuit on the propagation map.

Results: In the 16 patients studied, 18 atrial flutter circuits were observed. 11 (61%) re-entry circuits were consistent with counterclockwise CTI dependent atrial flutter, 2 (11%) clockwise CTI dependent atrial flutter and one (6%) example of intra-isthmus re-entry. 2 (11%) cases of upper loop re-entry were observed. Two (11%) circuits were consistent with left atrial flutter. Maps had a mean of 24202 ± 9939 points acquired in a mean of 21 ± 14 minutes. In 9 of 11 patients with counterclockwise CTI dependent flutter (diagnosed on activation and entrainment mapping), lower loop reentry appeared to be present with a wavefront crossing the crista terminals posteriorly. However in 6/9 pts (67%), entrainment mapping demonstrated that this location was not part of the active circuit. A passive ascending wave front meeting a passive descending wavefront created the visual appearance of break across the CT which was not actually present. In one further patient, an apparent complete circuit in the RA free wall represented passive circuitous activation only.

Conclusion: HD 3D electroanatomical mapping systems can rapidly produce highly accurate and dense maps of atrial activation patterns during a variety of atrial macro-reentry circuits. However, circuitous propagation not involving in the arrhythmia mechanism can mimic the appearance of a critical reentrant circuit. Simple entrainment mapping remains an important adjunctive tool when using latest generation HD mapping systems.

43 Bhupesh Pathik

Comparison of two-dimensional vs three-dimensional phase mapping in the detection of Rotors during human persistent AF.

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Background: Current mapping systems create 2D phase maps by projecting basket data onto an idealized grid of evenly spaced points. This assumes that the basket electrodes are evenly distributed in the atria, however this may not be correct. We developed novel three-dimensional (3D) phase mapping techniques that utilize the 3D locations of basket electrodes to project phase onto a patient specific 3D surface geometry. We sought to compare differences in AF activation patterns and the prevalence of rotors using 2D versus 3D phase mapping techniques.

Methods: 12 patients with PerAF (mean age 62 ± 8 yrs, median AF duration 4.7 yrs (2-6)) were mapped using a Constellation catheter. In each patient one minute of AF data was exported and analyzed offline using Matlab (Version R2015a). Raw unfiltered data was subjected to sinusoidal recomposition and then phase reconstruction was performed using the Hilbert transform. Customized software was then used to create 2D and 3D phase maps based on the same data. Activation patterns seen in 2D and 3D were classified into i) Wavefronts ii) Rotors (≥ 2 rotations of 360°) iii) focal sources with radial spread.

Results: Over 4000 individual wavefront patterns were analyzed. Using 2D phase mapping, AF was characterized by highly dynamic activation patterns made up of single (72.0±8.4%) and two simultaneous wavefronts (4.2±1.9%), focal activations (22.4±6.9%) and rotors (1.3±0.8%). Although rotors were seen in 8 patients during 2D phase analysis they were all transient and isolated lasting only a median of 5 [IQR 4,9] rotations. The most common (75%) site for rotor formation was the posterior left superior pulmonary vein. In 25% of cases, the rotor was located at the posterior right superior pulmonary vein. When the same data was analyzed using 3D phase mapping AF was characterized by single wavefronts (79.6±7.5%), two simultaneous wavefronts (5.3±1.2%), focal activations (14.5±5.3%) and rotors (0.6±0.3%). Transient isolated rotational activity was seen in only 3 patients lasting for median 4 [IQR 4,7] rotations. The location of the rotors was variable in each patient; anterior roof, anterior LSPV and posterior LSPV. None of the rotors seen in 2D were seen in corresponding time segments in 3D and conversely none of the rotors seen in 2D were seen in 3D.

Conclusion: The prevalence of rotors is highly dependent on the technique used to animate phase. 2D phase mapping oversimplifies spatial relationships and can create false rotors that are not present during 3D phase mapping.

44 Bhupesh Pathik

The efficacy of multipolar basket catheters in mapping the entire left atrium in human persistent atrial fibrillation

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Background: Novel methods of mapping the human atrium in atrial fibrillation (AF) include the multi-electrode basket catheter which allows simultaneous electrogram acquisition of the left atrium. However, the efficacy of this catheter in providing adequate electrode contact and electrogram recordings of the entire left atrium is unclear.

Methods: Global left atrial mapping was performed in 12 patients using the 56 bipolar electrode Boston Scientific Constellation basket catheter. Appropriate basket size was chosen based on pre-procedural cardiac CT imaging. A multi-procedural transesophageal echocardiography was performed to define components of the atrial anatomy. We analyzed specific spatial characteristics of the basket catheter and in particular its ability to provide global LA mapping for AF mapping including 1. Number of electrodes within 2 mm of the endocardial surface 2. Number of electrodes with suitable signal quality 3.
Percentage of LA mapped 4. Interspline distance (distance between adjacent splines).
Results: 12 patients were studied. 60mm basket catheters were used in 3 (25%) patients, 48mm catheters in 8 (67%) and the 38mm catheter in 1 patient. In 50% of patients, the Agilis sheath was used for basket catheter positioning. The mean number of electrodes within 2mm of the endocardial surface was 29 ± 3 (45%). Of the 56 bipolar electrograms, mean of 28 ± 7 (48%) had suitable signal quality to allow annotation for activation times. The mean percentage of LA mapped was 20.3%. There was marked variability in the inter-spline distance. The greatest inter-spline distance was at the equator (19.3±1.2mm) with the least inter-spline distance at the distal pole (12.4±0.9mm).
Conclusion: The constellation multipolar basket catheter provide limited coverage of the left atrium with poor signal quality and contact with the endocardial surface. Improved catheter technology is necessary to facilitate global mapping of the left atrium.

45 Bhupesh Pathik
Three-dimensional wavemapping of human persistent atrial fibrillation
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Background: The mechanism of persistent atrial fibrillation (AF) remains uncertain. We sought to determine the prevalence of driving rotors and drivers during human persistent AF using a novel 3D Wavemapping technique that projects local activation onto a patient specific 3D geometry.
Methods: Global left atrial mapping was performed during spontaneous AF in 12 patients using the multi-electrode basket catheter and analyzed offline using novel 3D wavemapping software. Continuous one-minute AF recordings were analyzed offline using customized signal processing software (CEPAS, Curotech). The local activation at each electrode site was determined using automatic annotation with manual correction to the peak of the bipolar electrogram. Activation data was then projected onto the 3D surface geometry using customized software. Activation patterns were classified into i) Wavefronts (single or multiple) ii) Rotational circuits (2 to 2 rotations of 360° iii) or focal sources with radial spread. In addition, the spatial distribution and origin of wavefronts was determined.
Results: Over 5000 activation patterns were analyzed. Mean AF cycle length per AF segment analyzed was 185±107ms. Activation patterns observed were highly dynamic and heterogeneous. The most common patterns were i. single wavefronts (75.9%), ii. two simultaneous wavefronts 6.4%, iii. transient focal activations in 17.7%. No sustained focal activity or rotors were seen. In the majority of maps (54.2%), the wavefronts appeared to originate from the anterior wall of the left atrium. Focal activity most commonly arose from the posterior wall adjacent to the left superior pulmonary veins. No wavefronts or focal activity was seen to originate from the left atrial appendage.
Conclusion: Activation patterns in persistent atrial fibrillation are highly heterogeneous with single wavefronts appearing to be dominant subtype. No rotors or sustained focal activity were observed.

46 Shobi Shivathambo
The prevalence of sleep disordered breathing in patients admitted for video-EEG monitoring
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Background: Sleep disordered breathing (SDB) is an increasing problem in sleep-disordered breathing patients with an increased risk of cardiovascular disease including stroke, hypertension, acute myocardial infarction, diabetes, and premature mortality, and affects 9-24% of the general population. Disturbances to sleep architecture can result in increased hypersomnolence, altered mood, and decreased cognition and quality of life. An underlying sleep disturbance may lower seizure threshold, decrease quality of life and cognitive functioning in this population.
Methods: We included 158 patients, admitted to our video-EEG monitoring unit who underwent polysomnography between February 2012 and September 2015. The polysomnography was analysed by a qualified sleep scientist, and reported by a respiratory and sleep physician. Sleep staging and scoring was in accordance with the current American Academy of Sleep Medicine (AASM) guidelines. Comparisons across groups were performed using Chi-Square test.
Results: There was an increased prevalence of SDB in patients admitted for VEM monitoring with 49/158 (31%) meeting the minimum diagnostic criteria (apnea-hypopnea index ≥5). Patients with epilepsy had the highest prevalence of SDB (33%) followed by PNES (29.5%) and those with both disorders (18.1%), though this did not differ significantly between groups. There were no significant differences in cognition, and quality of life measures across these groups.
Conclusion: Routine polysomnography is a useful diagnostic tool in patients admitted for video-EEG monitoring, and may lead to correct identification of nocturnal events. Treatment of an underlying sleep disorder may improve daytime functioning and psychiatric comorbidities, and also optimize seizure control in people with epilepsy.

47 Shobi Shivathambo
Cardiopulmonary function during the peri-ictal state of epileptic and psychogenic non-epileptic seizures
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Background: Sudden, unexpected death in epilepsy (SUDEP) is a significant cause of mortality in epilepsy, for which there are no known interventions. Terminal cardiopulmonary arrest, often in association with an epileptic convulsive seizure, is proposed to be the final mechanism of SUDEP. PNES can superficially resemble epileptic seizures, but are not accompanied with electrophysiological changes. Patients with PNES may also experience cardiopulmonary changes during their events, which are thought to be in relation to stress and trauma. Despite this, cardiopulmonary function is poorly understood during both epileptic seizures and PNES.
Methods: We studied 31 patients who were admitted to our video-EEG monitoring unit and routinely had a polysomnography between February 2012 and September 2015. A total of 88 events were recorded, which were classified as epileptic convulsive seizures, epileptic non-convulsive seizures, and PNES. Heart and respiratory rates, heart rate variability (HRV), and blood oxygenation using pulse oximetry were analysed for the pre-ictal, ictal and post-ictal phases of each event. Values were then averaged for each patient by seizure type. Comparisons across groups were performed using the Kruskal-Wallis test.
Results: There were significant and prolonged changes to cardiac function in the epileptic convulsive seizures. Changes to maximal heart rate differed across the three event groups, being more pronounced in the epileptic convulsive seizures (p = 0.024). HRV showed a distinctive bifasic pattern where there was a significant increase from the pre-ictal to ictal phase and then marked suppression from the ictal to the post-ictal phase, which differed from the non-convulsive epileptic and non-epileptic psychogenic groups (p = 0.0001). Epileptic convulsive seizures were also associated with a characteristic pattern of hyperventilation, which differed from that of PNES (p = 0.0002).
Conclusion: This study demonstrates clear associations between cardiac and respiratory dysfunction in convulsive seizures that may have significant implications for the pathophysiology of SUDEP. Cardiopulmonary monitoring, or polysomnography is currently not standard practice in video-EEG monitoring, but should be considered as it may provide crucial insights into cardiorespiratory function during seizures.
48 Natasha Smallwood

Utility of individualised patient breathlessness plans for refractory dyspnoea due to advanced chronic obstructive pulmonary disease – a pilot study

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Background: Up to 98% of patients with advanced Chronic Obstructive Pulmonary Disease (COPD) experience distressing breathlessness. Whilst some guidelines recommend using non-pharmacological strategies and opioids to palliate refractory dyspnoea, a standardised approach is lacking.

Aim: To assess the utility of an individualised Patient Breathlessness Plan (PBP) for managing refractory dyspnoea in patients with severe COPD.

Methods: The PBP and supporting educational leaflets were developed using both published literature and expert opinion. Consumer and health professional feedback were sought to optimise content. Patients with severe COPD and refractory dyspnoea attending the Advanced Lung Disease Clinic at The Royal Melbourne Hospital were offered a PBP and dyspnoea education. Demographic data and disease severity were recorded. Hospital Anxiety and Depression Scale (HADS), Self-Administered Standardised Chronic Respiratory Questionnaire (CRQ-SAS), and Modified Medical Research Council (MMRC) and Numerical Rating Scale (NRS) dyspnoea scores were measured at baseline and after 6 weeks.

Results: Twenty patients participated: 12 (60%) female, mean age 74.7 years (SD 8.9). Mean lung function: FEV1 0.7L (35%), FVC 1.8L (74%), and DLco 34%. Median MMRC dyspnoea score 3.6. Fifteen patients (75%) used home oxygen and 19 (95%) had completed pulmonary rehabilitation prior to study enrolment (1 declined to participate). Twelve patients (60%) used opioids for refractory dyspnoea and/or pain, with no dose change in the 6 weeks prior to start of enrolment. Median opioid dose was 27mg/24hours oral morphine equivalent (IQR 12-37mg).

To date, 16 patients have completed follow-up and are included in post-PBP data analysis. One patient died during the follow-up period, with palliative care from her GP in her nursing home. Pre-PBP (n=20), Post-PBP (n=16).

Post-PBP scores (pre-PBP scores in parentheses) presented below as mean±SD: Decrease in scores on the MMRC, NRS and HADS correspond to improvement; Increase in scores on the CRQ-SAS correspond to improvement; MMRC: 3.2±0.7 (3.6±0.5); NRS: Average 4.6±2.2 (5.9±1.4), Worst 5.4±3.0 (7.4±1.6), Exertion 6.3±3.0 (8.3±4.9), Depression 7.2±4.0 (7.9±5.0); CRQ-SAS: Dyspnoea 3.5±1.2 (3.3±1.3), Fatigue 3.0±1.2 (3.1±1.3), Emotional Function 4.2±1.4 (4.2±1.4), Disease Mastery 4.6±1.3 (3.9±1.5); A clinically significant improvement in dyspnoea was seen on the NRS, and in disease mastery on the CRQ-SAS.

Conclusion: We have conducted the first study evaluating the efficacy of a PBP in an Australian setting. Results demonstrate a trend towards improvement in multiple domains, and suggest this tool may be a useful adjunct in the complex management of refractory dyspnoea.

49 Andrea Hall

Development of multi faceted interventions to improve emergency department discharge processes

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Background: A quality improvement project was undertaken at Royal Melbourne Hospital to standardise clinical processes at discharge for adult patients. Although a significant improvement in vital sign documentation was recorded within one hour of discharge, a number of environmental, procedural and operational limitations were identified. This study aimed to explore the barriers and facilitators of safe discharge home from the ED and make recommendations for process improvement.

Methods: Qualitative research design at five EDs using focus groups with nurses, doctors, care coordinators and consumers. A practice development model (claims concerns issues) was used to unpack barriers and facilitators to current discharge practices.

Results: Nineteen focus groups were conducted involving 270 staff. Limitations to current discharge processes were consistent across sites. Five core themes emerged: vital sign issues (documentation, monitoring trends, escalating early review and thresholds for safe discharge); roles and responsibilities, time management, stream allocation and inter-disciplinary communication. Nurses focused on performing, interpreting and responding to vital sign abnormalities. Medical staff placed greater emphasis on individual responsibilities and medicolegal considerations. Care coordinators focused on the need for consistent discharge screening to occur for all patients as well as the need to integrated care between acute and community services. All participants shared the concern to clarify roles and responsibilities of staff at discharge, as well as improved communication using multiple modalities.

Conclusion: The core themes derived from the focus groups have informed the development of multi-faceted interventions designed to optimise patient safety and avert subsequent unscheduled return to the ED.

50 Emma Callegari

Bone turnover markers in young women: the Safe-D study

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Aim: The aim of this analysis was to examine the distribution and association of BTMs with relevant covariates.

Background: Interpretation of bone turnover marker (BTMs) relies upon robust normative data but this is limited in young women.

Methods: Subjects were 16 – 25 year-old females participating in the Safe-D study. Serum obtained from 312 participants was tested for BCTX and P1NP (Roche Elecsys automated analyser).

Results: After excluding 98 participants based on incomplete surveys, medical history, medication use or pathology results, the reference interval (central 95% of normalized values) was 0.2-1.1 ng/mL for BCTX and 16-143 ug/L for P1NP. BTMs were inversely correlated with age and years since menarche (p<0.001 for both). BCTX and P1NP were lower in hormonal contraception users (BCTX: users 0.52 vs. non-users 0.64 ng/mL; P1NP: 61 vs. 78 ug/L, p<0.001 for both). In a gamma regression model, BCTX was correlated with contraceptive use (β = 0.0066, p=0.001), lean mass (β = 0.091, p=0.001) and fat mass (β = 0.056, p=0.007) Restricting the analysis to those aged 20 and above, age and fat mass were no longer associated with P1NP. BTMs were not associated with 25OHD or whole body BMD.

Conclusion: To our knowledge, this is the first study to report BTMs in healthy women aged 16 to 25 years; these findings have important application in bone health research and in generating age-specific reference intervals.

51 Catherine George

Time to first dose of antibiotic in patients presenting to the Emergency Department with sepsis

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Aim: The Antimicrobial Stewardship (AMS) Clinical Care Standard (CCS9200) specifies that patients with severe sepsis or evidence of septic shock. The aim was to identify a suitable method for assessing time to antibiotics for patients with sepsis and severe sepsis after presentation to our emergency department (ED) and to determine the median time to antibiotic for these patients.

Method: This retrospective study was conducted at the Royal Melbourne Hospital, an adult tertiary referral hospital. All patients who...
received a dose of parenteral antibiotic in the ED during the one month audit period were assessed for inclusion. Time of triage and the time of antibiotic dispensing from Pyxis®, an automated medication dispensing cabinet used as a surrogate for time of antibiotic administration, were collected. Patient observations and pathology results, available electronically, enabled analysis based on presence of Systemic Inflammatory Response Syndrome (SIRS) criteria and markers of severe sepsis. Sepsis was defined as presence of two or more SIRS criteria thought to be due to infection. Severe sepsis was defined as sepsis with systolic blood pressure (SBP) <90mmHg or lactate >4mmol/L.

Results: The median time between ED triage and first dose of parenteral antibiotic was 152 minutes (range 17 to 1072 minutes) for the 348 patients in this study. 156 patients met the definition of sepsis, and the median time to first dose of antibiotic was 124 minutes (range 17 to 818 minutes). The median time to antibiotic for patients with sepsis and SBP <90mmHg was 60 minutes (range 18 to 195 minutes), and 68 minutes (range 18 to 448 minutes) for those with lactate >4mmol/L.

Conclusion: This study identified a method for assessing compliance with the AMS Clinical Care Standard, and showed that the median time to antibiotic administration for patients with severe sepsis was just over 1 hour, with a range that indicated evidence of room for improvement. This study provides baseline data for the development of targeted quality improvement initiatives in the ED.

52 John Moi

The management and outcome of low back pain presentations to the emergency department: a retrospective cohort study

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Background: Low Back Pain (LBP) is the most common musculoskeletal problem seen in hospital emergency departments (ED) and accounts for approximately 2% of all presentations. However, little is known about the management and outcome of LBP presentations to ED, and there are currently no evidence-based guidelines to inform best practice for managing LBP in ED and organising patient follow-up after discharge with severe sepsis just over 1 hour, with a range that indicated evidence of room for improvement. This study provides baseline data for the development of targeted quality improvement initiatives in the ED.

Aim: To review the management and outcomes of LBP presentations to an Australian tertiary hospital ED.

Method: We performed a retrospective cohort study of patients aged over 18 years that presented to the Royal Melbourne Hospital (RMH) ED with mechanical LBP between 1 January 2015 to 31 December 2015. ICD-10 codes were used to identify patients with LBP and clinical information was collected from the hospital health information systems.

Results: There were 1069 patient presentations for LBP to the RMH ED during the twelve-month study period. Patients had a median (SD) age of 47 (19) years, and males and females were equally represented (M:F ratio of 1:1.02). The majority of presentations were for acute (70%) or acute-on-chronic (30%) LBP, and most patients had self-referred without prior GP consultation (89%). 13% of all LBP presentations had one or more risk factors of whom 46% underwent spinal imaging and 56% had blood tests. Of patients without ‘red flags’, 25% had spinal imaging and 23% had blood tests. The most commonly prescribed analgesia in ED was opioids (71%), paracetamol (55%), NSAIDs (50%), neuropathic agents (13%) and benzodiazepines (23%). Oxycodone was the most frequently prescribed opioid (78%), 56% of patients were discharged home from ED, while the remainder were admitted to ED Short Stay Unit (SSU) (28%) or to an inpatient unit (16%). Physiotherapy review was more common for patients admitted to SSU (70%) compared to patients discharged from ED (15%). At discharge, 75% of patients were prescribed strong opioid analgesia, and 40% of patients were referred for GP or outpatient specialist follow-up and 11% for physiotherapy.

Conclusion: Our study findings demonstrate that the majority of LBP presentations to ED are for acute LBP and most patients have self-referred without prior GP consultation. Despite being prescribed strong opioid analgesia at discharge, many patients have no designated follow-up arranged. These results highlight areas for improved patient care and may help inform the future development of evidence-based guidelines for LBP management in ED.

53 Anton Musienko

Normal vital signs and chest x-ray are poor predictors of blunt thoracic aortic injury - 11 year experience at Level I Trauma Centre

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Aim: To analyse the presentation (clinical and radiological) and management of the Blunt Thoracic Aortic Injury over 11 year period at the Level I State Trauma Centre

Background: Blunt Thoracic Aortic Injury (BTAI) has a variable presentation and degree of severity and a missed injury can be catastrophic.

Methods: A retrospective study of the prospective trauma database of patients with BTAI at a Level I State Trauma Centre, from January 2003 to December 2013 was conducted. Demographics, presentation, management and outcomes were analysed.

Results: A total of 66 patients with BTAI were identified, with a mean Injury Severity Score of 38. BTAI was managed in 62 of these (3 died of other injuries, and 1 was transferred to another centre). Fourteen patients (21.2%) had normal vital signs. 63 patients had a CXR, and in nine (14.3%) it was normal. 42 (67.7%) patients were managed endovascularly, 16 (25.8%) conservatively and 4 (6.5%) had an open repair. 64.3% of patients (9 out of 14) with normal vital signs, and 55.6% patients (5 out of 9) with a normal CXR required a surgical intervention. Overall mortality was 15.2%, with 77.7% of fatalities occurring within 8 hours of arrival to emergency department.

Conclusion: Normal vital signs and chest x-ray do not exclude BTAIs, including those aortic injuries that require surgical repair. CT scan evaluation of the high-risk patients should be based on the mechanism of injury, rather than on the examination or chest radiographic findings.

54 Simote Foliaki

Prior acute synaptotoxicity at the CA1 region of the stratum radiatum

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Aim: To assess the acute preion synaptotoxicity at the CA1 region of the stratum radiatum.

Background: Although misfolding of normal prion protein (PrPC) into abnormal conformers appears critical for disease transmission and thereby initiation of pathogenesis, the precise molecular species causing neurotoxicity in prion disease is unknown. Evidence supports that misfolded PrP conformers, probably as soluble oligomers, are likely to be a principal determinant of neurotoxicity but this remains unproven and the specific biophysical properties of the relevant toxic species are unknown. Hippocampal synaptotoxicity within the CA1 region of the stratum radiatum is reported as a relatively early feature of prion disease pathogenesis. Long-term potentiation (LTP) within the CA1 region is an important neurophysiological correlate of hippocampal-dependent declarative memory and LTP disruption has been exploited to model other synaptotoxic peptides, such as soluble oligomeric Aβ42.

Methods: Ex vivo prions/misfolded PrP were sourced from terminal prion (M1000 strain) disease mouse brains including preparations following PPrp immuno-depletion and proteinase-K (PK) treatment to decrease total PPrp species and specifically select for PK-resistant PrP species (PPrP), respectively. Synaptotoxicity in the form of disrupted LTP was assessed in an electrophysiological model employing Multichannel Electrode Arrays interrogating the Schäffer collateral pathway within the CA1 region, with hippocampal slices derived from C57BL/6 wild type and genetically matched PrP knockout mice following exposure to various ex vivo preparations.

Results: LTP from both 12-week and 11-month old wild type mice was significantly impaired by 24-27% after brief exposure to 0.5% (w/v) crude M1000 brain homogenates. The LTP impairment was associated with reduced post-tetanotic potentiation suggesting likely coconcurrent presynaptic dysfunction. Specifically immuno-depleting 72% ± 9% of...
PrP species from M1000 brain homogenates significantly restored LTP by 70%, thus showing that the acute synaptotoxicity of ex vivo prion preparations is tightly linked to the presence of PrP species. Further, LTP remained significantly impaired by 24% following exposure to M1000 brain homogenate treated with 5 μg/ml PK (sufficient to completely degrade PrPC), demonstrating that PrPres is intimately linked to acute prion synaptotoxicity. LTP disruption was confirmed to be PrPC independent, with PrP knockout mice demonstrating significant impairment similar to wild type mice after exposure to crude M1000 brain homogenates. Studies of the pathophysiological basis to the synaptotoxicity employing biochemical analyses of treated hippocampal slices are ongoing.

Conclusion: We have developed a robust quantitative model of acute prion synaptotoxicity, demonstrating that PrPres species appear directly responsible and can act independent of PrP expression.

55 Chris French
Supercomputer modelling of antiepileptic drug effects on ion channels

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Aim: to identify the binding regions of a commonly used antiepileptic drug, phenytoin (PHT), with its ion channel target using atomic-resolution computer modelling. These interactions were compared with a common local anaesthetic, benzocaine (BZC).

Rationale: Many antiepileptic drugs and local anaesthetics are considered to inhibit voltage gated sodium channels in a state-dependent manner. It is commonly thought both classes of drug bind at an intracellular site. However, there remains much uncertainty as to the validity of these assumptions. We attempted to clarify these issues by performing extensive unbiased atomic scale (~8000 atoms) simulations of PHT and the local anaesthetic benzocaine binding to the bacterial NavAb channel structure derived from crystallography data.

Methods: Newly derived CHARMM models of PHT and BZC were used to explore interactions with lipid and the NavAB channel using the Anton supercomputer over a time scale of microseconds.

Results: PHT displayed relatively strong binding at the membrane interface with a minimum of ~4.1±0.1 kcal/mol allowing both aromatic rings to reside in the lipid region. It was found to cross the membrane on the sub-millisecond scale (35±3ms-1), but about 2 orders of magnitude more slowly than BZC, and in a much more restricted region of the channel compared to BZC. Surprisingly high affinity binding of PHT was found to the pore domain and voltage sensing domain interface.

Conclusions: These simulations provide potential explanations for a wide range of experimental observations, including the role of slow inactivation and voltage-sensing regions for sodium channel modulators such as phenytoin. They also provide very high resolution data about potential binding sites that will inform further pharmacological studies as well as drug design.

56 Chris French
Anti-epileptic drug combination efficacy in an in vitro seizure model – Phenytoin and Valproate, Lamotrigine and Valproate

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Aim: To study the relative efficacy of different classes of commonly used anti-epileptic drugs (AEDs) with different mechanisms of action, individually and in combination, to suppress seizure-like discharges in an in vitro model.

Background: Despite the undisputed efficacy of many AEDs, about 30% of the patients continue to have seizures. Although there is strong clinical evidence that combinations of drugs can be beneficial, the ‘gold standard’ monotherapy, there has been no clear demonstration of synergistic effects that might be expected from the use of different classes of drugs. The goal of ‘rational polytherapy’ has not yet been achieved.

Methods: Extracellular field potential were recorded in 450 μm thick transverse hippocampal slices prepared from juvenile Wistar rats, in which ‘seizure-like discharges’ (SLD’s) were produced with a high-K+ (8.5 mM) bicarbonate-buffered saline solution. Single and dual recordings at stratum pyramidale of CA1 and CA3 regions were performed with 3 – 5 M glass microelectrodes. All drugs: lamotrigine (LTG), phenytoin (PHT) and valproate (VPA), were applied to the slice by superfusion at a rate of 2 ml/min at 32 °C. Effects upon frequency of SLD’s were assessed for LTG, PHT and VPA applied at different concentrations, in isolation and in combination.

Results: High-K+ induced SLD frequency was reversibly reduced by LTG, PHT and VPA, at concentrations within the human therapeutic range of blood plasma concentrations. Under a repeated measures condition, PHT and VPA in combination displayed additive effect of effect with 50µM PHT and 350µM VPA reducing SLD frequency by 44% and 24% individually (n = 19), and together reducing SLD frequency by 66% (n = 19), 20µM LTG reduced SLD frequency by 32% and 350µM VPA by 16% (n = 18). However, in combination there was a supra-linear suppression of SLD’s of 64% (n = 18). In another independent set of experiments, similar results of drug combination responses were also found.

Conclusion: A combination of conventional AEDs with different mechanisms of action, PHT and VPA, relatively displayed linear additivity of effect on epileptiform activity. More intriguingly, a combination of AEDs considered particularly efficacious clinically, LTG and VPA, showed a tendency towards supra-additivity of effect. This approach may be useful as an in vitro platform for assessing drug combination efficacy.

57 Melissa Gresle
How does common genetic variation increase the risk of Multiple Sclerosis?

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Background: Multiple sclerosis (MS) is a life-long immune disease that affects the central nervous system, and the causes are still unknown. More than 100 variations in our genetic code or DNA (known as single nucleotide polymorphisms or SNPs), have been shown to increase the risk of MS by a small amount. MS risk SNPs do not change the protein code, so we don’t know how they work. Importantly, some studies have shown that ‘non-coding’ SNPs can work by regulating gene levels (or expression), and these are known as expression quantitative trait loci (eQTL).

Aims: In this study we characterize the effects of known MS risk SNPs on gene expression in five main types of immune cells previously implicated in the pathology of MS. We also investigate if there are differences in the way that MS risk SNPs regulate gene expression in MS cases compared to healthy controls.

Methods: Monocytes, NK cells, B-cells, and CD4- and CD8- T-cells were isolated using magnetic-activated cell sorting, from untreated relapsing MS cases (n=79) and healthy controls (n=101). To test for eQTL associations, we selected all genes within +/-500kb of an MS risk SNP (2500 pairs in total). The Illumina Immunochip was used to genotype for MS risk SNPs, and gene expression was measured for each cell type by microarray. The eQTL associations were identified by regression modelling (P<0.05, FDR <0.05).

Results: We have identified MS risk eQTL associations in each immune cell type, some of which are cell type specific. We also present preliminary data showing, for the first time, that MS risk SNPs could exert differential effects on immune gene expression in MS cases compared to controls.

Conclusions: We show that MS risk SNPs could function by contributing to immune heterogeneity. Importantly, we also present preliminary evidence to suggest that unknown disease associated factors could interact with MS risk SNPs to produce disease specific immune variation.
58 Mastura Monif

Interleukin-1β has trophic effects in microglia and its release is mediated by P2X7R pore.

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Background: Enhanced expression of the purinergic P2X7 receptor (P2X7R) occurs in several neuroinflammatory conditions where increased microglial activation is a co-existing feature. P2X7 receptors can function either as a cation channel, or upon continued stimulation, a large pore. P2X7R-overexpression alone is sufficient to drive microglial activation and proliferation in a process that is P2X7R pore-dependent, although the biological signaling pathway through which this occurs remains unclear. Once activated microglia are known to release a number of bioactive substances that include the proinflammatory cytokine interleukin 1β (IL-1β). Previous studies have linked P2X7R stimulation to the processing and release of IL-1β, but whether the channel or pore state of P2X7R is predominant in driving IL-1β release is unknown and is a major aim of this study. In addition we will determine whether IL-1β has trophic effects on surrounding microglia.

Methods: Electron microscopy and immunohistochemistry was used to delineate the sub-cellular localization of P2X7R and IL-1β in primary hippocampal rat cultures. FM1-43 fluorescent dye and confocal microscopy were used to quantify vesicular exocytosis from microglia expressing the pore forming P2X7R versus a non-pore forming point mutant, P2X7RG345Y. IL-1β in culture was quantified with an enzyme linked immunosorbent assay (ELISA). IL-1β intracellular processing was blocked with inhibition of caspase 1 (with a synthetic peptidic antagonist) and its extracellular form neutralized with an IL-1β neutralizing antibody. Microglial activation and proliferation was quantified immunohistochemically with confocal microscopy.

Results: P2X7R and IL-1β were co-localized in lysosomes. Vesicular exocytosis was higher in microglia expressing the pore forming P2X7R compared to those expressing the non-pore forming mutant. There was increased IL-1β in cultures expressing the pore forming P2X7R and this proinflammatory cytokine was found to mediate the trophic effects of P2X7R pore in microglia. Inhibition of IL-1β production and function resulted in a significant decrease in P2X7R-mediated microglial activation and proliferation.

Conclusion: IL-1β is a mediator of microglial activation and proliferation and its release/production is P2X7R pore-dependent. Blockade of P2X7R pore could serve as a therapeutic target in alleviating the degree of inflammation seen in neurodegenerative and neoplastic conditions.

59 Louisa Ng

Symptomatic management of Motor Neurone Disease

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Background and aim: This overview summarises the evidence from Cochrane systematic reviews of symptomatic treatments for Motor Neuron Disease (MND).

Method: We searched the Database of Abstracts of Reviews of Effects, MEDLINE, EMBASE, CINAHL Plus and the Cochrane Database of Systematic Reviews (CDSR) (August 2015) for systematic reviews of symptomatic treatments for MND. Methodological quality of the reviews was assessed using AMSTAR (Assessment of Multiple Systematic Reviews) and GRADE.

Results: We included nine systematic reviews, all of which were of high quality. Evidence for FES was limited to well conducted clinical trials with small sample sizes that showed improvements in measures of upper limb function and quality of life compared to the non intervention group. The significant changes in behaviour and increased clinician confidence are directly attributable to the use of the tailored education package, which provided staff the opportunity to transfer knowledge from workshops and clinical guidelines directly into patient demonstrations, scenarios and co-treatment sessions with the support of experienced key champions.

Conclusion: The implementation of evidence-based practices must target perceived barriers in order to change clinician behaviours and maintain staff confidence, knowledge and skills. Clinicians must have regular opportunities to transfer knowledge from workshops and clinical guidelines directly into clinical practice through a multifaceted training approach, which is dynamic and responsive to individual and organisational needs. The knowledge-to-action framework has provided a structured approach to ensuring the successful implementation of FES across the OT department of the Royal Melbourne Hospital.

60 Brittni Nielsen

Sustaining evidence in clinical practice: Introducing functional electrical stimulation (FES) across a large tertiary hospital

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Aim: The study explores how sustainable practice change was created to achieve consistent use of FES by occupational therapists (OT) at the Royal Melbourne Hospital.

Background: The National Stroke Foundation recommends functional electrical stimulation (FES) as one modality to address upper limb dysfunction post neurological event. Despite the availability of clinical guidelines, implementation to practice has been inconsistent.

Methods: The knowledge-to-action framework was adopted for its proven efficacy in sustaining changes across all levels of healthcare through addressing both individual and organisational barriers to uptake. A valid online survey tool was used to collect data pre and post the implementation of a tailored education package, measuring change in clinician’s behaviour and confidence over a 12 month period.

Results: Lack of experience as a perceived staff barrier decreased from 62% to 37%, with staff confidence increasing to 37% from 12%. 91% of staff who participated in the education package (intervention group) reported utilising FES in the past 12 months, compared to only 19% of the non intervention group. The significant changes in behaviour and increased clinician confidence are directly attributable to the use of the tailored education package, which provided staff the opportunity to transfer knowledge from workshops and clinical guidelines directly into patient demonstrations, scenarios and co-treatment sessions with the support of experienced key champions.

Conclusion: The implementation of evidence-based practices must target perceived barriers in order to change clinician behaviours and maintain staff confidence, knowledge and skills. Clinicians must have regular opportunities to transfer knowledge from workshops and clinical guidelines directly into clinical practice through a multifaceted training approach, which is dynamic and responsive to individual and organisational needs. The knowledge-to-action framework has provided a structured approach to ensuring the successful implementation of FES across the OT department of the Royal Melbourne Hospital.

61 Kim Powell

Chronic epilepsy causing an acquired cardiac channelopathy with altered expression of both T-type calcium channels and HCN channels

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Aim: Here we investigated whether there was altered cardiac expression of group of ion channels that importantly contributes to cardiac automaticity and excitability, T-type calcium channels and hyperpolarization-activated cyclic nucleotide-gated (HCN) channels in models of acquired and genetic epilepsy and in epileptic patients.

Background: Cardiac electrophysiological dysfunction is common in people with epilepsy; particularly in those with a longer duration of epilepsy. As a result people with epilepsy can suffer from serious cardiac arrhythmias, often precipitated by a seizure, which could...
62 Mujun Sun

A multi-factorial dietary treatment for traumatic brain injury

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Aim: To assess the effectiveness of a dietary supplementation targeting multiple TBI mechanisms in an experimental rat model of TBI.

Background: Traumatic brain injury (TBI) is a neurodegenerative disease that is induced by biomechanical forces applied to the brain. There is current no effective therapeutic intervention for clinical use in TBI patients. A major reason for the lack of effective TBI therapy is our poor understanding of TBI’s complex pathophysiology.

Neuroinflammation, oxidative stress and apoptosis are three of the major secondary injury pathways involved in the pathogenesis of TBI. Due to the complex relationship between these mechanisms, previous treatment studies that have targeted a single one of these mechanisms have been unsuccessful. However, a combination multifactorial treatment might allow for each of these pathways to be targeted simultaneously. Diet is a means to deliver neuroprotective agents that target a number of TBI pathogenic pathways. Considering the non-toxic nature of dietary agents, such compounds may be administered chronically and prior to injury.

Methods: 40 rats were randomly divided into 4 groups: 1. sham-injured with vehicle-diet; 2. sham-injured with diet supplement treatment; 3. lateral fluid percussion injury (FPI) model with vehicle-diet; 4. FPI with diet supplement treatment. Animals began their assigned treatment 4 weeks before their assigned injury and continued for one week post-injury. Behaviour tests were conducted on day 4 - 6 post-injury to assess cognitive, emotional, and motor functions. Brain tissue was collected on day 7 for MRI, biochemical, and immunohistochemical analysis.

Results: The FPI rats treated with the supplement diet had reduced cognitive and motor deficits compared to their vehicle-treated FPI counterpart. The supplement diet also reduced neuroinflammation after FPI compared to vehicle treatment. Analyses assessing apoptosis, oxidative stress, and structural brain damage are ongoing.

Conclusion: The preliminary results suggest that the multifactorial dietary supplement may be beneficial after experimental TBI.

63 Xin Lin Tan

Traumatic brain injury, Motor Neuron Disease, and TDP43

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Motor neuron disease (MND) is a neurodegenerative condition that is pathologically characterized by the progressive death of motor neurons and the presence of protein inclusions consisting of TAR DNA-binding protein 43kd (TDP-43). Sporadic MND, where the aetiology of the disease remains largely unknown, accounts for the large majority of MND cases. Traumatic brain injury (TBI) has been identified as a risk factor in the development of MND, and motor neuron loss, corticospinal tract degeneration, and TDP-43 pathologies, which are consistent with features of MND, have been observed in individuals with a history of TBI. However, the potential pathological mechanisms linking TBI and MND are poorly understood. Here we administered either a fluid percussion injury or sham injury to transgenic mice that overexpress TDP-43 or wild-type mice. After a one-week recovery, mice underwent behavioural testing to assess cognitive, motor, and emotional impairments before brains were collected for post-mortem analysis.

TDP-43 mice given a TBI had worse cognitive and motor deficits compared to their wild-type counterparts. While all mice given a TBI had significant neuronal death, it was worse in TDP-43 mice given a TBI. Notably, all mice given a TBI also had increased expression of phosphorylated TDP-43 relative to their sham-controls, with TDP-43 mice given a TBI having more than all other groups. We are currently conducting analyses to further probe other TDP-43 pathologies after TBI, however these initial finding suggest that TDP-43 phosphorylation may be detrimental in the aftermath of TBI.

64 Abu Mahomed Taiful Islam

Stereotaxic injection of M1000 prions to the CA1 hippocampal region of wild type mice induces molecular changes with acute transient ethological and memory disturbance

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Aim: Characterize the molecular, biophysical and cognitive changes of in vivo acute prion inoculation.

Background: Defining the toxic species underpinning pathogenesis in neurodegenerative diseases remains a major research goal. In Alzheimer disease (AD), good evidence exists for direct toxic effects of newly formed amyloid plaques rapidly inducing dysmorphic changes in juxtaposed neurites1 and for hippocampally injected pre-fibrillar oligomers of Aβ1-42 causing significant acute disturbances of synaptic function, dendritic spine ultrastructural changes and memory impairment2. With respect to prion diseases, size fractionation and sedimentation velocity fractionation approaches have shown that transmission efficiency (when normalized per total PrP) correlates with oligomeric forms of misfolded aberrant conformers (PrPSc) of the normal prion protein (PrPc)3,4. There is limited in vitro evidence to support direct toxic effects of recombinant soluble, oligomeric PrP enriched in β-sheet content5, as well as “purified” PrPSc and proteinase-treated PrPSc extracted from the brains of terminally sick rodents5,6. However, there has been no previous report of studies demonstrating direct, acute toxicity of PrPSc in vivo.

Methods: Stereotaxic surgery was used for injecting M1000 prions into female WT C57BL/6 mice brain. Brain homogenates derived from either terminally-sick mice infected with mouse-adapted M1000 prions or age-matched controls inoculated with normal brain homogenates, were stereotactically injected above the CA1 region of the hippocampus (coordinates -2.5mm from bregma, +/- 2.5mm laterally and 1.7mm depth) of 10 week old female WT C57BL/6 mice (n=10 per group). Five days following mice infection with stereotactic injection, brain homogenates were assessed in a series of motoric, behavioural/ethological and cognitive testing, which included Rotarod, Y-maze, Open Field, Burrowing and the Barnes Maze. Western blots of harvested brain homogenates were performed to assess cognitive, emotional, and motor functions. Brain tissue was collected on day 7 for MRI, biochemical, and immunohistochemical analysis.

Results: All testing was performed within 16 days of inoculation to minimise pathogenic contributions from de-novo M1000 prion propagation. No difference was observed in the Rotarod gross motor performance of the two groups. An increase in total errors was
observed in M1000 exposed mice in the Barnes Maze a Y Maze, appearing most notable on days 9 and 10 following stereotaxic injection. Brain morphological and biochemical analyses at different time-points confirm protein levels changes in different areas of the brain.

Conclusion: Taken together, these data support an acute, transient, in vivo toxicity of pre-formed M1000 prions in relation to neurons, astrocytes, behaviour and memory performances.

65  Patrick Tully
Reoperation for recurrent glioblastoma and its association with survival
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Aim: To investigate factors at initial surgery predictive of reoperation, and the prognostic variables associated with survival, including reoperation for recurrence.

Background: Glioblastoma is the most common and aggressive primary brain tumour. Despite current treatment, recurrence is inevitable. There are no clear guidelines for treatment of recurrent glioblastoma.

Method: A retrospective cohort study was performed including adult patients diagnosed with glioblastoma between January 2010 and December 2013. Student T-test and Fischer exact test compared continuous and categorical variables between reoperation and non-reoperation groups. Univariable and Cox regression multivariable analysis was performed.

Result: In a cohort of 204 patients with de novo glioblastoma, 49 (24%) received reoperation at recurrence. The median overall survival in the reoperation group was 20.1 months compared to 9.0 months in the non-reoperation group (p=0.001). Reoperation was associated with longer overall survival in our total population (HR 0.646 95%CI 0.543-0.922; p=0.016) but subject to selection bias. Subgroup analyses excluding patients unlikely to be considered for reoperation suggested a much less significant effect of reoperation on survival, which warranted further study with larger cohorts. Factors at initial surgery predictive for reoperation were younger age, smaller tumour size, initial extent of resection ≥50%, shorter IP stay and maximal initial adjuvant therapy.

Conclusion: Patients undergoing reoperation have favourable prognostic characteristics, which may be responsible for the survival difference observed. We recommend that a large clinical registry be developed to better aid consistent and homogenous data collection.

66  Frank Vajda
The Australian Pregnancy Register – How it is influencing our prescribing
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Aim: To determine how often birth defects occur in women who take antiepileptic medication (AEDs) and the influence it has on the prescribing patterns of these medications.

Background: The Australian Pregnancy Register has been collecting data on AED use in pregnancy and associated foetal outcomes in Australia since 1999. At least at yearly intervals, the accumulating data have been analysed and presented at conferences with the aim to inform neurologists, physicians, paediatricians, obstetricians, midwives, psychiatrists, general practitioners, and epilepsy support organisations. As we do not interfere in treatment the analysed and peer reviewed data is used to educate and/or influence prescribing.

Method: Three groups of women are enrolled with ethics approval and informed consent: Women with epilepsy and using these drugs for other conditions are eligible. Four telephone interviews are completed. Data base is confidential, analysis performed by standard statistical methods.

Results: We have an exceptionally low dropout rate compared to the other registers. We have shown a significant fall in the usage and doses of valproate in mono and polytherapy, this drug being the most likely to be associated with teratogenicity. We have shown that risk of birth defects is dose related, diminishing significantly from valproate doses of above 1500mg per day to less than 400 mg per day. With all antiepileptic drugs over the past 15 years here has been a drop of malformation incidence when used in monotherapy. The Register reported that seizure freedom during pregnancy was related to pre-pregnancy seizure control for at least 12 months. We documented the rise in the use of new antiepileptic agents versus the decline in use of the traditional ones, resulting in better tolerability and no rise in birth defects. We demonstrated for the first time that it is the content of polytherapy, not the use of several drugs per se which influences teratogenicity. Assessment of the babies 12 months after birth is able to detect about 20 per cent of additional defects. Amongst the extensions of the study we published data on cognitive outcome of babies, and attempt to find the mechanism of causation of spina bifida by collaborative translational research.

Conclusion: Multiple facets of investigation and wide-scale public education contributes to the value of the Australian Register, which is one of the major contributors to the international project, EURAP

67  Lucy Vivash
A pilot study of positron emission tomography with [18F]-FEMPA to image microglial activation in-vivo in patients with relapsing remitting and secondary progressive multiple sclerosis
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Background and Aim: The translocator protein (TSPO) is an 18kDa protein found on microglia, the primary immune cells of the central nervous system. As such TSPO expression is considered a marker of neuroinflammation and acute pathology, and has been widely associated with numerous neurological and psychiatric diseases including multiple sclerosis (MS). Positron emission tomography (PET) is a functional molecular imaging technique, which has unsurpassed sensitivity to localise and quantify specific proteins in the brain (and body) that are hypothesised to underlie the pathophysiology of diseases. The distinct advantage of PET is its ability to measure function noninvasively, and thus can be performed for diagnostic purposes, as well as for measuring disease progression. Therefore the development of novel PET radiotracers can greatly influence and inform clinical thinking, in terms of diagnosis, prognosis and efficacy of treatments. The aim of this study is to image neuroinflammation in MS using the novel TSPO-specific PET radiotracer [18F]-FEMPA.

Methods: Participants underwent a 120 min dynamic [18F]-FEMPA PET at the Melbourne Brain Centre Imaging Unit. Currently 3 patients with secondary progressive MS have been analysed and presented at conferences with the aim to influence our prescribing – How it is.
68  Kyria Webster

Progesterone treatment reduces neuroinflammation, oxidative stress and brain damage and improves long-term outcomes in a rat model of repeated mild traumatic brain injury

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Background: Repeated mild traumatic brain injuries, such as concussions, may result in cumulative brain damage, neurodegeneration, and other chronic neurological impairments. There are currently no clinically available treatment options known to prevent these consequences. However, growing evidence implicates neuroinflammation and oxidative stress in the pathogenesis of repetitive mild brain injuries, thus these may represent potential therapeutic targets. Progesterone has been demonstrated to have potent anti-inflammatory and anti-oxidant properties after brain insult; therefore, here we examined progesterone treatment in rats given repetitive mild brain injuries via the repeated mild fluid percussion injury model.

Methods: Male Long-Evans rats were assigned into four groups: sham-injury + vehicle treatment; sham-injury + progesterone treatment (8mg/kg/day); repeated mild fluid percussion injuries + vehicle treatment; and repeated mild fluid percussion injuries + progesterone treatment. Rats were administered a total of three injuries, with each injury separated by five days. Treatment was initiated one hour after the first injury, then administered daily for a total of 15 days. Rats underwent behavioural testing at 12-weeks post-treatment to assess cognition, motor function, anxiety, and depression. Brains were then dissected for analysis of markers for neuroinflammation and oxidative stress. Ex vivo MRI was conducted in order to examine structural brain damage and white matter integrity.

Results: Repeated mild fluid percussion injuries + progesterone treatment rats showed significantly reduced cognitive and sensorimotor deficits compared to their vehicle-treated counterparts at 12-weeks post-treatment. Progesterone treatment significantly attenuated markers of neuroinflammation and oxidative stress in rats given repeated mild fluid percussion injuries, with concomitant reductions in grey and white matter damage as indicated by MRI.

Conclusions: These findings implicate neuroinflammation and oxidative stress in the pathophysiologic aftermath of mild brain injuries, and suggest that progesterone may be a viable treatment option to mitigate these effects and their detrimental consequences.

69  David Wright

Behavioral, blood, and magnetic resonance imaging biomarkers of experimental concussion

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Background: Repeated concussions may lead to serious neurological consequences, especially if re-injury takes place within the period of increased cerebral vulnerability (ICV) triggered by the initial insult. Advanced magnetic resonance imaging (MRI) and blood-based proteomics, as opposed to symptom-based methods, might provide objective measures of identifying the pathophysiological changes in the concussed brain, indicating when the brain is no longer in a state of ICV, and monitoring recovery. This study assessed and compared behavioral, MRI, and blood-based biomarkers in a rat model of concussion.

Methods: Rats were given a sham or mild fluid percussion injury (mFPI), and behavioral testing, serial advanced multi-modal MRI, and blood collections were conducted up to 30 days post-injury. Results: There were cognitive impairments for three days after a single mFPI, before normalizing by day 5 post-injury. In contrast, both MRI (i.e., diffusion tensor imaging and tractography) and blood-based proteomics (i.e., tau and vascular endothelial growth factor) detected abnormalities that persisted beyond the resolution of cognitive impairments, some of which were still present 30 days post-mFPI.

Conclusion: These findings suggest that MRI and blood-based proteomics are sensitive and objective measures of the molecular and subtle structural changes following concussion.

70  David Wright

Traumatic brain injury induces pathophysiology resembling motor neuron disease

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Background: Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease (MND) and is pathologically characterized by the progressive death of motor neurons, degeneration of the corticospinal tract, and the presence of transactive response DNA binding protein 43 (TRDP-43) inclusions. To date the aetiology of ALS remains largely unknown, limiting our ability to prevent its occurrence or develop effective therapeutic treatments. Traumatic brain injury (TBI) is a common progressive neurodegenerative condition, and has been linked to the later onset of ALS. However, the notion that TBI may cause ALS remains controversial. As such, here we aimed to further study the potential relationship between TBI and ALS by performing experimental TBI in rats and assessing for the presence of progressive MND-like pathological and functional abnormalities.

Methods: TBI was performed using the lateral fluid percussion injury model. MRI data was acquired using a 4.7 T Bruker scanner at 1 and 12 weeks post-injury. Behavioral testing was performed at 12 weeks post-injury and brain tissue, spinal cords and muscle tissue were also examined post-mortem. Results: Volumetric analysis of in-vivo MRI found that rats given a TBI had progressive atrophy of the motor cortices compared to rats given a sham injury. Additionally, tensor-based morphometry and diffusion-weighted imaging revealed progressive degeneration and diffusion tensor changes within the corticospinal tracts of TBI rats. Immunofluorescence analysis of motor cortex revealed a reduction in neurons and an increase in the number of neurons overexpressing phosphorylated TDP-43. Further, rats given a TBI also had fewer motor neurons in the spinal cord, increased expression of muscle atrophy markers, changes in muscle fibre contractile properties, and muscle atrophy. Finally, assessment of motor function on a beam task revealed severe impairments in rats given a TBI. Conclusion: Taken together, these experimental TBI findings resemble the pathological and functional abnormalities common in ALS, and support the notion that TBI can induce a progressive disease process bearing similarities to those in MND.

71  Evonne Shum

The burden of atopic dermatitis in adults: direct and indirect costs on patients and the community

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Aim: This study aims to determine the direct and indirect costs of atopic dermatitis in adult patients attending an outpatient dermatology clinic in an Australian public hospital.

Background: Atopic dermatitis is a chronic skin condition requiring long-term management, which can be considerably costly. It is mostly a disease occurring during childhood but prevalence amongst adults is increasing and can be as high as 7%. Justification of the cost of atopic dermatitis is important as the condition can cause profound financial, social and emotional burden on patients and society. Currently, there are only a few Australian studies in this field and, overseas studies may not provide reliable estimates for the cost in the Australian health care system.

Methods: 27 adult patients with atopic dermatitis were recruited at the Royal Melbourne Hospital Dermatology Outpatient Department. Participants were stratified according to severity using the SCORing Atopic Dermatitis (SCORAD). Participants completed the Dermatology Quality of Life Index (DLQI) and a supplemental questionnaire on loss of income from the date of recruitment. They were also asked to complete an “Atopic Dermatitis (Eczema) Cost Diary” to record expenditures related to atopic dermatitis management over a 3-month period, starting from a month prior to two months from recruitment date.
Follow up with each participant was conducted by telephone or email every 4 weeks.

Results: Results show that average out-of-pocket cost per patient with mild to moderate atopic dermatitis was $981 while cost to a patient with severe atopic dermatitis can be up to $2989. Loss of income was significant only to patients with severe condition. Costs incurred to the public healthcare system increased with severity. No correlation was found between severity of the condition and quality of life.

Conclusion: Even though atopic dermatitis is not life threatening, it imposes financial costs on the individual and the health care system. Emotional and social burden should be evaluated as well when assessing patients with atopic dermatitis.

72 Yonatan Kok
A cross-sectional study assessing quality of life and depression in psoriasis patients

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Aim: This study aims to 1) analyse the DLQI's clinical sensitivity for detecting depression in psoriasis patients and 2) to evaluate the association between depression and the individual domains of the DLQI.

Background: Psoriasis is a chronic skin condition that significantly impacts quality of life. Treatment response is measured using the Psoriasis Area Severity Index (PASI) and the Dermatology Life Quality Index (DLQI). However, studies have shown that the PASI and DLQI are only modestly correlated, and recent literature suggests that quality of life is more strongly linked to depression than the severity of skin lesions. Concerns have also been raised regarding the sensitivity of the DLQI for detecting mental health problems. The Beck-Depression Inventory-II (BDI-II) is widely employed in clinical practice to screen for depression, but it is not currently part of standard care in psoriasis.

Methods: 45 adult psoriasis patients were recruited at The Royal Melbourne Hospital Dermatology outpatient's clinic from February to April 2016. Participants completed the DLQI and BDI-II. The PASI score was calculated by a clinician and patient demographic data were also collected. Patients were divided into the mild or moderate to severe group based on their DLQI score. The Mann-Whitney U test was used to calculate median differences in the PASI and BDI-II between groups. Spearman's rho was used to determine the correlation between the DLQI and BDI-II.

Results: The moderate to severe DLQI group showed significantly higher PASI (p value <0.00) and BDI-II (p value <0.00) scores. The sensitivity of a high DLQI or PASI score for depression was 50%. Certain domains of the DLQI are more highly associated with depression than others, and this was influenced by the patient's age, gender, lesion visibility and co-morbidities.

Conclusion: Both the DLQI and PASI can only modestly detect depression in psoriasis patients. As total DLQI and PASI scores may not screen for depression adequately, adding other screening tools such as the BDI-II may improve detection rates of depression. High scores in specific DLQI domains can guide clinicians to select for patients needing to be screened for depression.

73 Caryl Tay
Microbes on mobile phones in a public hospital setting

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Aim: To investigate the levels of contamination of mobile phones of doctors, nurses and patients at the Royal Melbourne Hospital using a novel methodology.

Background: The use of mobile phones is on the rise, with 94% of Australians now owning a mobile phone. They are commonplace in the hospital setting and are an essential tool for communication and information exchange. A number of studies have shown that mobile phones may play a role in pathogen transmission. Contamination rates of mobile phones range from 60% to 100%. This may be due to a lack of guidelines regarding the safe use of mobile phones in a hospital setting and an inadequate level of mobile phone hygiene. In this study, we compared the Aerobic Bacterial Count (ABC) of the mobile phones of doctors, nurses and patients to internationally recognized environmental bacteriological standards. We also looked for vancomycin-resistant enterococci (VRE), as we believe it can act as a specific surrogate marker for contamination.

Methods: Mobile phones from 50 doctors, 50 nurses, 20 patients, 5 allied health workers and 28 members of the community were investigated for bacterial contamination. In order to optimize our methodology, we first investigated the effect of different vortexing times on bacterial yield, which was recorded in colony forming units (CFU). Subsequently, each participant’s mobile phone was processed as follows: A moistened sterile swab is used to sample a mobile phone before being placed into 500µL of normal saline (NS). The NS is vortexed for 1 minute. 10µL of the NS is plated onto horse blood agar (HBA) and incubated aerobically at 37°C for 48 hours, at which, the number of CFU are counted. The rest of the sample is put into brain heart infusion (BHI) broth. After incubation at 37°C for 24 hours, 10µL of the broth is plated onto a ChromID VRE plate (bioMerieux), which is incubated at 37°C aerobically, and examined at 24 and 48 hours. The Aerobic Bacterial Count (CFU/cm2) is calculated by dividing the total CFU of a sample by the mobile phone’s surface area.

Results: Our investigation showed that different vortexing times of 1 minute, 2 minutes and 3 minutes do not produce a difference in bacterial yield. International standards suggest that high-touch environmental surfaces should contain an ABC of <5. Our study showed that 37.5% of mobile phones from doctors, nurses and patients do not meet this standard. However, no VRE has been recovered.

74 Sonet Chap
Profiloing proteases and protease-activated receptors in itchy, inflammatory skin conditions

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Aim: The aim of this study is to determine the level and expression of protease activity and protease-activated receptors in itchy, inflammatory skin conditions and to correlate with disease severity.

Background: Recent findings have highlighted the importance of the balance of many proteases, protease inhibitors, and protease-activated receptors (PARs) in maintaining epidermal barrier function. Increased levels and expression of protease activity and PARs are known to contribute to the pathophysiology of common itchy, inflammatory skin conditions such as atopic dermatitis (AD) and psoriasis. Proteases such as cathepsins X, B, S and legumain are known to activate PAR-2 whose physiological role is proposed as pro-inflammatory, mediator of immune reaction, and to promote endothelial cell proliferation. PARs are able to profile proteases in order to detect proteolytic activity that is not detected using traditional methods. Our study aimed to utilize activity-based probes (ABPs) and western blotting in order to detect proteolytic activity in inflammatory skin conditions such as atopic dermatitis (AD) and psoriasis.

Methods: This study included 157 patients with AD (Group I), 2 patients with psoriasis (Group II), 3 patients with unspecified inflammatory skin conditions (Group III), in addition to 10 healthy skin samples as controls (Group IV). These participants have been identified at the Dermatology Outpatient Clinic, Royal Melbourne Hospital. Punch biopsies were taken from lesional and non-lesional skin of the patients and part of non-lesional excised margins for controls. In order to elucidate the activity of proteases in inflammatory skin conditions, the levels of expression of cathepsins X, B, S and legumain were investigated by utilising activity-based probes (ABPs) and western blotting.

Results: This study will be expanding upon current literature studies, which report only on levels of protein expression. By using ABPs we are able to profile proteases in order to detect proteolytic activity that is dysregulated during active disease. Preliminary results have suggested an increase in protease activity in lesional skin as compared to non-lesional skin and controls. Higher levels of active proteases found in non-lesional skin as compared to controls suggest that patients with itchy, inflammatory skin conditions may have a higher background level of proteases.

Conclusions: Proteases may be implicated as important mechanisms in the pathogenesis of AD. Greater study numbers are required in order to determine whether significant correlation between the levels of proteases with disease severity scores to establish if proteases could be used as a useful marker to aid in clinical diagnosis.

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75  Hoie Kidd Leong

Serial ARFI measurements as a predictor of the natural history of chronic liver disease

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Aim: To investigate whether the change in ARFI reading over time is a better indicator of prognosis.

Background: In chronic liver disease, estimation of the degree of fibrosis is important in guiding management and prognosis. Acoustic Radiation Force Impulse Imaging (ARFI, Siemens, Germany) is an ultrasound elastography technique that has shown good diagnostic ability of fibrosis. However, all elastography techniques are affected by body habitus, liver steatosis and inflammation.

Methods: All chronic liver disease patients with at least two ARFI liver stiffness measurements between 08/2012-03/2016 were included in our study. Demographics, aetiology of liver disease, BMI, bloods, presence of cirrhosis and liver complications were obtained at baseline and follow up. The percentage change in ARFI scores per year were calculated. Initiation of treatment for HBV, HCV, AIH, abstention in alcoholic liver disease and DILI between ARFI measurements were documented. Data on the development of decompensation was collected up till 05/2016. Patients with follow up ARFI less than 6 months after baseline, or an IQI median velocity ratio >0.30 (=unreliable reading) were excluded from the study.

Results: 213 patients had 2 serial ARFI measurements a median 554 days apart (range 184-1186). 101 patients were excluded using the exclusion criteria. Of the remaining 112 patients, 50 (45%) were male. The median age was 49.5y (range:18-74). Liver disease was due to HBV (n=36, 32%), HCV (n=23, 21%), NAFLD (n=20, 18%), AIH (n=15, 13%), alcoholic liver disease (n=10, 9%), and other (n=25, 22%). 95 (85%) patients had stable ARFI over time (>20% change/yr), 8 (7%) got worse (>20% increase/yr) and 9 (8%) improved (>20% decrease/yr).

On follow up, 5 patients developed varices, 3 had DILI, 2 and 3 patients were newly treated for HBV, and HCV, respectively, and 3 patients ceased alcohol. Patients who developed new varices (median % ARFI change 15.4, p=0.005) or experienced a new DILI (median % ARFI change 28.4, p=0.03) had significant increases in percent change in ARFI yr, while new HCV treatment (median % ARFI change -17.2, p=0.04) was associated with significant decrease. There was no significant difference with new HBV treatment (median % ARFI change -14.7, p=0.21) and alcohol cessation (median % ARFI change 1.5, p=0.23). No patients decompensated during follow up.

Conclusions: Percentage change in ARFI may be a better indicator of disease progression or regression than individual values, as it allows for the individual confounding variables. Future studies with longer follow up are needed to confirm this.

76  Lakshmi Chitra Varanasi

Polycystic Ovarian Syndrome: prevalence and its impact on the wellbeing of Victorian women 16-29 years

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Aims: Polycystic Ovarian Syndrome (PCOS) is a common endocrine condition among women of reproductive age. We determined the prevalence of PCOS in a cohort of young Australian women using the National Institutes of Health (NIH) criteria (1990) and investigated the impact of PCOS on physical and mental wellbeing.

Methods: Participants were identified from the Young Female Health Initiative (YFHI) and Safe-D studies, in which females aged 16-25 years living in Victoria were recruited via Facebook advertising. Participants had already completed survey modules on multiple health domains including mental health, and had undertaken serum hormonal and metabolic profiles. In March 2016, two supplementary online questionnaires were distributed to participants. One comprising questions on diagnosis, treatment and fertility concerns, was sent to participants who reported having PCOS in the original YFHI or Safe-D studies. A second, comprising general questions on reproductive health, was sent to the remainder of the cohort. PCOS was diagnosed according to the NIH criteria: presence of both oligo/anovulation and biochemical (testosterone) or clinical (acne, hirsutism and androgenic alopecia) hyperandrogenism, and exclusion of other related anovulatory disorders.

Results: The prevalence of self-reported PCOS was 12% (31/253). After adjusting for age, socio-economic status and smoking status, we found that that more women with self-reported PCOS reported depression than women without PCOS (n=299, 55% vs 27%, p=0.005), after adjusting for age and BMI. Women with self-reported PCOS were also more likely to have a higher BM (≥25) than women without PCOS (n=296, 48% vs 28%, p=0.048). There were more women with self-reported PCOS who had a history of pregnancy than women without self-reported PCOS (n=221, 26% vs 7%, p=0.015). Additionally, among those that reported pregnancies, more women with self-reported PCOS had a history of miscarriages than women without self-reported PCOS (n=13, 57% vs 4%, p=0.021). Among those with self-reported PCOS, (65%, 15/23) were unhappy/worried about their diagnosis. Similarly, 72% (13/18) stated that concerns about fertility was the most distressing aspect of PCOS with 87% (20/23) believing their fertility was reduced.

Conclusion: The prevalence of PCOS in this sample was greater than previously reported in similar age groups when using the NIH criteria. However, it is within the range reported by other studies that have applied either the Rotterdam or AES criteria. Our findings also suggest that fertility concerns were a major cause of distress amongst women with PCOS, and should be addressed by clinicians early in the management of their diagnosis.

77  Shi Rou Zhang

BrightHearts: Using a biofeedback relaxation iPad app to reduce anxiety and pain during venepuncture.

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Background: Needle phobia is highly prevalent in the Australian population, with studies citing that as many as 22% of patients suffer from it in general practice settings. Biofeedback has been studied as a novel tool to reduce the pain and anxiety associated with a number of medical conditions: it is yet to be assessed for venepuncture. The BrightHearts app was developed and programmed by Dr George Khut to relax and distract children prior to medical procedures. However, this has yet to be piloted in research involving adolescents and young females.

Objective: Through this study, we investigated the impact of BrightHearts, a heart rate variability biofeedback iPad application app, on a single episode of venepuncture.

Methods: A randomised controlled trial was conducted with females aged 17-28 years recruited from the Young Female Health Initiative (YFHI) and Safe-D studies. 35 participants were randomly assigned to a control group in which normal venepuncture was conducted and 36 participants were assigned to the intervention group. The intervention group used BrightHearts during venepuncture, participants were instructed to take slow, deep breaths while aiming to reduce their heart rate with the aid of the app’s visual and audio feedback.

Results: There was a trend for lowers prolactin levels in the BrightHearts group compared to the control group (62% vs 39% with prolactin <284mU/L, p=0.07). There were no significant differences in pain and fear ratings between the two groups, nor with total State-Trait Anxiety Inventory (STAI) scores. However some individual component questions from the STAI did prove to be significant, or showed trends towards significance. A greater proportion of those in the BrightHearts group reported feeling “hardly ever unhappy” compared to those in the control group (44% vs 20%, p=0.03) in response to a STAI question. There were also no difference in participant heart rate across time points.

Conclusion: Although we did not measure any significant differences in pain, fear or STAI total scores between the two groups, trends in prolactin levels and some individual items from the STAI suggest a positive effect. This raises the issue of the sensitivity and specificity of the study questionnaire, designed for a paediatric audience, in measuring anxiety and pain in young adults. There is potential for future studies to increase sample size, and also to design a questionnaire more suited to assessing fear, pain and anxiety in adult populations.
Longitudinal Quality of Life and Neurocognitive conjunction with HRQoL. Particularly true in regards to longitudinal HRQoL, with even fewer studies investigating HRQoL in benign brain tumour patients are exploring the relationship between HRQoL and cognitive functioning. Patients at multiple time points, to establish HRQoL outcomes and assessing health-related quality of life (HRQoL) and neurocognitive function in brain tumours; low-grade gliomas, meningiomas and acoustic neuromas. With increased length of survival, it is essential to consider the quality of this survival and impact of post-operative morbidity and cognitive deficits on wellbeing, in order to ultimately optimise long-term patient outcomes. We present results from the third year in a five-year prospective study of 110 patients surveyed at multiple time points. HRQoL is found to be stable at a mean 50.8 months follow up. No significant cognitive impairments were detected using MMSE, however preliminary results from a subset of 21 using Cogstate testing indicate significant reduction in cognition in working memory (p < 0.001) and processing speed (p < 0.05) for all 3 tumour types compared to normal population data. There are stronger correlations between Cogstate and self-reported cognitive function than with MMSE, however these correlations are not statistically significant given current sample size. Further research is indicated to assess cognition using Cogstate testing to determine the degree to which patients are impaired and specific domains of impairment. These domains may ultimately prove to be amenable to cognitive rehabilitation and subsequent improvement in HRQoL.

Rehabilitation of spinal cord injury: Lessons learnt in disaster settings

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Background and aim: On April 25th and May 12th 2015, two mega earthquakes struck Nepal, resulting in 8,600 casualties, >100,000 injured. The aim is to present a rehabilitation Foreign Medical Team’s (FMT) effort for spinal cord injury (SCI) patients following these earthquakes; focusing on lessons learnt and shortcomings in disaster management.

Methods: Settings: A specialised rehabilitation centre for SCI. Participants: 101 consecutive earthquake victims with SCI admitted to SIRC. Intervention: In the week of the earthquake, an approved FMT from the Royal Melbourne Hospital (RMH) was deployed to an established rehabilitation centre for SCI in Nepal (approved by the WHO and Nepal Ministry of Health and Population). The RMH team activity included addressing priorities identified by SIRC; barriers and enablers; develop rehabilitation triage process (documentation, treatment approaches, systems of care); integration with acute facilities; and training of local healthcare professionals for specific rehabilitation issues. All data were collected prospectively during the ward rounds by the FMT with local physician; and a triage tool was validated.

Results: The mean age of participants (n=101) was 34.4±15.1 years (range: 11-86 years), majority were female (53.5%). Over two thirds had SCI (78%). Common non-neurological issues were: pain (74%), bladder disorder (73%) and bowel problems (58%); and pressure ulcers (33%). Participants reported some form of psychological trauma (severe anxiety, fear, sleep disturbance) and symptoms consistent with post-traumatic stress. A rehabilitation triage tool was developed (based on ‘needs’ assessment) and validated during the disaster with positive feedback from staff. Processes for systems of care were facilitated (documentation, communication and training of local staff); and identification of barriers for future action.

Conclusions: A collaborative multidisciplinary (FMT and local staff) rehabilitation management of earthquake victims with a SCI resulted in better coordination and effective care. Long-term planning for disasters should include early aggressive medical rehabilitation.

Long-term functional and psychological outcomes in persons with traumatic brain injury

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Background and Aim: With advances in medical care, the survival rates and functional outcomes of persons with traumatic brain injury (TBI)
have improved dramatically. However, TBI survivors often have long-term physical, cognitive and behavioural disabilities, residual neurological deficits, medical complications and lifestyle consequences. The aim of this study was to examine factors impacting long-term functional and psychological outcomes in persons with moderate to severe TBI. 

Methods: A prospective cross-sectional study assessed the long-term (up to 5 years) impact of TBI on participants (n=103 non-compensable patients registered in a tertiary hospital Trauma Database from 2009 to 2011) current activity and restriction in participation using validated questionnaires. 

Measures: Global outcomes: Glasgow Outcome Scale-Extended, Functional Assessment Measure (FIM-FAM); Cognitive Log. Centre for Epidemiologic Studies Depression; Health status: Community Integration Questionnaire, Community Integration Measure, Satisfaction with Life Scale; Caregiver outcomes: Caregiver Strain Index, Caregiver self-reported burden. 

Results: Participants’ mean age was 48.6±7.9 years, majority were male (77%), 49% had some form of previous rehabilitation. The common causes of TBI were falls (42%) and motor vehicle accidents (27%). The TBI-related symptoms were: pain/headache (47%), dizziness (36%), bladder/anal incontinence (34%), sensory-perceptual deficits (34%). Participants reported minimal change in their physical function and cognition (FIM-FAM: motor (median: Md): 102, Inter Quartile Range (IQR): 93-111) and cognition (Md: 89, IQR: 78-95). Participants were well-adjusted to community-living, however, reported high levels of depression. Factors significantly associated with poorer current level of functioning/wellbeing included: older age (>60 years), preexistence of TBI-related symptoms, a lack of previous rehabilitation and those classified in ‘severe disability categories’ at admission. 

Conclusions: Cognitive and psychosocial problems are more commonly reported by TBI survivors in the longer-term than physical disability. More focus on participation and aging with disability in these persons is needed.

82 Sarah Hanieh

Exclusive breast feeding in early infancy reduces the risk of inpatient admission for diarrhea and suspected pneumonia in rural Vietnam: a prospective cohort study

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Aim: To identify maternal and early infant factors associated with inpatient admission for suspected pneumonia or diarrheal illness during the first 6 months of life in Ha Nam province, Vietnam. 

Background: Acute respiratory infections and diarrhea remain the leading causes of infant morbidity and mortality, with a high burden of both pneumonia and diarrhea in Southeast Asia. Information on maternal and early infant predictors of inpatient admission for these illnesses could greatly assist in the planning of prevention strategies, and early interventions could be targeted towards those most at risk. 

Methods: A prospective cohort study of 1049 infants, born to women who had previously participated in a cluster randomized controlled trial of antenatal micronutrient supplementation in rural Vietnam, was undertaken between 28th September 2010 and 8th Jan 2012. Infants were followed until 6 months of age, and the outcome measure was inpatient admission for suspected pneumonia or diarrheal illness during the first 6 months of life. Risk factors were assessed using univariable logistic regression and multiple logistic regression. 

Results: Of the 1049 infants seen at 6 months of age, 8.8 % required inpatient admission for suspected pneumonia and 4 % of infants required inpatient admission for diarrheal illness. One third of infants (32.8 %) were exclusively breast fed at 6 weeks of age. Exclusive breast feeding at 6 weeks of age significantly reduced the odds of inpatient admission for suspected pneumonia (Odds Ratio (OR) 0.39, 95% Confidence Interval (CI) 0.20 to 0.75) and diarrheal illness (OR 0.37, 95% CI 0.15 to 0.88). 

Conclusions: Exclusive breast feeding in early infancy reduces the risk of severe illness from diarrhea and suspected pneumonia. Public health programs to reduce the burden of inpatient admission from diarrheal and respiratory illness in rural Vietnam should address barriers to exclusive breast feeding.

83 Kudzai Kanhuu

Research and development of a purpose-built software solution to enhance refugee patient management

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Aim: To develop a care model to enable clinical research and respond to the needs of people from refugee-like background. 

Background: Each year Australia receives 13,750 refugees via the United Nations High Council for Refugees (UNHCR) Humanitarian Programme. Many of these people will have had interrupted or poor access to adequate healthcare prior to being resettled in Australia. Achieving comprehensive and equitable health assessments and care for refugees often involves multiple care providers. Efficient communication and data management is necessary for optimal patient outcomes.

Method: A mixed methods research approach was employed in the design and implementation of the CAReHR™ (Clinical Audit Research electronic Health Record) package. This involved: Collaboration and focus group analysis between clinicians and the information technology team Aritecta®; Input from refugees and refugee advocates; Quantitative analysis of the epidemiology of non-communicable and communicable diseases in the Victorian refugee population using pre-existing hospital and external data. A paper-based clinic record has been supplemented with this solution, which improves clinical management and enables the collection of de-identified data for research purposes. 

Results: Using the CAReHR™ electronic health record patients can now be managed onsite at RMH or alternatively remotely via a telehealth programme. 1250 patients have been managed with CAReHR™ for over 3000 clinic visits since 2012, delivering: An electronic health record that can be configured by clinician; The option of directly linking to other software systems (such as cdmNet®) allowing GPs to view clinic summaries online; Electronic requesting of pathology; Electronic prescribing; Automatic development of modifiable clinic letters for referring doctors; Consistent data collection; The option of giving the patient a summary at the time of the appointment; Letters for referring doctors being sent on the day of clinic visit. 

Conclusion: A bespoke software, CAReHR™ has been developed for the refugee and immigrant population. It can be adapted by the clinician at the user interface to coordinate the care of patients with other acute and chronic conditions, and is now in use by most infectious diseases clinics at RMH. CAReHR™ also allows for the collection of de-identified data for research purposes, which is uploaded to BioGrid (a federated data sharing platform for collaborative translational health and medical research) for easier research access. This improves patient care by improving the timeliness and flow of information between patients, primary care, hospital specialists and other health professionals. 

84 Kevin Chow

Monocyte-derived dendritic cells promote Th polarization, whereas conventional dendritic cells promote Th proliferation

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Aim: To determine the respective roles of monocyte derived dendritic cells (moDCs) and conventional dendritic cells (cDCs) in mediating adaptive CD4+ T cell responses. 

Background: moDCs dramatically increase in numbers upon infection and inflammation. We found that this also occurs in response to allotransplantic encounters, such as those that occur in the setting of organ transplantation. Despite their prominence in these settings, how
emergent moDCs and resident conventional DCs (cDCs) divide their labor as APCs remain undefined.

Methods: Since, unlike nominal antigen, transplant antigen can be recognised by direct and indirect presentation, we compared both direct and indirect antigen presentation by murine moDCs versus cDCs.

Results: We found that, despite having equivalent MHC-II expression and in vitro survival, moDCs were 20-fold less efficient than cDCs at inducing CD4+ T cell proliferation through both direct and indirect Ag presentation. Despite this, moDCs were more potent at inducing Th1 and Th17 differentiation (e.g. 8-fold higher IFN-γ, 2-fold higher IL-17A in T cell co-cultures) whereas cDCs induced 10-fold higher IL-2 production, suggesting moDCs potently reduced the ability of cDCs to stimulate T cell proliferation in vitro and in vivo, partially through nitric oxide production.

Conclusion: These results suggest a clear functional specialisation between moDCs and cDCs in mediating various aspects of CD4+ T cell responses. We surmise that this division of labor has implications for their respective roles in the immune response.

85  Rachel Cooke
Comparative immunobiology of variations of the Vk*MYC mouse model and human multiple myeloma

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Aim: To examine how cellular immunity is affected within the bone marrow (BM) microenvironment of the Vk*MYC mouse models and compare that to human immunology in patients with newly diagnosed and relapsed/refractory (R/R) multiple myeloma (MM).

Background: The Vk*MYC transgenic and transplant mouse models of MM are well established as a research tool for anti-myeloma drug research. Understanding the immunological relevance of these models is critical for developing effective immunotherapies.

Methods: Using 6-8 colour flow cytometry, we analysed T cells from PBMC and BM from MM patients enrolled on two clinical trials at baseline: LitVac (ANZCTR trial ID ACTRN12613000344796, which recruited newly diagnosed, untreated patients), and RevLite (ANZCTR trial ID NCT00492261, which recruited relapsed/refractory patients). As a control group, PBMCs from Australian Red Cross Blood Service (ARCBS) donors were used. Ages of ARCBS donors is unknown and the average age of these donors is likely to be significantly lower than MM patients; therefore, we also analysed PBMCs from healthy, elderly individuals. Tumour burden in the mice was assessed by BM trephine immunohistochemistry, the presence of extramedullary disease on dissection and serum protein electrophoresis.

Results: We found that there were significant immunological responses in mice with developing spontaneous (transgenic) or transplanted MM as a consequence of the degree of tumour burden. Particularly striking were the association of MM development and profound B cell lymphopenia and the expansion of IFNγ-producing CD8+ T cells and antigen-experienced CD8+ effector memory T cells. Our findings most closely mirrored the patterns seen in patients with R/R MM, rather than those with newly diagnosed MM, and suggest that the immunity of Vk*MYC models may more accurately resemble the effects of R/R MM rather than those present at initial diagnosis.

Conclusions: Our findings indicate that T cell profiles differ in patients with newly diagnosed MM from that seen in advanced MM. However, transgenic and transplanted Vk*MYC mouse models of MM more closely mirror the immunology of patients with advanced (R/R) disease rather than newly diagnosed MM. This is an important consideration when interpreting the pre-clinical findings of therapies tested in the Vk*MYC mouse model.
show durable responses to treatment. Here, we suggest that assessment of specific immune parameters in peripheral blood (PB) of patients at diagnosis may discriminate between individuals who will or will not respond favourably to this combination. PB from MDS patients on a randomised clinical trial of Azacytidine with or without Lenalidomide was assessed by multi-parameter flow cytometry. MDS patients showed discrete changes in a number of immune cell subsets compared with healthy donors. Patients showed significant reduction in Natural Killer (NK) cell and Myeloid-Associated Invariant T (MAIT) cell populations, along with a shift of T cells towards a terminally differentiated phenotype. Expression of the costimulatory molecule CD28 was significantly reduced on cytotoxic T cells, and was indicative of response to treatment within the MDS cohort. Similarly, MDS patients showed significant populations of CD3+CD11b+CD14+HLA-DR~ myelo-derived suppressor cells (MDSCs) that correlated with poor response. Taken together, these data suggest that assessment of a wide range of immune cell subsets may provide a measure of ‘immune fitness’ in newly diagnosed patients and identify biomarkers to better inform treatment decisions in the clinic.

88 Katherine Nicholas
Perioperative anaphylaxis audit: Royal Melbourne Hospital
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Background. Perioperative anaphylaxis (PA) is a medical emergency with potential for mortality. Skin testing (ST) of agents used in the perioperative period is considered the gold standard for the identification of likely causative agents. Neutrophilic blocking agents (NMBA) (58%), antibiotics (12-15%) and latex (16-19%) are the most commonly implicated causative agents. Chlorhexidine allergy is described although its prevalence is not well established and likely underreported.

Method. Medical histories were reviewed for all patients referred for PA who underwent testing in our centre over a 2-year period from September 2013 to August 2015. Data collected included severity grading, acute elevation in mast cell tryptase (MCT) (>12ng/mL or >135% basal level), and causative agent indicated by the presence of a biomarker to better inform treatment decisions in the clinic.

Aim. We conducted a retrospective audit of all patients who underwent ST and specific IgE testing (SpIgE) for investigation of a perioperative allergic event in order to identify the proportion of patients who had a likely causative agent identified and also the prevalence of reactivity to different agents within our cohort.

Method. Medical histories were reviewed for all patients referred for PA who underwent testing in our centre over a 2-year period from September 2013 to August 2015. Data collected included severity grading, acute elevation in mast cell tryptase (MCT) (>12ng/mL or >135% basal level), and causative agent indicated by the presence of a biomarker to better inform treatment decisions in the clinic.

Results. Of 47 patients identified during this period, ST testing was positive to at least 1 agent in 22 (47%), with NMBA and beta-lactam antibiotics accounting for 10 (46%) and 7 (32%) positive results respectively. Of the 27 patients with MCT results, 14/19 (74%) patients with an acute MCT rise had positive skin tests, compared with only 1 (13%) of 8 patients with no reported MCT rise (P<0.01). Over the same period, 4 patients had positive SpIgE to chlorhexidine (range 0.43-55.8kUa/L). Severe reactions (grade 3) were associated with an increased proportion of positive ST (16/31, 52%) compared with grades 1 and 2 (6/16, 38%), however this result did not reach statistical significance.

Conclusion. The prevalence of causative agents reflects current literature, with an increased proportion of reactions to antibiotics, and decreased proportion to latex. Our audit indicated a significantly higher proportion of positive ST in those with acutely elevated MCT. In our cohort, chlorhexidine appeared to be a common allergen.

89 Edward Smith
Calciprotein particle ripening is associated with priming and activation of the NLRP3 inflammasome in the human macrophage
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Background: Mineral nanoparticles may directly link inflammatory and calcification processes that often appear to co-exist in patients with CKD and in other age-related vascular diseases. Synthetic mineral nanoparticles are strong activators of a pro-inflammatory response in the macrophage in vitro, inducing IL-1β secretion via activation of the NLRP3 inflammasome. Here, we studied the ability of amorphous (CPP-I) and crystalline (CPP-II) serum-derived mineral nanoparticles, which are abundant in these conditions, to prime and activate the NLRP3 inflammasome in human macrophage derived from peripheral monocytes.

Results: Both CPP-I and CPP-II were internalised via scavenger receptor (SR)-A-mediated endocytosis to the endolysosomal compartment. CPP-I failed to prime or activate the NLRP3 inflammasome even at very high levels. In contrast, exposure of naïve cells to high levels of CPP-II, primed inflammatory cytokine synthesis via TLR/NF-κB-dependent signalling. Priming was potentiﬁed by immunochenical blockade or siRNA silencing of SR-A, demonstrating the competitive binding of CPP-II to these two innate pattern recognition receptors. Cell surface binding and uptake of CPP-II resulted in marked changes in intracellular calcium flux that were not apparent with CPP-I. Intracellular trafficking of internalised CPP-II, but not CPP-I, lead to lysosomal destabilisation and partial redistribution to other subcellular compartments. Some CPP-II were found to be in close proximity to mitochondria. CPP-II induced a dose- and time-dependent change in mitochondrial (mt) morphology, fission, loss of membrane potential, increased mitochondrial reactive oxygen species and a release of mtDNA. Direct activation of the NLRP3 inflammasome by these danger signals, as well as sustained elevations in intracellular calcium, amplified mitochondrial damage via opening of the mitochondrial transition pore, induced IL-1β secretion and ultimately, pyroptotic cell death.

Conclusion: crystalline serum-derived mineral nanoparticles prime and activate the NLRP3 inflammasome in the human macrophage in vitro via effects on mitochondrial integrity.

90 Katie Dale
Comparing Tuberculosis management under public and private healthcare providers: Victoria, Australia, 2002-2014
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Aim: In the interests of providing recommendations to improve the management of tuberculosis (TB) in Victoria we sought to compare the healthcare received by TB cases in the public compared to the private sector.

Background: Victoria, Australia, has low tuberculosis (TB) incidence and universal health care. TB cases are predominantly managed in the public sector, however a proportion do attend private healthcare providers. International experience in a variety of settings has suggested different TB-related outcomes in private and public care contexts.

Methods: Retrospective cohort study; 2002-2014. Private healthcare provision was included as an independent variable in statistical analyses in addition to demographic, clinical, pathological and risk factor characteristics. Survival analyses were used to assess various time periods from symptom onset, healthcare presentation, investigations and treatment commencement. Multivariate logistic regression was used to analyse symptoms, laboratory tests, treatment regimens and treatment outcomes.

Results: Of 4,757 cases, 284 (6.0%) were seen exclusively by private healthcare providers, and 4,233 (89.0%) by public. In multivariate analyses private patients were significantly less likely to have genotypic TB diagnosis (Odds ratio [OR] 0.66, p<0.009, 95% confidence interval [CI] 0.48-0.90); and a sputum smear positive (OR 0.48, p=0.003, 95%CI 0.30-0.78), if there was pulmonary involvement; but were not significantly more likely to have a bronchoscopy (OR 1.11, p=0.699, 95%CI 0.66-1.85). The time between healthcare presentation and first specimen collection or chest X-ray was significantly longer (Hazard ratio [HR] 0.76 p=0.001, 95%CI 0.64-0.89) but the time between first positive chest X-ray or laboratory result and treatment commencement was not (HR 0.83 p=0.168, 95%CI 0.63-1.08). Patients attended private providers significantly sooner after symptom onset than public patients (HR 1.81, p=0.002, 95%CI 1.25-2.64) (symptom onset analysis restricted to 2012-2014) and, were significantly less likely to have a...
positive sputum (OR 0.40, p=0.006, 95%CI 0.21-0.77). Private patients were less likely to receive ethambutol (OR 2.30 p=0.001, 95%CI 1.41-3.74), and more likely to be lost to follow up (OR 2.83, p=0.012, 95%CI 1.25-6.40). Improvements over time were observed for several disparities.

Conclusions: Our results indicate that patients may attend private healthcare providers earlier during their disease progression than those that attend public, however the disparities in TB treatment and outcomes between settings prompt the need for whole-of-sector strengthening approaches. These approaches may include educational engagement with private practitioners and improvements in private-to-public referral pathways.

91 Victoria Lewis
Matrix metalloprotease processing of the prion protein

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Background & Aims: Post-translational processing of the cellular prion protein (PrPc) includes several proteolytic cleavage events, namely the well-described alpha- and beta-cleavages, cell surface PrPC shedding, and the newly described gamma-cleavage. The precise purpose of PrPC endoproteolysis is not yet understood, though there is increasing evidence for distinct biological roles of the full-length protein and various N- and C-terminal fragments, as well as links to prion disease susceptibility, prion protein misfolding and prion propagation. The dominant PrPc proteolytic cleavage event in normal (healthy) cells is alpha-cleavage, which occurs within the potentially neurotoxic and amyloidogenic central region of PrPc, producing the N1 and C1 fragments. Despite this, the exact identity of the protease responsible for alpha-cleavage is contentious, with evidence both for and against the involvement of the ADAMs family of proteases. We previously identified the matrix metalloprotease (MMP) family of proteases as capable of PrPC endoproteolysis, in particular MMP2, which could produce C1 from full-length recombinant human PrP (recPrP) in vitro. Additionally, treating cultured cells with prionomastat, a pan-MMP inhibitor, significantly increased C1 levels, and decreased PrPSc levels in M1000 prion infected cells. These novel and dichotomous findings prompted our continued investigation of the role of MMPs in PrPC processing and prion propagation, also incorporating the comparison of biologically relevant PrPc variants (codon 129MV and codon 127GV).

Methods & Results: Utilizing the recombinant protein in vitro assay we found that similar to MMP2, MMP7, and to a much lesser extent MMP9, also cleave PrPc, largely at the alpha-cleavage site. We observed several differences in the processing of recPrP by the various MMPs, including differences in the proteolysis of the recPrP N-terminus, the digestion of higher molecular weight (dimerized) recPrP species, and the involvement in recPrP gamma-cleavage. Interestingly, we also detected differences in the processing of cell derived PrPc and PrPSc by the recombinant MMPs. Of possible relevance to prion diseases, the two codon 129 variants showed similar MMP cleavage profiles, however in contrast, the codon 127V recPrP appeared less susceptible to MMP-induced gamma-cleavage.

Conclusion: Our results indicate the MMP family of proteases are key regulators of PrPC endoproteolysis. Deduction of the precise mechanistic pathway/s of MMP-regulated prion protein proteolysis, and its impact on normal PrPc function and prion diseases, are the subject of ongoing investigation.

92 Jennifer MacLachlan
Antiviral treatment for chronic hepatitis B in Australia: a nationwide analysis of treatment uptake and prescribing trends according to individual antiviral agent

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Background: Antiviral treatment for chronic hepatitis B (CHB) in Australia: a nationwide analysis of treatment uptake and prescribing trends according to individual antiviral agent

Methods: Aggregate, population-level data regarding expenditure for CHB treatment through Medicare were obtained for all approved therapies (adefovir, entecavir, lamivudine, pegylated interferon, telbivudine, and tenofovir). Numbers of patients receiving therapy were derived from these data, and prescribing trends by individual agent were assessed for the period 2011-2013. Individualized data were also obtained for 2013 to examine prescribing patterns for combination antiviral therapy.

Results: The number of patients treated for CHB in Australia increased from 9,000 in 2011 to 10,900 in 2013, for an estimated proportion of all people living with CHB in 2013 of 5%. Patients receiving recommended first-line oral therapies represented an increasing majority, with those receiving entecavir increasing from 44.1% to 46.8% and tenofovir increasing from 26.3% to 34.6%. Usage of lamivudine and adefovir decreased, however together these drugs still represented 17.4% of prescribing expenditure in 2013. Very small numbers of patients received either telbivudine (<1%) or pegylated interferon (1.2%). Combination therapy was used in 9.7% of all patients receiving treatment in 2013, with the most common combinations being lamivudine/tenofovir (546 patients, 4.9% of the total receiving therapy) or lamivudine/adoefovir (454 patients, 4.0%). Combination therapy represented the majority of prescribing for lamivudine (64.4%) and adefovir (82.4%).

Conclusions: The analysis of national prescribing data can provide valuable insight into current pharmaceutical management of people living with CHB, and into prescribing trends in an environment where all CHB therapies are subsidised for use. These data demonstrate that the majority of CHB patients in Australia are receiving entecavir or tenofovir alone or in combination, in accordance with clinical guidelines, however there are still opportunities to optimize treatment outcomes for patients. The finding that the majority of patients treated for chronic hepatitis B receive first-line oral antiviral monotherapy supports expansion of treatment access outside of specialist centres, as identified as a priority in Australia’s National Hepatitis B Strategy.

93 Nompilo Moyo
Evaluation of tuberculin skin testing in tuberculosis contacts in Victoria, Australia, 2005–2013

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Aim: To review the programmatic use of the tuberculin skin test (TST) following tuberculosis (TB) exposure in Victoria, Australia.

Background: Tuberculosis (TB) ranks alongside HIV as the world’s leading cause of infectious disease mortality. Although Australia has a low incidence of TB, TB continues to pose a significant public health threat in Australia with 1,263 cases of tuberculosis notified in 2013.

Methods: A retrospective review of data collected for public health surveillance was performed to identify contact demographic factors, including bacille Calmette-Guérin (BCG) status and age and outcomes of TST.

Results: Contact tracing was performed for 15,094 people, of whom 13,427 (89.0%) had a TST performed. The TST was positive in 31.4% (95%CI 30.6–32.2) of all contacts, and 48.8% of contacts born outside of Australia. Amongst contacts who were TST-negative at baseline, the conversion rate following exposure was 14.8%. Conversion was most common in those aged 45–54 years, with <12% positivity in both the youngest (<5 years) and oldest (>65 years) age groups. Active TB developed in 1.1% of all contacts. Contacts aged <65 years had the highest risk of developing active TB following exposure (3.8%), while low risk was seen in those aged >65 years (0.3%).

Conclusion: Overall, contact tracing and TST in this setting appear to yield a high proportion of people at risk for the development of active TB. The yield of testing in some groups, particularly those aged >65 years, was low, and investigation of alternative strategies should be considered.
94 Susan Tadros
Pneumocystis jirovecii pneumonia in connective tissue diseases: A case-control study
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Background: Pneumocystis jirovecii pneumonia (PJP) is an opportunistic fungal infection that affects the immunocompromised. Patients with connective tissue diseases (CTD) are increasingly recognised as at-risk clinical population with a high mortality.

Aim: This case-control study examined differences in the characteristics and peripheral blood parameters between patients with CTDs who developed PJP and gender, age and disease-matched controls.

Methods: Retrospective data were collected between 2002 and 2013 at the Royal Melbourne Hospital, Australia. Cases were defined by having a CTD and a diagnosis of PJP (either a positive toluidine blue O stain or P.jirovecii PCR, with a concurrent respiratory illness that was clinically consistent with PJP). Controls were matched for age, gender and CTD in a 4:1 ratio. Peripheral blood results were retrieved from an in-house pathology database.

Results: After adjustment for corticosteroid exposure and C-reactive protein, lymphocyte count on admission (0.4 v 1.3; p=0.04) and at nadir (0.2 v 0.7; p=0.05) were significantly lower in cases than in controls. Cases (n=11) were more frequently Caucasian rather than non-Caucasian (81.8% vs 65.9%; p=0.04). In addition, cases more commonly presented in autumn (March to May) than in other seasons (OR 7.3, 95% CI 1.4 to 38.7; p=0.02).

Conclusion: These Australian data demonstrate that CTD patients that develop PJP have significantly greater lymphopenia than age, gender and disease-matched controls, independent of corticosteroid exposure, as well as a potential ethnicity and seasonal predilection to PJP. This may help to inform prophylactic guidelines for PJP in CTD patients.

95 Bang M Tran
The Hepatitis B virus surface and precore proteins may promote the development of liver cancer via upregulation of Wntβ-catenin signalling
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Aim: This study is to examine and characterise the potential impact of the hepatitis B virus surface and precore proteins on the Wntβ-catenin signalling in liver cancer.

Background: Chronic infection with hepatitis B virus was well established to be the main risk factor for development of primary liver cancer, known as hepatocellular carcinoma (HCC), with the presence of infection in approximately 40% to 90% of cases. Among various cellular signalling pathways, the Wntβ-catenin signalling was clinically found to be the most frequently activated oncogenic pathway leading to HCC in up to 60% of HCC cases. However, the connection between Wnt pathway and HBV infection is not well understood. Most of studies focused on the X protein while little was known about the role of viral surface and precore proteins, even though these proteins are known to affect viral replication and establishment of chronic infection.

Methods: To measure Wnt signalling, a TCF/β-catenin transcriptional reporter (sTOPflash) was co-transfected into cells with or without a plasmid encoding active β-catenin. Cells were then stimulated with Wnt3a in the supernatant, and luciferase activity (relative to renilla transfection control) was measured using the Promega Dual Luciferase assay. In addition, western blot was also used to confirm the results.

Results: (1) Using HuH7 cells, we have shown that co-expression of the HBV S protein could enhance receptor/ligand-mediated Wnt signalling. It also further increased the activity of co-transfected constitutively active β-catenin. This enhancement of Wnt signalling by HBs occurs in a dose-dependent manner. In addition, there might be distinct mechanisms between the endogenous and exogenous effects of HBV S protein on Wnt pathway. (2) HBe protein precursor was also found to promote the TCF/β-catenin pathway at a significantly higher level than the HBV X protein. The upregulation effect was consistent in different cell lines. Early results so far suggested this upregulation may happen at the lower downstream level of the Wnt signalling pathway.

Conclusions: These results suggest that while HBV S protein stimulates additive Wnt/β-catenin signalling from both the receptor and transcription complex, the HBe precursor protein upregulates the TCF/β-catenin pathway at the lower downstream level. This may be the mechanisms by which HBV promotes the development of liver cancer.

96 Emma Callegari
Vitamin D status, bone health and depressive symptoms in young women
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Aim/Background: Vitamin D deficiency has been associated with poor musculoskeletal and mental health outcomes but the interplay between these indices remains uncertain. The Safe-D study is a comprehensive study of vitamin D status and a range of clinical, behavioural and lifestyle factors in young women, an understudied demographic.

The aim of this analysis was to investigate the associations between serum 25-hydroxyvitamin D (25OHD), bone mineral density (BMD) and depressive symptoms in young women.

Methods: Female participants aged 16-25 years living in Victoria, Australia, were recruited through Facebook. Participants completed an extensive online health survey and attended a site visit. Dual-energy X-ray absorptiometry was used to measure BMD at the lumbar spine, total hip and femoral neck. Osteopenia and osteoporosis were defined using WHO criteria (Z-score was used in participants aged ≥20). Serum 25OHD was measured using liquid chromatography tandem mass spectrometry (LC-MS/MS). The Patient Health Questionnaire (PHQ-9) was used to measure depressive symptoms.

Results: To date, 197 participants have been fully evaluated. The mean serum (± SD) 25OHD concentration was 74.3±28.8 nmol/L: 41 (20.8%) participants were vitamin D-deficient (25OHD <50 nmol/L). One hundred and twenty-eight (66%) participants had normal BMD; 59 (30%) had osteopenia and 8 (4%) had osteoporosis at one or more skeletal sites. Serum 25OHD of <50 nmol/L was significantly associated with a diagnosis of osteopenia or osteoporosis when compared to 50 nmol/L or above. Osteopenia and osteoporosis were defined using WHO criteria (Z-score was used in participants aged ≥20). Serum 25OHD was measured using liquid chromatography tandem mass spectrometry (LC-MS/MS). The Patient Health Questionnaire (PHQ-9) was used to measure depressive symptoms.

Conclusions: These results suggest that while HBV S protein stimulates additive Wnt/β-catenin pathway at a significantly higher level than the HBV X protein. The upregulation effect was consistent in different cell lines. Early results so far suggested this upregulation may happen at the lower downstream level of the Wnt signalling pathway.

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Conclusion: Analysis revealed significant associations between vitamin D deficiency and BMD in vitamin D-deficient young women. The Safe-D study will recruit up to 500 participants to further investigate the associations between vitamin D status, musculoskeletal health and mental health in young women, aiming to optimise their health and wellbeing.

97 Laura Finlayson-Short
Who am I? fMRI and identity in youth borderline personality disorder
FINLAYSON-SHORT L(1,2), Whittle S(1), Davey C(1,2,3), Jovev E(1,4,5) and John D. Wark(1,5) on behalf of the YFHI and Safe-D study groups
1 The University of Melbourne; 2 Murdoch Childrens Research Institute; 3 Royal Women’s Hospital; 4 Melbourne EpiCentre, Royal Melbourne Hospital, University of Melbourne; 5 Bone and Mineral Medicine, Royal Melbourne Hospital.

Aim: This project investigated the neural bases of identity disturbance in youth borderline personality disorder (BPD). Further, the exploratory aim of this study was to examine the neural correlates of depression in young people with BPD.

Method: Participant recruitment occurred via snowball sampling. Inclusion criteria were: age between 16 and 25 years; a current diagnosis of BPD; and a history of depression and/or anxiety. Exclusion criteria were: a history of head injury; no history of speech therapy; and no current suicidality.

A structural T1-weighted MRI was obtained for each participant. Each participant underwent a unique block design fMRI paradigm that included a baseline, an episodic memory, and a semantic memory task. The fMRI data were analysed using SPM12. A within-subjects analysis was performed for the episodic and semantic memory task.

Results: An exploratory analysis revealed significant decreases in activity in the default-mode network in the right angular gyrus in the group with BPD compared to the control group. In the control group, there was significant activity in the dorsal anterior cingulate, the right middle frontal gyrus, and the left supplementary motor area. In the group with BPD, there was significant activity in the right middle frontal gyrus, the left middle frontal gyrus, and the left insula.

Conclusion: These results suggest that while HBV S protein stimulates additive Wnt/β-catenin pathway at a significantly higher level than the HBV X protein. The upregulation effect was consistent in different cell lines. Early results so far suggested this upregulation may happen at the lower downstream level of the Wnt signalling pathway.

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this trait will improve our knowledge of the disorder and present possible future targets for treatment.

Methods: This study involved two groups of young people between the ages of 15 and 25, those with borderline pathology who met three or more of the SCID-II criteria for BPD (n=14, nine female) and healthy controls (n=14, nine female). Participants underwent fMRI scanning while they completed a task designed to examine processing of self-related information. Previous studies have found that this task engages the default mode network (DMN). The task contained two conditions. The first asked participants to determine whether trait-adjecitves applied to them. The second was a control condition in which participants counted the number of vowels in a matched set of adjectives. Participants also completed the Self Concept and Identity Measure (SCIM) to determine their level of identity disturbance.

Results: When comparing the groups’ neural activity observed during the self-referential task compared to the control task, significant differences were found in regions of the DMN. However, there was also a significant interaction between group and gender in a number of DMN regions. BPD females showed greater neural activity during the self task than their healthy counterparts. In contrast, BPD males had significantly less neural activity during this task than healthy males. BPD patients had significantly greater identity disturbance than controls, evidenced by higher SCIM scores. Regional activations in the self-referential condition correlated positively with these SCIM scores in the two groups showing greatest activation, BPD females and healthy males. Conversely, activity and SCIM scores correlated negatively in the two remaining groups.

Conclusions: Disturbed processing of self-related information, reflected in abnormal DMN functioning, may underlie identity disturbance in BPD. However, the pattern of dysfunction observed differs between males and females with the disorder. These disparate results may be due to differences between the genders in the efficiency of neural network organisation or to the clinical presentation of BPD. These results should inform future treatment research.

98 Eleni Ganella
Widespread reductions in resting-state functional connectivity in a treatment-resistant schizophrenia cohort

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Introduction: Despite advances in antipsychotic medications, approximately 5-10% of schizophrenia patients do not experience a clinically significant reduction in psychotic symptoms with pharmacological therapy, and have thus been said to be experiencing ‘treatment resistant’ schizophrenia (TRS). The “default mode network” (DMN) has been found to show aberrant connectivity in early and established schizophrenia groups. However, little research has investigated the functional connectivity (FC) of the DMN in a TRS cohort. Therefore, this study aimed to investigate resting-state FC in a group of TRS patients in comparison with a group of matched healthy controls and explore what relationship FC abnormalities, if any, have on symptomatology and global social functioning.

Methods: Resting-state functional magnetic resonance imaging was used to evaluate DMN FC in 43 TRS participants prescribed clozapine (mean age=41.3(10), 30 males) and 42 healthy controls (mean age=38.4(10), 24 males). Head motion was controlled for with the Friston 24-parameter. Whole-brain FC across was examined by anatomically parcellated the registered fMRI volumes into 116 nodes using the AAL. We then measured the temporal correlation coefficients between each nodal pair (116x115) to investigate the extent to which the nodes were functionally connected. The network-based statistic was used to correct for multiple comparisons. The Global Assessment of Functioning (GAF) and the Social and Occupational Functioning Assessment Scale (SOFAS) were used to determine global functioning across the entire sample, and the Positive and Negative Syndrome Scale (PANSS) was used to measure symptom severity in the TRS group.

Results: We found reduced mean global brain FC in TRS patients (p=0.002), as well as reduced FC between multiple nodal pairs (153) in TRS patients compared with controls. Nodal pairs showing reduced FC in TRS patients were widespread, however the majority were localized to frontal-temporal, temporal-parietal, and frontal-occipital areas.

Sample wide, mean global brain FC, and FC between the temporal lobes and regions showing reduced FC in the TRS group positively correlated with SOFAS and GAF scores, that is, the greater the FC, the better the global functioning.

Conclusions: These results suggest that FC is widely reduced in TRS patients. This network dysfunction may suggest inefficient system processing that could in turn impact a number of neural processes that are found to be especially impaired in TRS patients. Furthering our understanding of neurobiological impairments in this chronic TRS group can help elucidate brain regions and networks that may be important targets for alternative treatment strategies in the future.

99 Danielle Hitch
A program of knowledge translation for mental health sensory approaches

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Aim: The aim of this project is to describe how a series of research projects have formed a program of knowledge translation for mental health sensory approaches in occupational therapy.

Background: The brain needs to be able to organise sensory input (including touch, movement, proprioception, sight, sound, smell, taste and gravity) to fully make use of them, but research suggests that people with mental illness often experience difficulties with the modulation of their senses. Sensory approaches in mental health aim to support consumers to understand their response to sensory input, and regulate and organise input as a means for attaining better functional performance of meaningful activities. While there is much anecdotal evidence for their effectiveness, research in this area remains in its infancy.

Method: This project will use a recognised model of knowledge translation to describe the program (including a sensory modulation working group, four research studies and associated changes in practice), and critique its impact on both clinical practice and consumer outcomes.

Results / Discussion: The sensory modulation working group meets monthly, and has influenced process guidelines, documentation and practices in the broader organisation. Four research studies will be summarised, all of which have found positive outcomes for consumers from the implementation of sensory approaches. Changes the occupational therapy workforce have made from the program will also be presented, along with further plans for evaluation.

Conclusion: Formulating a program which includes multifaceted knowledge translation strategies has proven to be an effective way of applying research and other evidence into practice. This program has built capacity at all levels of the occupational therapy workforce, and enabled the rigorous and methodical implementation of sensory approaches for consumers. It has also placed the occupational therapy department at the forefront of research into sensory approaches, both nationally and internationally.

100 Jonathan Knott
Management of mental health patients in Victorian emergency departments, a 10 year follow-up study

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1 Melbourne Medical School, University of Melbourne, 2 Emergency Department, Royal Melbourne Hospital, 3 Emergency Department, Dandenong Hospital, 4 Department of Medicine, Monash University, 5 Emergency Department, Geelong Hospital, 6 Emergency & Trauma Centre, The Alfred Hospital, 7 Department of Epidemiology & Preventive Medicine, Monash University.

Aim: Despite efforts to restructure mental health (MH) services across Victoria, the social and economic burden of MH illness continues to grow. This study compares MH presentations to Emergency Departments (ED) with a study undertaken 10 years earlier.

Methods: A retrospective observational study of MH presentations to four Victorian EDs between May and October 2013. Subjects were included if the presentation was mental health related as determined by an ICD-10 discharge diagnosis, referred to emergency crisis assessment team or had a documented presenting psychiatric complaint. Variables were extracted from electronic medical records and compared with 2004 data from a previous published study.
Results: There were 5659 MH presentations over the five months compared with 2788 in 2004. The median ED length of stay (LOS) decreased from 4.18 hours in 2004 to 3.20 hours in 2013 (p<0.001), with a significant reduction in LOS > 4 hours from 22.5% to 34.4% (p<0.001). There was a 22-fold increase in short stay units as discharge destination from 0.9% to 20.2% (p<0.001). Patients presenting with concurrent methamphetamine exposure doubled from 2.2% of presentations to 4.3% (p<0.001).

Conclusions: Despite increasing MH related presentations, changes in ED practice have allowed improvements in delivery of care through a shortened ED length of stay and the virtual elimination of very long stays over 24 hours. However, there continues to be significant variability in management and performance across hospital sites. Identifying which interventions lead to standout site performance, and subsequent application more broadly, may improve future ED delivery of care.

101 Samantha Loi
Tracking challenging behaviours - the Symptom Assessment Manager

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Aims: This program aimed to track and monitor behavioural and psychological symptoms of dementia (BPSD) so that these could be assessed more thoroughly and appropriate interventions implemented.

Background: BPSD are a common manifestation of dementia. In order to design appropriate interventions to manage BPSD, knowing what these are, when they occur, the duration, the triggers, the context, and the distress for the person with dementia (PWD) and their carers is important information. While there are many validated and reliable tools available, in the clinical context, these are not often utilised. Real-time monitoring of BPSD may provide more useful information in order to implement interventions and then monitor how these are affecting the BPSD. Previous literature has commented that although BPSD is an important management aspect of dementia, assessment of BPSD has not been usual part of routine care (Gillin et al. 2014).

The Symptom Assessment Manager (SAM) was developed using information gathered by key clinicians and based on existing literature which reviewed available BPSD measures. The SAM is based on the Neuropsychiatric Inventory (NPI, Cummings 1994), but is web-based for real-time data entry, and is available on a computer or tablet format, rather than traditional paper-based methods.

The SAM was trialed in the Neuropsychiatry Unit (NPU) which is an assessment and diagnostic hospital ward for people with complex psychiatric and neurological symptoms. This also includes people with dementia. Nursing staff were asked to use the SAM in order to test its feasibility, utility and ability to monitor BPSD.

Methods: An evaluation of the SAM which consisted of 10 statements and a 5-point Likert scale for responses was administered to staff.

Results: An evaluation of the SAM was completed by a number of staff. These included nursing staff and medical staff. Overall, almost 90% of respondents stated that completing the SAM took 10 minutes or less and 90% would use the program again. Up to 70% stated that having definitions of each BPSD was useful. Up to 70% of respondents stated that entering data was “easy”.

Conclusion: The SAM appears to be a quick and easy method of monitoring BPSD. Further studies in different settings are recommended. Ongoing refinement of this program is ongoing.

102 Deborah Leighton
Patient satisfaction with the RMH outpatient neuropsychology services: Preliminary data

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The Royal Melbourne Hospital (1), The Alfred Hospital (2)

Aim: This project aimed to quantify patient satisfaction with the Royal Melbourne Hospital Outpatient Neuropsychology Clinic services in Allied Health at the City Campus.

Background: Services in the Clinic include assessment of memory and other cognitive skills, and provision of compensatory strategies to manage difficulties.

Method: Patients were asked to complete a survey following their neuropsychological assessment appointment; 21 surveys were completed between August and December 2015.

Results: Responses to the survey indicated a high level of satisfaction with the service provided by the Clinic. Patients felt that they were given an opportunity to ask questions, had their questions answered in a way that was easy to understand and felt that the neuropsychologist respected what they had to say (average ratings of 9.7, 9.5 and 9.8 out of 10, respectively). While a majority of respondents (over 85%) were aware that they had been referred to neuropsychology, some did not know what to expect prior to the appointment (average rating of 7.5 out of 10). Ninety-five % of respondents indicated that the appointment length was appropriate to meet their needs – this is significant as appointments can last for more than 150 minutes. Finally, close to 62% of patients preferred both written and verbal feedback from their appointment, with less than 15% of respondents indicating that they preferred verbal feedback only. qualitative comments supported satisfaction with the services provided (e.g. “respectful, open-minded, understanding”, “very helpful and informative”).

Conclusion: Patients indicated a high level of satisfaction with the Outpatient Neuropsychology Clinic services at the Royal Melbourne Hospital in a survey conducted in 2015. Identified areas for improvement of the service include: (1) developing procedures to improve patients’ understanding of what to expect during a neuropsychology appointment and (2) the development of written materials to supplement the verbal feedback provided to patients at the conclusion of neuropsychological assessments. Future research will implement this protocol to measure patient satisfaction with outpatient neuropsychology services at the Royal Park Campus (in the Community Therapy Services and Cognitive, Dementia and Memory Service).

103 Eva Staunton
Head to toe: the role of psychology in supporting the Diabetic Foot Unit

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1) Melbourne Health

Aims: Diabetes related foot ulcers are well established to impact physical, mental, social and economic dimensions of quality of life. Few health services have a dedicated psychologist in their multidisciplinary wound teams. The aim of this presentation is to highlight the importance of having access to a clinical psychologist within a diabetic foot unit. They have an invaluable role in supporting the mental health impact of foot wounds, to improve treatment adherence, patient care, and outcomes, as illustrated by a complex case study.

Case Study: A case study of Mr X, a 52 year old male who presented to hospital with a dorsal diabetic foot ulcer caused by a piece of wood, describes the role of psychology in the management of this patient. The wound was infected, requiring urgent surgical debridement, IV antibiotics and revascularisation. Premorbid anxiety, complex and invasive interventions, and a long inpatient stay caused the patient significant distress and anxiety, resulting in him initially declining consent for limb salvage surgery.

Outcomes: Using a cognitive behavioural framework incorporating: cognitive restructuring, relaxation techniques and anxiety management strategies, Mr X was able to consent to numerous surgeries, angioplasty, split skin graph and multiple medical interventions, enabling complete wound healing in 3 months.

Discussion: Diabetic foot ulcers require a multi disciplinary approach in order to achieve best practice and improve patient outcomes. Having a clinical psychologist as a part of the DFU, is an invaluable resource in the management of psychosocial factors that impact wound management and prognosis.

104 Peter Colman
The North West Diabetes Quality Improvement Project – taking Endocrinologists to general practices improves GP confidence in managing diabetes

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(1) Dept. Diabetes and Endocrinology; (2) North West Melbourne Primary Health Network

Background: The burden of diabetes in the Inner North West of Melbourne is high with at least 3.6% of residents affected. A
collaborative network including RMH, Melbourne Primary Care Network, CoHealth and Merri Community Health Services has focussed on improving diabetes outcomes in the region. A needs assessment indicated that improving health professional knowledge and confidence in managing patients with diabetes was a priority.

**Aim:** To increase the capacity of primary care health professionals to effectively manage patients with diabetes in the community and reduce the need for unnecessary specialist care in hospital.

**Methods:** We undertook audits and a tailored quality improvement initiative in eight general practices [24 general practitioners (GPs) and 10 practice nurses]. GPs were asked to select 2 to 4 patients with type 2 diabetes to discuss in a small group setting with a visiting endocrinologist and diabetes nurse educator within their own general practice. Each practice was visited twice. Four endocrinologists undertook visits. Pre and post-visit surveys sought information from GPs regarding their expectations of the program and post program knowledge, confidence in diabetes management and overall usefulness of visits.

**Results:** • 100% of GPs agreed that they attained increased knowledge about diabetes management; • 100% felt that clinical outcomes for the patients discussed were improved; • 100% of practices had improved data collection following visits; • 75% believed that the program increased the quality of care provided within their practices; • 50% felt that participation in the project would reduce the need to refer to hospital outpatient services; • Endocrinologists established valuable links with the practices involved and had a much improved understanding of the disparate needs of GPs and their practices.

**Conclusion:** Specialist outreach programs with a strong educational focus are clearly seen as highly valuable by GPs. Resources need to be made available to continue to extend this successful program.

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**105 Hongyuan Jiang**

**Peripheral quantitative computed tomography (pQCT)** measures contribute to the understanding of bone fragility in older patients with low-trauma fracture

**HONGYUAN JIANG (1), Christopher J Yates (1,2), Alexandra Gorelik (3), Ashwini Kale (1,2), Qichun Song (1,4), John D Wark (1,2)**

Dpt. of Medicine RMH, University of Melbourne (1); Bone and Mineral Medicine, RMH (2); Melbourne EpCentre, UoM and MH (3); Dpt. of Orthopaedics, the Second Affiliated Hospital, Xi’an Jiaotong University, China (4)

**Background and Aims:** Dual energy X-ray absorptiometry (DXA) as currently utilised has limitations in identifying patients with osteoporosis and predicting fractures, since most low-trauma fracture (LTF) patients have osteopenia not osteoporosis based on DXA assessment. We aimed to express peripheral quantitative computed tomography (pQCT) variables of patients with low-trauma fracture as T-scores by using T-score scales obtained from healthy young women, and to evaluate the potential clinical utility of pQCT to complement DXA for the assessment of bone fragility.

**Methods:** Fracture patients were recruited from a fracture liaison service at a tertiary hospital. Reference pQCT data were obtained from studies of women’s health conducted by our group. A study visit was arranged with fracture patients, during which DXA and pQCT measures were obtained to assess their bone strength.

**Results:** A total of 59 fracture patients were recruited, and reference data were obtained from 78 healthy 19 – 25 year-old females after screening for medical exclusions. All DXA variables and most pQCT variables were significantly different between healthy young females and fracture patients (p < 0.05), except polar stress strain index (SStip; p = 0.15). Fracture patients were divided into osteoporosis and non-osteoporosis groups according to their DXA T-scores. Significant differences between these groups were observed in most pQCT variables (p < 0.05), except trabecular area and cortical density (p > 0.9 and p = 0.5, respectively). By applying pQCT T-scores, 15 (37%) LTF patients who were classified as low-medium risk of fracture on DXA T-scores alone were reclassified as high risk. Results of logistic regression suggested trabecular volumetric BMD and SStip were independent predictors of fracture risk status.

**Conclusions:** More patients can be identified as having high fracture risk by applying pQCT T-score variables in older people with low-trauma fracture. Peripheral QCT T-scores contribute to the understanding of bone fragility in this population.

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**106 Mervyn Kyi**

**Glycaemic variability and diabetes inpatient outcomes**

**KYI M, Italiano S, Colman PG, Fourlanos S**

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**Background:** Hospital inpatients with diabetes have poorer clinical outcomes than those without diabetes. In critical care, glycaemic variability (GV) is a predictor of mortality, and in general ward patients GV has been associated with increased length of stay (LOS) and 90-day mortality. We aimed to assess GV in diabetes inpatients to determine its relationship to clinical features (age, HbA1c, insulin therapy, type 1 diabetes (T1D), acute kidney injury, chronic kidney disease, delirium and glucocorticoids), and hospital outcomes (hypoglycaemia, critical hyperglycaemia, length of stay (LOS), and 1-year mortality).

**Methods:** Diabetes inpatients in medical and surgical wards (n=210) with a minimum three days LOS had glucose control monitored in the first 72 hours after admission. GV was assessed by standard deviation (SD) of capillary blood glucose levels (BGL), and coefficient of variation (CV) calculated as the ratio of SD to mean glucose.

**Results:** The cohort had a mean age of 70±15 years, HbA1c: 7.4±1.6%, and 38% were receiving insulin prior to admission. The median LOS was 9 days. The mean BGL was 9.8 mmol/L. Hypoglycaemia (BGL <4.0mmol/L), Hyperglycaemia (BGL >10.0mmol/L), and critical hyperglycaemia (BGL >20.0 mmol/L) occurred in 6%, 64%, and 6% of patient-days respectively.

**Overall measures of GV were SD: 2.9±1.4 mmol/L and CV: 29±11%. On bivariate analysis, GV was significantly greater in patients treated with insulin (SD: 3.2±1.2 mmol/L vs. 2.6±1.5 mmol/L, p=0.0001), and T1D (SD: 4.4±1.2 mmol/L vs. 2.8±1.4 mmol/L, p<0.0001). GV correlated with admission HbA1c (r=0.486, p<0.001). On multivariable analysis, GV was associated with age, HbA1c, insulin therapy, T1D, and delirium. GV on Day 1 correlated with GV on Days 2-3 (r=0.509, p=0.001). When adjusted for other clinical features, GV was independently associated with hypoglycaemia and critical hyperglycaemia. Each 10% increase in CV was associated with 4 times increased risk of hypoglycaemia. There was no association between GV and LOS or 1-year mortality.

**Conclusion:** Glycaemic variability is greater in patients with insulin therapy, type 1 diabetes, and higher HbA1c. GV was persistent during the admission and predicted the risk of hypoglycaemia and critical hyperglycaemia. Earlier intervention in higher risk patients to reduce GV may decrease adverse effects related to inpatient hypoglycaemia and hyperglycaemia.

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**107 Mervyn Kyi**

**Use of a glucose alert pathway and connectivity blood glucose meters reduces inattention to hospital diabetes management**

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Department of Diabetes and Endocrinology, Royal Melbourne Hospital

**Background:** In hospitalised patients, hypoglycaemia and hyperglycaemia are associated with infections, mortality and increased costs. Clinical inertia and inattention to diabetes are major barriers to achieving optimal glycaemic control. We investigated the effect of a novel Glucose Alert Pathway (GAP) and Connectivity Blood Glucose Meter (CBGM) technology on nursing and medical staff action in response to suboptimal glycaemia.

**Methods:** The study was a prospective, pre- and post-implementation audit on two wards (medical and surgical) at the Royal Melbourne Hospital. The intervention consisted of two components: GAP (a paper-based glucose management and clinical escalation guideline) coupled with CBGM with visual alerts for out-of-range capillary blood glucose levels (BGL). A study visit was a prospective, pre- and post-implementation audit on two wards (medical and surgical) at the Royal Melbourne Hospital. The intervention consisted of two components: GAP (a paper-based glucose management and clinical escalation guideline) coupled with CBGM with visual alerts for out-of-range capillary blood glucose levels (BGL)

**Consecutive inpatients with diabetes admitted with length of stay (LOS) ≥ 1 day were assessed for capillary BGL measures, diabetes treatment and hospital outcomes. BGL data was analysed per patient-day.**

**The primary outcome was appropriate staff action on patient-days with reportable low or high BGLs (defined as BGL < 4.0 mmol/L, or > 15.0 mmol/L, or two consecutive BGL > 10.0 mmol/L at least 4 hours apart).**

**Appropriate nursing staff action was defined as documented evidence noting medical staff. Appropriate medical staff action was defined as documented evidence of reviewing or adjusting diabetes management.**

**Secondary outcomes were adverse glycaemic days (patient-days with...**
**ROGASCH S(1), McCann J (1) Wright, P (1)
1: Melbourne Health**

Background: Appropriate footwear is an important aspect of treatment for patients with diabetes. Peripheral neuropathy, peripheral vascular disease and foot deformity places these people at high risk of foot complications such as ulceration and infection. Appropriate footwear is difficult to obtain for patients in the community. Barriers to using appropriate footwear were identified including cost, access, availability and education of patients and footwear providers. A gap in accessibility and service provision was identified based on anecdotal evidence reported by patients within the HARP (Hospital Admissions Risk Program) Diabetic Foot Unit (DFU) – Community, a high risk foot service affiliated with the Royal Melbourne Hospital. Clinicians identified health impacts associated with this including re-ulceration and subsequent increased risk of infection and/or hospitalisation.

Method: An evaluation of two brands of footwear was performed by a group of expert podiatrists. The three DFU-Community sites were provided with a range of stock and standardised fitting devices allowing provision of appropriate footwear within the community at an affordable price. All DFU-Community staff were educated regarding the provision of footwear before the service was implemented in May 2015.

Results: Retrospective data from year before the service development (2013 – 2014) showed 13 applications for footwear from the HARP Brokerage fund with a total cost was $12173.00. The cost of footwear currently available is a minimum of $435. The new Dr. Comfort footwear costs $165 a pair with the neoprene style at $85 a pair.

Conclusion: We have successfully implemented a new footwear provision program within the DFU-Community to allow patients access to appropriate footwear across multiple sites within our service. Phase 2 of the project will investigate the costs associated, the number of patients utilising the service and the timeliness of the service to measure its ongoing success.

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**BGL < 4.0 mmol/L or BGL > 15.0 mmol/L, hospital complications and LOS.**

Results: Over the study period, 157 patients with diabetes were recruited. In the 6-weeks baseline and 8-weeks intervention periods, there were 72 patients (359 patient-days) and 85 patients (311 patient-days) respectively. Reportable BGLs occurred in 148 (42%) and 114 (37%) of patient-days in the baseline and intervention periods respectively (p=0.12). Of patient-days with reportable BGLs, appropriate nursing staff action increased from 34% at baseline to 58% at intervention period (p<0.001). Similarly, appropriate medical staff action increased from 33% to 50% (p=0.004). However, there was no increase in diabetes medication adjustment (baseline 24%, intervention 29%, p=0.3) or endocrinology consults (baseline 14%, intervention 17%, p=0.6). There was a significant 24% decrease in adverse glycaemic days as a proportion of all patient-days (baseline: 29%, intervention: 22%, p=0.03). There was no difference in hospital complications or LOS.

Conclusion: The GAP coupled with CBGM technology, increased nursing and medical staff attention to diabetes, however there was evidence of ongoing clinical inertia with little action to adjust diabetes medications or seek endocrinologist assistance. Overall, the intervention resulted in a quarter reduction of adverse glycaemic days in hospital.

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**108 Jane McCann**

To identify whether the systolic pressures of toes two to five are consistent with the first toe systolic pressure in people with diabetes

MCCANN J (1), Karahalios E(2), Morrow F(1), O’Keefe S(1), Rogasch S(1), Smith K(1), Iacobaccio L (1), Freeman A(1), Wraight P(1)
1 - Melbourne Health 2- The University of Melbourne

Aim: To identify whether the systolic pressures of toes two to five are consistent with the first toe systolic pressure in people with diabetes

Background: Australian data suggests that every three hours, one Australian loses a limb as a consequence to diabetes related foot ulcerations. First Toe systolic pressures are a reliable bedside tool, however the agreement between the the first and lesser toe systolic pressures. To identify whether the systolic pressures of toes two (i.e. toes 2-5) compare to the first toe.

Method: The study recruited 99 adults with diabetes from The Royal Melbourne Hospital. Podiatrists used handheld doppler to conduct toe systolic pressures on all five toes. Blank-Altman plots determined the agreement between the the first and lesser toe systolic pressures. Sensitivity and specificity analyses were performed, using the appropriate clinical cut off (45 mmHg) and the first toe systolic pressure as the reference.

Results: The second toe systolic pressure had the best agreement to the first toe systolic pressure with a mean difference of 7.96 mmHg (95% CI 5.06, 10.87). The limits of agreement ranged from -29.63mmHg (95% CI -49.94, -9.34) to 45.56 mmHg (95% CI 25.25, 65.87). The second toe systolic pressure had high sensitivity 86.7% (95% CI 69.3, 96.2), specificity of 95.5% (95% CI 90.4, 98.3), positive predictive value of 51.3% (95% CI 66.3, 92.0) and negative predictive value 96.9% (95% CI 92.4, 99.2) compared to the first toe systolic pressure. The sensitivities were high for the third (93.3% (95%CI 77.9- 99.2)), fourth (75.0% (95%CI 53.3-90.2)), and fifth toe (78.6% (95% CI 59.0-91.7)) systolic pressures. The specificities were also high for the third (94.7% (95%CI 89.5-97.9)), fourth (93.2% (95% CI 87.5-96.8)), and fifth toe (96.9% (95% CI 92.9-98.1)) systolic pressures.

Conclusion: Where a first toe systolic pressure cannot be obtained, the toe systolic pressure from toes 2 to 5 is a clinically appropriate substitute.

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**109 Sonja Rogasch**

Now you’re healed, let’s get you heeled; footwear for the high-risk foot.
Conclusion: Asians with T2DM living in Australia developed diabetes at an earlier age than Caucasians and had lower BMI at the time of diagnosis. The BMI difference was maintained over years. They required insulin therapy at younger age. The diabetes complication rate is overall similar to that seen with Asians living in their homeland with retinopathy and nephropathy been more common than foot ulcers and macrovascular disease.

111 Marjan Tabesh
The link between metabolic syndrome and osteoporosis

TABESH M(1), Garland SM(1-3), Callegari ET(1), Gorelik A(4), Rivers A(1), Nankervis A(5), Kale A(1,6), and Wark JD(1,6) on behalf of the YFHI and Safe-D study groups
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Osteoporosis is an important public health issue due to increased fracture risk, significant health care costs and high mortality and morbidity. The association between osteoporosis and hypertension, dyslipidaemia and abnormal glucose metabolism, which are components of metabolic syndrome, has been extensively studied. Results are conflicting and it remains unclear how osteoporosis and metabolic syndrome interact.

The aim of this study was to (1) assess the relationship between metabolic syndrome components and bone health measures [bone turnover markers (BTM) and bone mineral density (BMD)] and (2) evaluate whether 25-hydroxyvitamin D (25OHD) levels provide a link between osteoporosis and metabolic syndrome.

Safe-D is a cross-sectional study evaluating vitamin D status, physical health and mental health in young women. Women aged 16-25 years old living in Victoria, Australia, were recruited through Facebook advertising. Participants completed an online survey and attended a study site visit where metabolic profiles, blood pressure, serum 25OHD levels, bone turnover markers and bone density were measured. 390 participants were recruited in this study. The mean (±SD) age, body mass index (BMI) and energy intake were (22.1 ± 2.8 year, 24.1 ± 5.1 kg/m2 and 6940.9 ± 2843.5 kJ/d, respectively). All measurements were on fasted血液.

Participants with osteoporosis had higher high density lipoprotein (HDL) levels (p=0.008). Significant negative associations were observed between CVD (C-terminal telopeptide) and HDL (β = -0.164, p = 0.001), P1NP (Procollagen I N-Terminal) and HDL (β = -0.142, p = 0.004), and femoral neck BMD and triglycerides (β = -0.135, p = 0.004) after adjustment for BMI, physical activity, season, age and oral contraceptive use. A significant independent association between HDL and 25OHD was also observed (β = 0.217, p = 0.001) after adjustment for BMI, physical activity, season and age. However, sensitivity analyses showed that 25OHD had no impact on any association between HDL and BTMs. No significant associations were found between other components of the metabolic syndrome (e.g., systolic and diastolic blood pressure and fasting glucose levels) and 25OHD, BTMs and BMI, respectively.

These findings suggest that indices of bone health and 25OHD levels are independently associated with various components of the metabolic syndrome in young women. These associations may relate to future disease risk. Possible underlying mechanisms warrant further investigation.

113 Emma Callegari
Vitamin D status and skin damage in a sunny climate: The SAFE-D study

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Skin damage has increased with exposure to sun and ultraviolet (UV) radiation. Vitamin D plays an important role in skin health and skin cancer prevention.

Aim/Background: Maintaining adequate vitamin D status without increasing skin cancer risk may be difficult in sunny climates. We therefore examined the relationships between circulating 25-hydroxyvitamin D (25 OHD) levels, ultraviolet (UV) exposure and actinic skin damage in young Victorian women.

Methods: Safe-D study participants completed an online questionnaire, were a UV dosimeter for 14 days and attended a site visit. Serum 25 OHD was measured using liquid chromatography-tandem mass spectrometry. Melanin density was measured at the upper, inner arm using spectrophotometry. Actinic skin damage was measured by scoring silicone skin casts of the hand using the Beagley-Gibson grading system on a 1-6 scale (higher score indicating greater damage).

Results: Data for 204 participants were available for analysis. Mean (SD) serum 25 OHD was 74.0 (28.7) nmol/L. In women with mild skin damage, 23% were vitamin D-deficient (25 OHD < 50 nmol/L) compared to 21% with moderate-to-severe damage (p=0.080). The median skin cast score was 3/6 (Q1-Q3 2-4). Adequate vitamin D status correlated with increasing sun exposure (OR 1.50, p=0.008) and preference to go into the sun to tan when adjusted for season, body mass index (BMI) and melanin density (OR 2.18, p=0.002). Participants with higher melanin density were less likely to have adequate vitamin D when adjusted for season and BMI (OR 0.24, p<0.010).

Conclusion: This analysis indicates a high prevalence of moderate-to-severe actinic skin damage in young women despite vitamin D deficiency being common, raising concern whether it is feasible to maintain adequate vitamin D levels while minimising skin damage and skin cancer risk.
of information delivery, evidence underpinning information, engagement of the right health professionals at the right time, and a non-judgemental approach to infant feeding. Themes included practices for primary prevention of chronic disease and their sequelae, the importance of contraception and planning pregnancy and breastfeeding, close monitoring of medications, supporting mental wellbeing, managing disease activity and providing practical support for early parenting.

Conclusions: A cross-disciplinary clinical panel highly supported key information and clinical practices in the care for women with RA across the continuum of contraception to early parenting within a whole-person, chronic disease management approach

116 Michele Chen
Displaying visual cues to increase compliance of using a gait aid
Michele Chen

Aim: To identify how frequently a gait aid is misplaced and if visual cues such as a photo can help to increase compliance to using a gait aid correctly.

Background: Forgetfulness, misidentification and wandering are common in people with dementia. These behaviours could potentially increase the likelihood of refusal to use a gait aid, mistaking another person’s gait aid with their own, or walking off forgetting the need to use a gait aid. Secure Geriatric Evaluation Management (Secure GEM) specialises in caring for people with dementia. Non-compliance with gait aid is high among people with dementia which can lead to increase falls.

Methods: All patients admitted to Secure GEM, Royal Park Campus, Royal Melbourne Hospital who use gait aids were asked to have their photos taken while holding their given gait aids. Mobility photos are displayed in patient’s room and on their given gait aid. Pre and post intervention audits were conducted two months pre-intervention and three months after intervention is implemented.

Results: During the pre-intervention period, there were 10 falls from patients who use gait aids. Gait aid was not within reach or being used 21% of the time. In comparison, there were 4 falls from patients who have mobility photos and use gait aids during the post intervention period, and that gait aid was not within reach or being used 7% of the time.

Conclusion: This study demonstrated that visual cues, such as a photo, can help to reduce gait aids from being misplaced. It also helps to remind a person to use the recommended gait aid and potentially reduce the risk of falls.

117 Anita Goh
Engagement via technology of residents with dementia in aged care facilities

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Aim. This project involved a specialist multidisciplinary dementia team - comprising of a neuropsychologist, consultant psychiatrist, occupational therapist, nurses, lifestyle coordinators and facility key staff, to deliver interactive education workshops to staff to focus on the benefits of using touchscreen technology (TT) in their residents with dementia (including increased engagement, reducing anxiety and depression, improving quality of life, and reducing the behavioural and psychological symptoms of dementia, BPSD).

Background: Recently, technology such as robotics and global positioning systems technology has been used to assist in the quality of life for the dementia population. Another potential approach to improving quality of life which has not been formally utilised is touchpad technology (TT), such as iPad and similar tablets. TT may provide a resource that can unlock many interventions to harness the welfare of older residents, people with dementia and care staff through a person-centred approach.

Methods. Education workshop topics discussed included:
1. The ageing process and dementia, including information about memory changes, symptoms and diagnoses and the common BPSD
2. The evidence behind using TT in the care of those with dementia
3. The practical day to day logistics of using TT and engaging a resident
with TT (such as when and how to use TT, damage and breakage risk, storage of the TT).

Results: Introduc... the care of people with dementia.

Conclusion: This project found TT effective and impactful on the day-to-day lives of people with dementia and the staff engaged in their care, thus providing more evidence that TT can make a positive contribution to helping people to live well with dementia.

118 Jacqueline Kay

Can a culture change make Aged Care a more attractive rotation for junior Physiotherapy staff?

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Background: Poor culture was identified by the Aged Care (AC) Physiotherapy team leader through observation and informal feedback in February 2012. A staff satisfaction survey was conducted, followed by a team-building planning day. Themes from the feedback indicated lack of support for junior Physiotherapy staff, increased caseload pressure, decreased access and subsequent poor relationships with the Multidisciplinary ward-based team members, and difficulty with patient transport to gym-based exercises.

Aim: To instigate and evaluate if changes based on principles of supportive leadership and equality within a Physiotherapy team can result in an overall culture change.

Methods: As a result of the identified themes, a multiple strategy approach was undertaken. This included shifting Physiotherapy assessments and treatments from gym-based to ward-based interventions; caseload reallocation to relieve pressure on junior staff; allowing Physiotherapists to discharge patients when intervention is futile and no goals identified; and the allocation of patients’ with increased complexity to senior staff, or to junior staff with extra support, including senior presence during family meetings.

AC Physiotherapy staff were re-surveyed using the original survey in March 2015. Results were collated with themes analysed. The participants were the AC Physiotherapy team, at a large metropolitan hospital in Melbourne, Australia (approximately fourteen Physiotherapists and Allied Health Assistants).

Results: Surveyed staff listed senior support and teamwork as the best features of working as an AC team. Caseload pressure was noted as a positive or negative. Overall team culture and the relationship with ward staff has improved. Grade One rotation preferences selecting AC increased over the past three years.

Conclusion: By addressing specific issues identified, there has been a positive cultural outcome from implementing changes driven by the AC Physiotherapy team. It is concluded that providing increased support to Junior Physiotherapy staff during AC rotations, particularly with patients and families grieving the loss of function and independence can have a positive impact on team culture. Junior staff also need guidance and support for discharging patients when intervention is futile.

119 Joanne Tropea

Poorer outcomes for hospitalised people with dementia and delirium

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Background: Approximately 20% of general medical inpatients have cognitive impairment (delirium and dementia), with prevalence higher among older patients and following orthopaedic surgery. However, there is a paucity of literature on the acute hospital costs associated with cognitive impairment.

Aim: The aim of the study was to compare healthcare utilisation outcomes among older hospitalised patients with and without cognitive impairment and to compare the costs associated with these outcomes.

Methods: Retrospective cohort study of administrative data from a tertiary hospital in Melbourne, Australia from 1 July 2006 to 30 June 2012. People with cognitive impairment were defined as having dementia or delirium coded during the admission. Outcome measures included length of stay, unplanned readmissions within 28-days, and costs associated with these outcomes. Regression analysis was used to compare differences between those with and without cognitive impairment.

Results: The adjusted median length of stay was significantly higher for those with cognitive impairment compared to those without (7.4 days vs. 6.7-10.0 vs 6.6 days, IQR 5.7-8.3; p<0.001). When only those discharged back to their usual residence were included in the analysis, the risk of 28-day readmission was significantly higher for those with cognitive impairment compared to those without. The adjusted cost of admissions involving patients with cognitive impairment was 51% higher than the cost of those without cognitive impairment.

Conclusion: People with cognitive impairment had greater length of stay and among those discharged home were more likely to be readmitted within 28-days compared to the non-cognitively impaired. The costs associated with hospital utilization were significantly higher for those with cognitive impairment.

120 Neha Kaul

Considerations for the use of the ketogenic diet as treatment for refractory status epilepticus in the intensive care unit – A case report

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Background: The resolution of refractory status epilepticus (RSE) is critical to reduce the risk of complications including, hypoxic brain injury, cardiac arrhythmia and respiratory distress. It requires specialist neurological and intensive care unit (ICU) management including, sedation, anti-epileptic drugs (AED’s), magnesium infusion, immunotherapy and potentially surgery.

The ketogenic diet (KD) is a high fat, low carbohydrate diet that is a well-established treatment in paediatric refractory epilepsy. The underlying mechanism of the KD remains unknown, but is likely a combination of increased fatty acid and Kreb’s cycle metabolism and neurotransmitters and ion channel regulation. Acute complications of KD include hypoglycaemia, metabolic acidosis and gastrointestinal intolerance. KD use is contraindicated with concurrent use of some AED’s and sedative agents.

The Case: A 59-year-old male was admitted to RMH for elective cranioplasty. Two years prior, the patient underwent decompressive craniectomy following a motorcycle accident resulting in traumatic head injury with residual acquired brain injury and hemiparesis. The patient was taking levetiracetam for anti-seizure prophylaxis and had no reported seizures prior to admission.

Following surgery, prolonged focal seizures were observed. Multiple AED’s were administered without resolution and the patient was transferred to the ICU. After six days, sedation was unable to be weaned without increased seizure activity. The patient was on multiple AED’s including midazolam and propofol infusions, levetiracetam, sodium valproate and phenytoin. Subsequently, the patient was referred for initiation of KD. KD formula was commenced via nasogastric tube. On Day 3 post commencement, beta-hydroxybutyrate levels were 2.2-2.5 mmol/L and blood glucose levels were 6.2-8.5 mmol/L. Lacosamide was commenced. The patient remained on ketogenic formula and no further seizures observed.

Discussion: Although it cannot be definitively determined that the KD was directly responsible for the resolution of RSE in this case, it is likely to be a contributing factor along with medications and other supportive care. The use of sedative agents, AED’s and metabolic monitoring require careful consideration when selecting KD as a treatment. These may be contrary to standard practice within the ICU.

Conclusion: Traditionally KD is used as treatment of chronic paediatric epilepsy, but this case demonstrates a likely benefit in an older patient in the acute setting. Evaluating the efficacy of KD for RSE is difficult due to heterogeneity of patient presentations and concurrent treatments. A robust clinical trial is required to answer this question, but the emerging number of published case series reporting resolution of RSE with KD treatment is promising.
Transition to non invasive ventilation from invasive ventilation via Tracheostomy - a multi disciplinary approach - Case study: Respiratory Care Unit 2015 Royal Melbourne Hospital

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Respiratory Medicine1, Medicine and community 2

Introduction: The Respiratory Care Unit (RCU) is a four-bed unit within the ward SSouth West (Respiratory and General Medicine) at the Royal Melbourne Hospital, which specialises in managing patients with acute respiratory issues, admitted from ICU and ED and post met call patients. Non invasive ventilation (NIV) is the delivery of mechanical ventilation without the need for artificial airway through the larynx or trachea. There is very limited literature available on the transition to NIV from Invasive Ventilation via Tracheostomy.2

Mrs. LH is an 81 years old patient transferred from ICU to RCU for tracheostomy weaning and ventilator support from hypoaxia and hypercapnea.

- Patient had 18 days of ICU stays and 11 days of tracheostomy tube instilu.
- Type 2DM, HTN, hypercholesterolemia, obesity, BMI>35, OSA? Total right knee joint replacement complicated by post operative hypoaxia.
- Requiring emergency intubation,made difficult due to narrowing of trachea second to a retrosternal goiter.
- Post removal of goiter patient had tracheostomy for ventilator support.
- ABGs on arrival to RCU on Fio2 of 0.3, Ph; 7.37; Paco2:54, Haco3:29, Paco2:52, Sao2:86.

Aim of this case study: Review of Transition to NIV from Invasive ventilation via Tracheostomy.

Methods: Verbal consent obtained from patient for Transition to NIV from Invasive ventilation.

Steps involved: 1. Referrals to: To ENT (ENT review to exclude large suprastomal granulation, diameter of the airway etc; Speech pathology for swallowing and cuff deflation trial including assessment for PMV suitability; Physiotherapist for mobilization (exercises to maximize knee range of movement and strength);and cuff deflation trial; Tracheostomy team involvement to oversee tracheostomy wean. Tracheostomy team includes, ICU liaison CNC, Physiotherapist, Speech pathologist, Resp Clinical Nurse Consultant; Nursing staff full nursing care and mobilization out of hours.

2. Implementation or Transition to NIV from Invasive ventilation via tracheostomy: With both the Respiratory physicians and Respiratory Clinical Nurse Consultant (ICU back ground) in attendance the initial NIV trial was commenced using a nasal mask when the tracheostomy cuff was deflated and the PMV was insitu. Patient tolerated NIV for 2 hours at a time and followed by more than 9 hours tolerated. Three days later the patient was decannulated and discharged to Rehab. Upon discharge ABGS are on room air PH7.4, Paco2:44, Paco2:92, Hco3:27, Sao2:94%

Conclusion: Transition to NIV therapy from invasive ventilation via Tracheostomy is challenging due to patient’s tolerance and Claustrophobia, anxiety, communication difficulties. However the involvement of multi specialty teams made in this case more effective treatment.

Further evidence for POLE as a predisposition gene in Lynch Syndrome

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Respiratory Medicine1, Medicine and community 2

Background: Genetic susceptibility accounts for up to 35% of colorectal cancer (CRC) predisposition; high penetrance germline mutations in known CRC-susceptibility genes are found in 3-5% of all CRC. High risk genes include the DNA mismatch repair genes, APC, MUTYH, STK11, BMPR1A, SMAD4, PTEN and more recently, the POLE and POL21 genes. Lynch syndrome in an autosomal dominant inherited cancer susceptibility syndrome, where carriers of mutations in the mismatch repair genes are predisposed to cancers especially of the colorectum and endometrium. The POLE c.1270C>G, p.(Leu424Val) mutation has been emerged as a low frequency but highly penetrant variant in familial CRC and polyposis patients, explaining approximately 0.25-1.4% of the heritability in CRC.

Case study and Conclusion: We report a novel POLE variant c.1708C>A p.(Leu570Met) in a 28 year old man with suspected Lynch syndrome. Individual testing for this gene may not be cost effective. With the transition from genetics to genomics, with multigene testing panels and whole exome sequencing, inclusion of this gene in the investigation of the heritability of CRC is warranted. Given the evident phenotype, with its similarity to LS, consideration of risk management colonooscopic surveillance as for LS seems prudent, as more data is gathered about the clinical utility of mutations in this gene.

Evolution in progress: the intriguing case of the lambda (type III) interferons

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Background: Gene duplication, a ubiquitous biological phenomenon, is arguably the major driver of evolution and contributor to genetic robustness. Large-scale gene duplications, including whole genome duplications, occurred very early during the evolution of anninotes and subsequent smaller scale duplications have continued to occur, along with gene losses. In the short term, gene duplication provides insurance against genetic damage; in the longer term homologs may accumulate mutations and become non-functional or acquire complementary or new functions. Duplicated sets of interacting genes tend to be retained since loss of interaction stoichiometry usually decreases network robustness.

Evolution by gene duplication is epitomised by the recently-discovered type III (lambda) interferons (IFNLs), a group of small homologous cytokines encoded by a gene cluster located within a ~50kbp region on the long arm of chromosome 19. The canonical members (IFNL1, 2 and 3) were discovered in 2003. A fourth homolog (IFNL4), expression of which was found to be restricted to specific ethnic groups, was discovered in 2009. IFNLs are functionally similar to type I interferons, but their activities are restricted to cells of epithelial origin. They have attracted considerable interest since several genome-wide association studies revealed that single nucleotide polymorphisms in their non-coding regions strongly influence both spontaneous and treatment-induced clearance of some viral infections as well as influencing severity of sterile inflammatory responses underlying allergic conditions such as asthma. IFNLs clearly play pivotal roles in inflammation and immunity, but many aspects of their regulation and function remain unexplored.

Methods and Aims: Various genomics and bioinformatics resources, all of which are freely accessible via the internet, were used to investigate the phylogeny and structure of the IFNL locus and its products in an attempt to discover more about the evolution biological effects of genetic variation at this locus.

Results and Conclusions: Early duplication of an ancestral type I interferon produced a primordial IFNL gene (probably corresponding to IFNL1), further duplications of which generated IFNL2 and IFNL3. The phylogeny of IFNL4 and reason(s) for recent selection against this expression are still unclear. Despite their close sequence homology, differences in IFNL gene and transcript structure predict differences in turnover rates. Likewise, predicted interactions of their protein products and differences in the potential for post-translational modification support the idea that IFNL genes are “modern” genes that are still actively evolving in response to environmental pressure. Future investigation of this area should prove interesting and informative.
124  Emily Higgs
A new model of care for clients at low-moderate risk of familial breast cancer

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Background: Familial cancer services in Victoria are funded by the Department of Health to provide services to high risk individuals/families. Currently at The Royal Melbourne Hospital Familial Cancer Centre all high risk referrals undergo standard verification of cancers and family history, with a subset of referrals then re-assessed as moderate or low risk with the additional information. These individuals, who have already engaged with the FCC, generally have an expectation of an appointment. Previously, these clients were allocated a 45-60 minute telephone appointment with a consultant. A novel model of care was developed to address the growing number of individuals at low-moderate risk of familial breast cancer.

Method: Clients deemed to be at low-moderate risk of familial breast cancer, based on the National Breast and Ovarian Cancer Centre guidelines, were invited to attend a 45 minute group information session. Following this, attendees were invited to a 5-10 minute individual consultation with a genetic counsellor and medical oncologist to address any specific concerns and to receive tailored advice. They were also given the option of arranging self-funded genetic testing at this point. Attendees were asked to complete a feedback questionnaire at the end of the session. All attendees received a standard summary letter following the session, with additional tailored advice if they attended the individual consultation.

Results: For the pilot group information session, 19 clients were invited to the information session, with nine accepting the invitation. Two clients brought a relevant family member, comprising 11 attendees. Of these, seven elected to take up the brief individual consultation with one proceeding with self-funded BRCA testing. None of the clients’ risk assessments changed following the individual consultations. Summary family history data are presented, as well as a summary of client feedback. Feedback from clients who attended the group information session suggests this model was well-received.

Conclusion: Genetic counselling research has highlighted the need for flexible approaches to delivery of services in response to increasing demand. Our experience, together with published evidence, supports consideration of group counselling as a potential approach for some areas of healthcare.

125  Tim Shaw
Computing with nucleotides: the mitochondrion as an evolvable, self-regulating power oscillator

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Introduction: During the past two decades, the “big data” explosion and the advent of omics and nanotechnology has allowed the concept of the cell as a supercomputer to materialise from theoreticians’ dreams into practical, testable reality. A new field named synthetic biology has developed, inspired by the striking similarities between evolved (genetic) and engineered (computational) control systems. It aims to analyse and emulate complex biological by using electronic models and vice versa.

Self-Organizing Criticality (SOC) and Highly Organized Tolerance (HOT) are two well-established conceptual frameworks for studying the behaviour of complex networks. Besides complexity, both identify essential network characteristics as meta-stability, robustness and the ability to self-regulate. “HOTSOCS” networks cope easily with “normal” fluctuations in input but freeze or disintegrate when challenged by input signals that are outside the “expected” frequency and amplitude range, when the responses can vary from organized power-up to burnout or power-down to switch-off. Engineered networks rely on appropriately coupled and regulated power supplies for optimal performance.

Mitochondria, the organelles that have evolved to orchestrate these processes in eukaryotic cells, provide a platform for integration of the signals that control vital reactions as well as the energy needed for their execution. In multicellular organisms, individual cells’ power requirements vary enormously, depending on many factors that include developmental stage, nutrient availability and ionic microenvironment. Respiring mitochondria supply most cells’ power as ATP, producing the signalling molecule superoxide as a by-product. Significantly, respiration is also required to generate UMP, the common precursor of all other pyrimidine nucleotides. Regulated nucleotide production is essential for a plethora of cellular functions including mitochondrial maintenance.

Aim and Methods: To produce an electronic analogue model of mitochondrial nucleotide metabolism using biochemical and genetic data in conjunction with design concepts from synthetic biology.

Results and Conclusion: We designed a simplified electronic model that has the potential to be tested theoretically by computer simulation and experimentally using hard-wired circuitry. The model is consistent with experimental data which show that (1) except under “unexpectedly” stressful conditions, the mitochondrial reserve capacity for nucleotide supply in most cells exceeds demand and (2) flux through the mitochondrial network is normally repressed by negative feedback which if removed beyond a critical period will result in network failure. Gene duplication and alternative processing of gene products ensures that suitable protein components are available to maintain function under different “expected” conditions. Network behaviour displays both HOT and SOC characteristics, depending on circumstances.

126  Dominica Zentner
Can ‘high-risk’ selection criteria improve the identification of mutation positive individuals in the cardiogenetics clinic?

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Background: Greatest value in cardiac genetic testing comes from identifying families carrying a pathogenic mutation. In these families the mutation result can confirm the diagnosis, guide risk management and facilitate predictive testing for relatives. In practice, although detection rates vary, most index case testing will not identify a mutation. We sought to capture features of the clinical history identifying a higher chance of positive mutation detection and measure their performance as clinical checklist.

Aims: To determine whether a standardised approach to determining when genetic testing should be undertaken could contribute to a higher likelihood of a positive mutation detection result. In order to determine this, the clinic created a Clinical Tool Checklist.

Methods: A checklist of features associated with a higher risk of a gene mutation was created and applied retrospectively to all cases undergoing next generation sequencing (NGS) mutation detection through a single cardiogenetics clinic. 126 cases were identified, including familial arrhythmia, cardiomyopathy and aortopathy, with a positive mutation detection rate of 36.5%. Clinical histories were reviewed by 2 clinicians in a de-identified manner and a checklist score assigned, using only information available at the time of testing. Result: A cut-off score ≥3 on the clinical checklist was reached for 35/46 (76%) mutation and 39/78 (50%) mutation negative cases, giving a 47% positive predictive value and 78% negative predictive value. The likelihood ratio for positive mutation detection at this threshold was 1.59.

Conclusion: Clinical features can be utilised in a simple checklist to standardise selection of cases for mutation testing and increase the probability of mutation detection. Further refinement of the criteria may be able to improve their performance.

127  Kirstie MacGill
Surgical education and training at RMH: an HMO perspective

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Introduction: Recent changes in health care, including reduced working hours, shift work and short rotations, increased bureaucratic requirements and a culture where efficiencies of care delivery, patient safety and accountability are more important than teaching, all combine to impact on the training of future surgeons. In the years between completion of internship and selection into specialist training Hospital Medical Officers (HMOs) need to balance their professional development with their service commitment to their employers.
Research questions: “How do junior doctors balance their service commitments and learning needs to progress in a surgical career?; “In what ways do junior doctor’s perceptions of the SET application process guide their learning choices?”

Methods: A qualitative study was conducted using semi-structured interviews of 11 Post-Graduate Year 2 doctors at Royal Melbourne Hospital. They were asked about their learning and how they were preparing for SET selection. The transcribed audio recordings were analysed using a constructivist grounded theory approach.

Results: Themes that were identified as effecting learning included the need to “go beyond”, time pressure, the role of the team and the need for consultant contact. The central themes that emerged from the study were the importance of individual agency, participation and relationships for learning. Individual endeavour is insufficient due to the surgical unit and organisational factors that also impact on their training. The SET selection process, including scored curriculum vitae and referee reports has both positive and negative effects on junior doctor’s professional development.

Discussion: This study explored how junior doctors learn in the clinical workplace and how the requirements for SET selection impact on their learning and learning choices. Many of the themes will be familiar, however the impact of the changing healthcare environment has not been previously explored. By focusing on factors that influence relationship building and participation in the workplace it should be possible to maximize learning opportunities for junior doctors and facilitate their professional development and career progression.

128 Meng Tan
Dissecting the worm: what can real-time web-polling tell us about medical school lectures?
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(1) The University of Melbourne (2) The Royal Melbourne Hospital

Aim: We sought to implement a novel web-based real-time method of estimating student comprehension during medical school lectures, and to determine whether this method can provide useful feedback on lecture presentations and materials.

Background: Effective pedagogy requires clear learning objectives and evaluation of achievement of those objectives. Specific, comprehensive feedback from learners, obtained retrospectively, can be time-consuming and is subject to low response rate and imperfect recall. We propose to overcome these limitations by acquiring student feedback using a web interface through which learners estimate their own level of understanding in real time, as lecture content is presented.

Methods: Second-year medical students of RMH Clinical School were asked during lectures to navigate to a designated website featuring a 5-star rating widget and a graph showing the class’s average ratings over time. Students used this to rate their own understanding of lecture content (on a scale of 1 to 5) and to submit ratings anonymously, as often as they wished throughout the lecture. Simultaneously, a researcher observing the lecture documented a timeline of content presented. Students were surveyed twice regarding usability and usefulness of the interface.

Results: Data were collected for 15 lectures during six weeks from 41 participants, with one lecture excluded from analysis because of website malfunction. Ratings were submitted by 12 students (median per lecture (range 4-23), with 3.4 ratings submitted per student per lecture (range 2.4-9.5). Subsequent to the first week, participant numbers remained stable until the end of the study period. Variability in ratings potentially identified poorly understood content in 8 of 14 lectures (57%), especially in lectures with higher user numbers (> 12) and more ratings per user (> 3.2). All survey respondents (N = 11) agreed that the interface was easy to use, and 55% indicated they would be inclined to continue using the system, however opinions were more neutral regarding its usefulness (36% agreement). In free-text comments, respondents acknowledged that the interface was a distraction, albeit an acceptable one, and described the information as interesting, but probably more useful for lecturers than students.

Conclusion: This pilot study suggests that continuous real-time web-polling during lectures is feasible, sustainable and potentially informative. Poorly understood concepts are more likely to be identified when more than 12 students participate. The value of sharing this feedback with educators will be studied in the next planned stage of research.

129 Joanne Young
Medicines education: What matters most to patients and carers
JOANNE YOUNG (STOECKEL)
Melbourne Health

Aim: To collect qualitative data from patients and carers regarding their preferences for content and delivery of medicines information, to guide actions to improve medicines education.

Background: Hospital-wide post discharge patient experience survey results indicated that patients were not satisfied with the information they had received about their medicines. Out of the 1,496 patients who responded, 34% were not completely satisfied with the information they received about medicine side effects.

Methods: A consumer focus group was coordinated by the Pharmacy Department, in consultation with the hospital’s Community Engagement Manager. Consumers were recruited by inviting current and recently discharged patients (or their carers) and those listed on the hospital consumer register to participate. Prior to the session, consumers were provided with an information sheet outlining the purpose of the focus group and targeted questions. This allowed time for consumers to reflect on their experiences and prepare responses to specific issues highlighted in the survey. Seven patients or carers, of various ages and experiences, attended the two hour session. Responses were recorded and displayed during the session, then analysed to identify themes and preferences of the group.

Results: The consumer focus group identified consistent themes and preferences of patients and carers with regard to medicines information content and delivery. Overall, consumers would like information about medicines to be: Individualised according to their needs and preferences identified at admission; Provided earlier and throughout hospital admission; Delivered by all staff (not just pharmacists); Not just about side effects (to include purpose and how/when to take); Utilise and refer to electronic tools or websites.

Conclusion: Conducting a consumer focus group provided qualitative data to identify patient/carer preferences for content and delivery of medicines information. The results demonstrated the importance of establishing “what matters most” to patients and carers when considering improvements to medicines education to ensure they are consumer focused.

130 Fary Khan
Medical rehabilitation in Madagascar: challenges in implementing the World Health Organization Disability Action Plan
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Background and objective: In Madagascar, similar to other sub-Saharan African countries, much effort has gone to improve acute health care sector, and post-acute care system, including rehabilitation, is undeveloped at many levels. This article provides an update on medical rehabilitation in Madagascar by using local knowledge to outline the potential barriers and facilitators for implementation of the WHO ‘Disability Action Plan’ (DAP) of 2014-2021.

Methods: A 14-day extensive workshop program (Sep-October 2014) was conducted at the University Hospital Antananarivo and Antsirabe, with the Department of Health Madagascar, by rehabilitation staff from Royal Melbourne Hospital, Australia. Attendees were rehabilitation professionals (n=29) from three main rehabilitation facilities in Madagascar, who identified various challenges faced in service provision, education and attitudes/approaches to people with disabilities. Their responses and suggested barriers/facilitators were recorded following consensus agreement, using objectives listed in the DAP.

Results: The barriers and facilitators outlined by participants in implementing the DAP objectives include: engagement of health professionals and institutions using a multi-sectorial approach, new partnerships, strategic collaboration, provision of technical assistance, future policy directions, research and development. Other challenges for basic policies on rehabilitation included: access to rehabilitation
services, geographical coverage, skilled work-force shortages, limited info-technology systems; lack of care-models and facility/staff accreditation standards; limited health services infrastructure and ‘disconnect’ between acute and community based rehabilitation (CBR).

Conclusion: The DAP summary actions were useful planning tools to improve access, strengthen rehabilitation services and CBR, and collate data for outcome research.

131 Louisa Ng

Effectiveness of a structured sexual rehabilitation programme following stroke: a randomized controlled trial

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Background: Sexual activity is an integral part of life and the importance of addressing sexual health after stroke is well accepted but poorly done in general.

Objective: To assess the effectiveness of a comprehensive structured sexual rehabilitation program compared with written information alone, on sexual functioning and psychological function (anxiety, depression, stress), and on functional independence and quality of life in an Australian stroke cohort.

Methods: Sixty-eight participants randomized to a treatment group (N=35) for comprehensive structured sexual rehabilitation program or a control group (N=33) for written information alone. Outcome measures included: Sexual Functioning Questionnaire Short Form (CSFQ-14), Depression, Anxiety Stress Scale (DASS), Functional Independence Measure (FIM) and Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39g). Assessments were made at the baseline, six weeks and six months following intervention. Participant preferences of how they would like to receive information, who from and how frequently were collected at baseline.

Results: No difference between groups was noted in any of the outcome measures. Half the participants (51%) wished to receive information and were equally divided into preferring written information vs face-to-face counselling with majority (54%) patients preferring information after discharge from an inpatient setting.

Conclusion: Written information alone appears as effective as a more comprehensive individualised sexual rehabilitation program in an inpatient setting. Further research is needed for longer-term outcomes and for outpatient settings.

132 Louisa Ng

Promoting smoking cessation in an inpatient physical medicine and rehabilitation setting in Australia through a comprehensive smoking cessation program: a clinical controlled trial

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Background: Every year, smoking kills approximately 15,000 Australians and costs Australia $31.5 billion in social (including health) and economic costs.

Aim: To conduct a clinical non-randomized controlled trial over 6 months with blinded patients and outcome assessors to compare the feasibility and effectiveness of a comprehensive smoking cessation program which combines training with organisational components (specifically i) health professional training, ii) alerting patients prior to admission that the rehabilitation unit is non-smoking through written brochures iii) systematic smoking screening questions on admission to rehabilitation and brief advice and treatment where applicable iv) written brochure on smoking cessation to patients who smoke v) single reminder follow up phone call at 6 weeks) compared to usual care. The aim is to improve health professional behaviour in providing smoking cessation advice, patient self-efficacy relating to smoking cessation, rates of smoking cessation and continued abstinence 8 weeks after discharge from the inpatient rehabilitation unit.

Methods: 25 smokers (out of 168 admissions, 22 were excluded due to cognitive issues and those 7 were smokers) in inpatient rehabilitation were allocated by date of admission into 2 groups - the first three months of the study into control usual care (N=12) and the second three months of the study into intervention with comprehensive smoking cessation program (N=13). Outcome measures included: Fagerström Test for Nicotine Dependence, Smoking Abstinence Self-efficacy Questionnaire (SASEQ), Functional Independence Measure (FIM) and Patient Health Questionnaire-2 (PHQ-2). A smokerlyser device was used as an objective confirmation of smoker status. Assessments were made at baseline, discharge and eight weeks post discharge. All staff underwent smoking cessation education and training 3 months into the study before intervention commenced.

Results: Significant improvement in all measures (all stats to be presented once finalised): Fagerström Test for Nicotine Dependence (1 person quit smoking in the control group and 6 people quit in the intervention group), SASEQ, FIM but not PHQ-2. All improvements were sustained at 8 weeks post discharge. Examinations conducted confirmed that staff education was effective in increasing smoking cessation knowledge.

Conclusion: A comprehensive smoking cessation program in the rehabilitation setting appears both feasible and effective. Larger studies with more robust methodology are needed to confirm these findings.

133 Hayley O'Sullivan

Neuromuscular rehabilitation improves strength and reduces functional impairment following moderate-severe wrist injury

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1 Melbourne Health

Aim: To improve patient outcomes, including grip strength and pain, following moderate-severe wrist injury.

Background: Historically, wrist rehabilitation has focused primarily on active range of motion (AROM) and strength training. More recent studies have identified the importance of proprioceptive retraining and endurance. Failure to address these latter aspects can reduce the effectiveness of rehabilitation and impact on long term outcomes.

Whilst clinical research indicates the benefits of neuromuscular rehabilitation programs, there is little evidence of how to design and implement these programs. This study outlines an 8-week neuromuscular program to enhance functional outcomes for patients following a moderate-severe wrist injury.

Problem: Neuromuscular rehabilitation is indicated to enhance patient outcomes following moderate-severe wrist injuries. There is a lack of information on either the structure or effectiveness of such programs.

Intervention: Patients were identified following acute hand therapy intervention. Patients attended a 45 minute wrist group weekly for 8 weeks. Individualised programs were developed accordingly. 6-7 exercises were completed each session and upgraded as progress was achieved. Pre and post measures were taken including: Jamar hand dynamometer, Patient Rated Wrist Evaluation (PRWE).

Evaluation: Twenty patients were recruited to the study over a 12 month period. Preliminary results indicate improvement in all outcomes measured. PRWE scores indicated a decrease in functional impairment.

Recommendations: Patients with moderate-severe wrist injuries benefit from an 8 week neuromuscular rehabilitation program. Further research comparing effectiveness of a neuromuscular approach would further develop the evidence.

134 Jennifer Beavis

Using the Patient Outcome Scale to address symptom burden in patients with end-stage renal disease

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The Royal Melbourne Hospital

Aim: To determine whether intervention based on Patient Outcome Scale-Renal (POS-R) confers a reduction in symptoms in patients with End-Stage Renal Disease (ESRD).

Background: There is a high symptom burden in patients with ESRD. POS-R is a validated tool for measuring 17 physical and psychological symptoms on a scale of 0-4. The POS-R is in use at our facility as a supportive tool in directing treatment strategies.

Method: 92 ESRD patients receiving different care modalities (dialysis and conservative) completed a baseline and at least one follow-up
POS-R. Symptom scores of 3-4 were deemed severe and triggered Supportive Care referral with treatment based on our symptom control ladder (available at www.rmkkidney.com), and further directed referrals if appropriate.

Results: No significant changes from baseline aggregate score were detected after a mean follow-up time of 150 days. Most domains suggested a relative worsening in symptoms e.g. nausea (29vs43,p<0.01) and poor sleep (97vs119,p<0.05). Pain, itch, decreased mobility and weakness/fatigue were rated as most distressing.

However this masked marked improvement in patients scoring 3 or 4 in any domain, who were therefore referred for intervention, who showed the following percentage improvement on follow-up: Pain 55%; shortness of breath 100%; weakness 42%; nausea 67%; vomiting 50%; appetite 88%; constipation 71%; mouth problems 67%; drowsiness 71%; mobility 50%; itch 60%; sleep 47%; restless legs 67%; anxiety 63%; depression 60%; skin changes 75%; diarrhoea 100%. Very few patients got worse.

Conclusions: The symptom burden of ESRD patients’ needs further attention. Patients referred with high symptoms appeared to have benefited from intervention. Overall symptom burden in other patients increased, meaning that symptom burden in our population demands more resources and a longer monitoring period.

135 Tim Hewitson
Fibroblast growth factor 23 is synthesised locally by renal proximal tubule cells and is pro-fibrotic

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Background: Physiologically, fibroblast growth factor-23 (FGF23) synthesis occurs predominantly in bone and it regulates mineral handling in the kidney. In chronic kidney disease, circulating levels are very high and are strongly predictive of disease progression, yet changes in FGF23 are not adequately explained by increased osteocytic synthesis.

Aim: Since extra-osseous FGF23 production is observed in diseased heart and vascular tissue, and is associated with the activation of pro-fibrotic cascades, we sought to evaluate local production and pro-fibrotic action of FGF23 in the kidney.

Methods: Kidneys were harvested from mice at day 0 or 3 days post-unilateral ureteric obstruction. Paraffin-embedded sections were stained for FGF23 and with lectins to identify specific nephron segments. Total RNA was extracted from whole kidney tissue and the carboxy-terminal fragment of FGF23.

Results: Generalised low-level FGF23 protein staining was observed in proximal tubules at day 0, with more intense focal staining at day 3 post-UUO. Normalised FGF23 mRNA expression increased 11-fold in day 3 UUO relative to day 0 and 23-fold in the contralateral unobstructed kidney. Local FGF23 synthesis was confined to proximal tubular cells, and not glomeruli. Treatment of rat fibroblasts with exogenous recombinant human FGF23 and transforming growth factor-β1 (TGF-β1). Cells were stained for alpha-smooth muscle actin (αSMA) to assess myofibroblast differentiation, and a panel of markers was used to evaluate fibrogenesis.

Conclusion: Local renal FGF23 synthesis occurs in proximal tubular cells, is enhanced by tubulointerstitial injury, and may be pro-fibrotic.

136 Susan Fisher
A qualitative review of medication errors made by new kidney transplant recipients

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Aims: To identify the rate and types of medication administration errors made by patients after renal transplantation; to explore reasons for these errors and to develop strategies to prevent further deviation from the prescribed regimen.

Background: After kidney transplantation, patients are required to follow a complex and frequently changing medication regimen. Non-adherence to the prescribed schedule is associated with increased rates of rejection and graft loss, but detecting patients who make unintentional errors or who are intentionally non-adherent can be difficult. To assist with improving medication management in this group, the Renal Transplant Outpatient Pharmacist (RTOP) role was established.

Methods: The RTOP reviews all new renal transplant patients in clinic after hospital discharge, providing medication education and early identification of medication errors. Medication administration errors were recorded in the nephrology patient database (Nephworks). Records were reviewed retrospectively for the first 84 transplant patients since the RTOP role was established to identify and characterise those errors.

Results: The RTOP identified 71 errors made by 35 patients (41.7%). These included numerous dangerous mistakes such as: confusion over medication strengths leading to under and overdosing; tablets halved inappropriately; incorrectly packed dose administration aids; incorrect administration times and failure to make prescribed dosage changes. Also of great concern was the error rate with immunosuppressant - 32 errors made by 22 patients. Demographic data was compared between patients who made errors and those who made no errors including age, NESP, help from a carer and number of transplants but little difference was identified between the two groups.

Conclusions: Medication errors were common in the early post-transplant period. The majority of errors identified at this early stage were unintentional and related to poor medication knowledge, the complexity of the medication regimen and misunderstandings about changes. The RTOP provided close follow up with patients identified as being non-adherent to improve their medication management and to help avoid further errors.

137 Anne Hong
Impact of ERT on the prevalence of hearing loss and tinnitus in Fabry disease

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Aim: 1. Describe the nature and prevalence of hearing loss (HL) and tinnitus in Fabry disease. 2. Explore correlations between HL with cardiomypathy, stroke, renal disease and the type of enzyme mutation (missense or nonsense). 3. Determine the response of HL and tinnitus to enzyme replacement therapy (ERT).

Background: Fabry disease (FD) is an X-linked lysosomal storage disorder due to mutations in the GLA gene encoding α-galactosidase A. Subsequently, globotriaosylceramide accumulates and causes multi-organ dysfunction, including nephropathy, neuropathy and cardiomypathy. Additional manifestations include hearing loss (HL) and tinnitus. Our aims were to describe the nature and prevalence of HL and tinnitus in FD, correlations between HL and tinnitus with cardiomypathy, stroke, renal disease and the type of enzyme mutation (missense or nonsense), and the response of HL and tinnitus to enzyme replacement therapy (ERT).

Methods: Prospectively collected audiogy data, RMM Fabry database, patient registry data and medical records of patients >16 years who attended the Fabry service at the Royal Melbourne Hospital since year 2000 were accessed. Routine audiogy tests included pure tone thresholds for frequencies at 0.25, 0.5, 1, 2, 3, 4 and 8 kHz, speech audiometry and tympanometry. A pure tone average (PTA) across frequencies of 0.5, 1, 2 and 4 kHz was calculated for each ear and a PTA>20dB was considered as HL. Cross sectional and longitudinal analyses were performed.

Results: A total of 55 patients (32 males, 23 females) were included. HL was present in 47.3% of 110 ears tested. This translated to 60.9% of male ears and 28.3% of female ears having HL. HL was predominantly sensorineural and affected the high frequencies (4 and 8 kHz). Tinnitus was present in 47.3% of patients (60.9% of males and 28.3% of females). Patients with HL were also older in age (Mann-Whitney U, p<0.01). Reduced renal function (χ²=13.6, p<0.01), stroke (χ²=6.0, p<0.05) and left ventricular hypertrophy (χ²=7.0, p<0.01) were also
correlated with HL, but only reduced renal function and increasing age were independently associated when analysed using multivariate linear regression. The type of enzyme mutation did not have a significant effect on HL. In ERT treated patients, HL remained unchanged during follow up. There was a significant but slight increase in prevalence of tinnitus during follow up (χ²=12.0, p=0.05).

Conclusion: Hearing is significantly impaired in adult FD patients, especially males, and appears to be stabilised by ERT. Tinnitus was not affected by ERT.

138 Michael Cai

The role of calciprotein particles in the mineralisation paradox in chronic kidney disease

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Background: In health, tightly controlled processes restrict mineralisation to bone and teeth. The process is disturbed in chronic kidney disease (CKD), where there is a parallel, but paradoxical, development of vascular calcification, and reduction in bone mineralisation. The mechanism behind this phenomenon is not clear. Recently, we have discovered the presence of circulating nanometer-sized particles in CKD patient serum containing a calcium phosphate mineral core with a fetuin-A rich protein shell. Serum CPP levels are associated with arterial stiffness and arterial calcification in CKD patients.

Aim: The aim of the study was to investigate the effect of CPP on mineralisation of osteoblasts and vascular smooth muscle cells (VSMC) in culture.

Methods: CPP were synthesised by mixing human serum with buffered calcium chloride and sodium phosphate. Saos-2 (an osteosarcoma cell line) and MOVAS-1 (murine VSMC) were grown to confluence, and treated for 7 days with either control media (CM, 1 mM phosphate (Pi)), osteogenetic media (OM, 4mM Pi), CM supplemented with CPP (CM+CPP) and OM supplemented with CPP (OM+CPP). Mineralisation was detected with alizarin red staining, and quantified as calcium (Ca) corrected for protein. Monolayer cell counts were also determined.

Results: OM treatment resulted in the mineralisation of Saos-2 (p<0.001 vs CM), but not MOVAS-1. OM+CPP treatment yielded a dose-dependent decrease in Saos-2 mineralisation (P<0.001 vs OM), which was associated with a reduction in free Ca and Pi media concentrations over 24 hours (50% and 13% reduction, respectively). In contrast, treatment with OM+CPP (10µg/ml) in MOVAS-1, resulted in a 22-fold and 13-fold increase in mineralisation compared to OM and CM+CPP respectively (both P<0.001 vs OM). OM+CPP on its own did not reduce cell viability, while OM+CPP resulted in reduced cell viability in both cell lines (both P<0.001).

Conclusion: In an in vitro model, CPP reduce mineralisation of an osteoblast-like cell line but increase mineralisation of a VSMC cell line. Our findings suggest that circulating CPP in CKD serum is a novel mediator of the calcification paradox in CKD.

139 Rosemary Masterson

Low versus high dialysate calcium concentration in alternate night nocturnal hemodialysis: a pilot randomised controlled trial

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Background: Higher calcium dialysate is recommended for quotidian nocturnal hemodialysis (NHD) (56 nights/week) to maintain bone health. It is unclear what the optimal calcium dialysate concentration should be for alternate night NHD. We aimed to determine the effect of low calcium (LC) versus high calcium (HC) dialysate on cardiovascular and bone parameters in this population.

Method: A randomised controlled trial where participants were randomised into LC (1.35mmol/L, n=24) or HC dialysate (1.5 or 1.75mmol/L, n=26) over a 12-month period. Primary outcome was change in mineral metabolism markers. Secondary outcomes included change in vascular calcification (VC) scores (computed tomography (CT) of abdominal aorta (AA) and superficial femoral arteries (SFA)), pulse wave velocity (PWV), bone mineral density (BMD) and left ventricular mass index (LVMI).

Results: In the LC group, there was a decrease in pre-dialysis ionised calcium of -0.12mmol/L (-0.18-0.06, p=0.0001) and a rise in PTH of 16pmol/L (3.5-28.5, p=0.01) from baseline to 12 months with no significant change in the HC group. In both groups, there was no progression of VC in AA or SFA and no change in PWV, LVM or BMD over 12 months. At 12 months, calcimimetics were prescribed in a higher percentage in the LC vs HC groups (45.5% vs 10.5%) with a lower proportion of the HC group being prescribed calcitriol (31.5% vs 72%).

Conclusion: Although dialysate calcium prescription influenced biochemical parameters it was not associated with difference in progression of VC between HC and LC groups. An important finding was the potential impact of alternate night NHD in preventing progression of VC and inducing stabilisation of LVMI and PWV.

140 Jo-anne Moodie

Smoothing the transition from Peritoneal Dialysis and Haemodialysis

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Background: A review of the service delivery in the peritoneal dialysis (PD) unit, including time on therapy for PD patients, provided insights into technique failure rates and causes in our unit. Patients stopped PD due to a variety of reasons including inadequate solute and fluid removal and inability to cope with the demands of a self-care treatment.

Aim: The aim of this paper is to identify whether dialysis access was planned, as evidenced by the creation of an arterio-venous fistula (AVF) prior to it being required for Haemodialysis (HD), for patients stopping PD due to these reasons and transitioned to permanent HD to learn what can be done to plan for future patients needing to stop PD.

Results: Of the 225 patients to undergo PD between July 2010 and February 2014, 56 (22%) ceased PD. 55 patients commenced permanent Haemodialysis (HD). 23/56 (42%) switched to HD due to inadequate solute or fluid removal (ANZDATA national figure 21%). 14/23 (61%) of these people started HD with a functioning AVF because we had noted failing PD. 9/23 patients started PD on a tunneled catheter. 7/23 (30%) patients went on to perform Home HD. 8/56 patients (14%) were unable to cope with the demands of a self-care treatment and changed to satellite HD (18% ANZDATA). 3 had AVF created prior to stopping PD and 1 chose not to continue dialysis. 4 patients had central catheters for HD. Early identification of failing PD is important given the need to plan for dialysis transition and to make this process as easy as possible for the patients. We failed to provide an optimal access plan for 11 (7+4)/56 patients, as they started on HD with a tunneled line. We are examining factors that might have alerted us to create HD access sooner.

Conclusion: Communication regarding the continuum of dialysis modalities may assist the transition process along with early surgical access creation. Introduction to the benefits associated with home HD should also be discussed early to allow for home dialysis choice.

141 Blazhe Nedanovski

Analysis of pre-treatment water supplies to our dialysis facilities in Victoria from 2009 to 2015

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1 University of Melbourne 2 Royal Melbourne Hospital Department of Nephrology

Aim: Determine the water feed levels of toxins needed to be removed in each water region for haemodialysis use.

Background: Water quality is a major factor in safe haemodialysis practice and purification requires a series of filtration, adsorption and reverse osmosis (RO) steps. The water quality of the feed water that is supplied for our dialysis patients in Victoria varies enormously. Microbiological safety is often discussed but other impurities and toxins are under reported but are vital for water safety. We set out to establish the values that our pre filtration and filtration systems are exposed to and expected to deal with, to ensure the highest quality dialysis water.
Methods: Retrospective audit of all our water quality data. Levels below the limits of detection were dealt with by substituting (limit of detection/2) for analysis. RO output water is routinely tested and meets Association for the Advancement of Medical Instrumentation (AAMI)-RD62:2009 standards (not data presented). Feed water results are verified pre installation and 12 monthly thereafter.

Results: Data is presented as; toxin: units, AAMI acceptable limit, maximum level detected and where maximum taken.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Units</th>
<th>AAMI limit</th>
<th>Maximum detected</th>
<th>Maximum supply district level</th>
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<tr>
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<td>144</td>
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<td>98.9</td>
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</table>

Conclusions: Our equipment is expected to deal with large fluctuation in feed water quality. Knowing what limits we can reasonably expect to find in various regions allows us to plan pre-filtration equipment and allows estimation of replacement frequency.

142 Irene Ruderman

Anti-blood group antibody titres in blood group A and B transplant wait listed patients

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Royal Melbourne Hospital

Background: Historically, deceased donor ABO-incompatible renal transplant (DD-ABOi) has been limited to kidneys from A2 or A2B blood group donors transplanted into group B recipients with low anti-A titres. Recent successful living donor ABOi from all blood groups into recipients with low titre anti-blood group antibody (ABGAb) using standard immunosuppression alone suggests DD-ABOi may be possible into selected recipients with limited or no antibody removal pre-transplantation. Methods: ABGAb titres of wait listed patients were compared with our institutional threshold for transplantation of ≤ 1:8 (Ortho) to determine how many might accept a DD-ABOi kidney with one or no antibody removal treatments prior to transplantation.

 Aim: We sought to systematically measure ABGAb titres in our deceased donor wait listed group A and B patients.

Results: To date 36/106 (34%) group A and 16/55 (29%) group B patients have had titres measured. Of the group A patients, 66% had an anti B titre ≤ 1:8 with 69% of group B patients having an anti A titre ≤ 1:8. Of the 52 patients who have had titres measured, 25 (48%) have titres <1:4

Conclusion: A significant number patients have ABGAb sufficiently low to enable DD-ABOi with limited or no antibody removal.

143 Irene Ruderman

Late antibody mediated rejection in renal transplant: retrospective review of outcomes and prognostic indicators

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Background: Late antibody mediated rejection (AMR) is recognised as a major contributory cause to long allograft failure with current therapies having little impact on long term allograft outcomes.

Aim: Our aim was to identify predictors of allograft outcomes in late AMR in the context of a previously normal three-month protocol biopsy in a single centre transplant population.

Methods: We conducted a retrospective review of all renal transplant recipients between January 2005 and December 2014. We identified 106 transplant patients with late AMR and analysed the impact of histological and clinical factors on graft survival compared with 968 patients without late AMR transplanted during the same period.

Results: Median time to diagnosis of rejection was 58 months post-transplant (range 26-97 months). Preceding acute cellular rejection (ACR) was found in 31% of patients. De novo donor specific antibodies (dnDSA) were present in 60% of patients with late AMR. Thirty three percent of the cohort was ABOi incompatible (ABOi). Compared with the control group the late AMR group were older and had higher rates of ABOi transplants.

Late AMR was associated with a two-fold increased risk of graft loss compared to non-AMR controls. In the late AMR group, high chronicity scores on diagnostic biopsy and high serum creatinine but not history of ABOi, C4d positivity or de-novo DSA were associated with worse graft outcomes. Graft survival was poor in the late AMR group regardless of treatment, with 50% graft loss 29 months after late AMR diagnosis.

Conclusion: Late AMR is associated with high rates of graft loss, current treatments are poorly effective and chronically score on biopsy is a marker of poor graft survival. This highlights the need for better diagnostics and interventions for late AMR.

144 Stella Setyapranata

Autosomal dominant polycystic kidney disease does not in itself appear to cause thrombocytopenia.

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Background: Platelet volume in patients with autosomal dominant polycystic kidney disease have been reported higher, than in the general population. Platelet counts, however, have been reported to be reduced or similar compared to a healthy population.

Aim: To determine whether patients with autosomal dominant polycystic kidney disease have low platelet counts

Methods: This is a single centre retrospective study. We examined our patient database and compared platelet counts with an age and sex matched control group.

Results: There were 3 cohorts of subject patients with corresponding control groups (chronic kidney disease non-dialysis=59, transplanted n=171, on dialysis n=60). We analysed 21,120 individual blood results from subject patients and 21,852 tests in the control groups from 290 patients in each group. Patients with autosomal dominant polycystic kidney disease on dialysis had statistically higher haemoglobin values (114±10 vs controls 105±10g/L, p<0.0001) and lower platelet counts (213± 63 vs 238 ± 69 x109/L, p<0.01) despite using less erythropoiesis-stimulating agent. In the transplant and non-dialysis groups there were no significant differences in the haemoglobin or platelet counts. Conclusion: Platelet counts appear lower in subject patients on dialysis and this may be related to less erythropoiesis-stimulating agent use.

Non-dialysis or transplant patients with autosomal dominant polycystic kidney disease who have chronic kidney disease or who have been transplanted have similar platelet numbers to controls. The magnitude of the difference in platelet numbers was small and unlikely to be clinically significant. Patients with low platelet counts with autosomal dominant polycystic kidney disease should have further investigations to establish the cause.

145 Ashish Sharma

High resolution MRI to assess bone microarchitecture in patients with chronic kidney disease

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Aim: To validate high resolution magnetic resonance imaging (HR-MRI) assessment of bone microstructural parameters compared to micro computed tomography (μCT) of transillic bone biopsies in renal transplant recipients at the time of transplantation.

Background: Renal osteodystrophy (ROD) adversely affects bone quantity and quality, compromises bone strength, and is associated with increased incidence of fractures in patients with chronic kidney
147 Matthew Sypek

Optimising paediatric renal transplantation utilising the australian paired kidney exchange program

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Aim: To describe the Australian experience of paediatric renal transplantation through the Australian Kidney Exchange (AKX) program.

Background: Despite many patients with End Stage Kidney Disease (ESKD) having friends and relatives volunteer to donate an organ for transplantation, many barriers exist that can prevent safe direct donation. Paired Kidney Exchange (PKE) programs offer the opportunity to enable living donation for incompatible pairs by matching them with other pairs or chains of donor-recipients with whom they are compatible. Children are likely to require multiple transplants during their lifetime and hence high standards of organ matching should be aimed for to prolong graft life, minimise the risks of exposure to immunosuppression and prevent future sensitisation. Since its inception in 2010 the AKX has facilitated over 150 transplants for incompatible pairs.

Cases: We describe the 7 paediatrics recipients transplanted through the AKX to date. Five patients were HLA incompatible with their registered donor due to preformed donor specific antibodies (DSAb). Three of these were highly sensitized with a calculated Panel Reactive Antibody (cPRA) >90%, significantly limiting their chances of receiving a compatible organ. One patient was ABO incompatible with his registered donor and the final patient entered the AKX to mitigate the risk of exposure to hepatitis B virus. We discuss the balancing of immunological risk against access to transplantation in a variety of situations and explore the use of a novel HLA epitope based matching in assessing this risk.

Conclusion: PKE programs present a viable strategy to overcome many of the barriers to living donation for paediatric patients who have an otherwise suitable donor, including ABO blood type and HLA incompatibility, and risk of transmission of chronic infection. Opportunities exist to potentially mitigate immunological risks, improve graft outcomes and reduce sensitisation by minimising donor-recipient HLA epitope mismatches through PKE.
Cardiovascular Function: Case 1: Interventricular and posterior wall thickness increased from 10 and 12mm to 22 and 17mm respectively over 13yr ERT. Diastolic dysfunction progressed with increased left ventricular filling pressure. Severe Mitral regurgitation developed; Case 2: Wall thicknesses reduced from 14 and 12mm to 10 and 10mm respectively. Diastolic dysfunction progressed with increased left ventricular filling pressure. Cardiac Histology: Post-ERT – Both cases showed hypertrophied myocytes, intracellular vacuolation and patchy interstitial fibrosis.

Conclusions: Post-mortem biopsies yield organ-specific information regarding tissue response to ERT in Fabry disease. Initiation of ERT prior to reaching CKD 5 (Case 2) resulted in stabilisation of renal function and histology. While ERT did not prevent the occurrence of cerebrovascular or cardiac events in either case, the progression of cardiomyopathy and cerebrovascular disease was more pronounced in Case 2, in whom ERT was initiated after reaching CKD 5.

149 Sven-Jean Tan
Changes in markers of mineral metabolism following living kidney donation
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Aim: To evaluate the effect of nephrectomy on markers of mineral metabolism in living kidney donors (LKD) compared to healthy volunteers (HV) over 12 months.

Background: LKDs experience reduction in kidney function however serum phosphate (sPi) levels are lower when compared to eGFR-matched CKD patients. Mineral metabolism adaptations that occur in LKDs have not been adequately investigated.

Methods: Twenty-one adult LKDs and twenty HVs were evaluated with respect to renal function and mineral metabolism parameters, including sPi, intact parathyroid hormone (PTH), fibroblast growth factor-23 (FGF23), soluble Klotho (sKl) and urinary phosphate, prior to donation (T0), 1-month (T1), 6-months (T6) and 12-months (T12) post kidney donation/baseline. Statistical analyses were conducted on normalised variables and changes were assessed using two-way ANOVA.

Results: Median (±SD) age of LKDs and HVs were 54.1 ± 14.7 and 52.6 ± 8.0 years respectively. There were no baseline clinical or biochemical differences between LKDs and HVs. At T1, mean (±SD) serum creatinine (sCr) increased from 75 ± 12 to 114 ± 22 μmol/L, with FGF23 elevation (52 ± 15 to 70 ± 19 pg/ml) and sKl reduction (564 (469-662) to 424 (375-523) pg/ml), all p<0.001. Changes were sustained at T12. Following donation, LKDs consistently demonstrated lower sPi compared with T0 (1.08 ± 0.15 mmol/L) though maximal sPi change was detected at T6 (0.19 ± 0.17 mmol/L), p<0.001. Other markers of mineral metabolism were unchanged in LKDs. There were no differences in parameters over 12 months in HVs.

Conclusion: Prospective evaluation of mineral metabolism parameters in LKDs provides valuable insight into compensatory mechanisms following reduction in kidney function. Further reduction of sPi at T6 despite early alterations in FGF23 and sKl suggest adaptation of mineral metabolism continues long-term in LKDs.

150 Sven-Jean Tan
Effect of exercise on serum α-klotho, phosphate and glucose in healthy volunteers: a pilot study
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Aim: To investigate the effect of exercise on soluble α-klotho (sKl) in healthy adults.

Background: Membrane-bound α-klotho, predominantly expressed in the kidney, functions as a co-receptor for fibroblast growth factor-23 (FGF23) to regulate phosphate excretion. Circulating sKl, derived from membrane α-klotho cleavage, has extra-renal actions. sKl can affect ion channels and insulin signaling pathways and is inversely associated with mortality. Effects of physical exercise on sKl are unknown.

Methods: Ten fasting healthy volunteers underwent a standard Bruce protocol exercise test on a treadmill. sKl, serum phosphate (sPi) and blood glucose levels were measured in samples collected 1-week prior, immediately pre (Tpre), 0 (Tpost), 30 (T30), 240 (T240) minutes and 1-week post exercise. Changes were assessed using repeat measures ANOVA or Friedman’s test with Dunn’s multiple comparison.

Results: Median (IQR) age of participants was 47.5 (44-51) years; five (50%) were male. All study participants achieved at least 90% predicted maximum heart rate. Compared with Tpre, an acute increase in sKl was seen at Tpost (median 483pg/ml vs 602pg/ml, p<0.01) followed by non-significant decline in sPi at T30 (mean 0.94mmol/L vs 0.83mmol/L). Exercise led to a reduction in blood glucose by T240, following an initial non-significant rise, with median glucose levels at Tpre, Tpost, T30 and T240 of 6.0, 6.5, 6.3 and 5.7mmol/L respectively.

Conclusion: High intensity exercise is associated with a transient increase in sKl, decrease in sPi levels and delayed blood glucose reduction in healthy adults. Evaluation of long-term effects of cardiovascular fitness programs on sKl and sPi in healthy individuals and disease cohorts are required to identify potential lifestyle modifications to improve chronic disease management and long-term outcomes.

151 Sven-Jean Tan
Circulating soluble-Klotho levels modestly increase after renal transplantation
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Background: Klotho, a co-receptor for fibroblast growth factor-23 (FGF23), is predominantly expressed in the kidney and reported to have anti-oxidant and anti-fibrotic properties. Soluble-Klotho (sKl), the circulating protein cleaved from membrane-bound Klotho, is reduced significantly with kidney disease and is inversely associated with mortality. sKl has not been thoroughly evaluated prospectively after kidney transplantation.

Methods: Incident kidney transplant recipients (KTRs) were prospectively evaluated pre-transplantation, 1-week, 12-weeks and 52-weeks post-transplantation. Samples were assayed for basic biochemical, sKl and intact FGF23. Within-subject comparisons were evaluated using repeat-measure ANOVA or Friedman’s analysis. Effects of immunosuppression and biochemical parameters on sKl over time were evaluated using mixed effects modelling.

Results: Samples from 29 KTRs were available for final analysis. Median (IQR) age of KTRs was 49 (35-55) years and 17 (59%) were male. Twenty-six (90%) were living kidney allografts and 10 (34%) were pre-emptive. Median serum creatinine (sCr) at 1-week was 116 (92-142) μmol/L and at 52-weeks all 29 KTRs had a functioning graft with median sCr of 111 (97-131) μmol/L. Compared with baseline, sKl exhibited an increase at 52-weeks following initial decline at 1-week (p<0.005 and p<0.01 respectively) while FGF23 displayed sustained sizeable reduction (p<0.001) though >30% (n=10) of KTRs still had levels >70 pg/ml at 52-weeks. In a mixed effects model, sKl increase was not associated with reduction in immunosuppression or evaluated biochemical parameters.

Conclusions: A modest increase in sKl is observed one year post kidney transplantation with excellent early graft function suggesting factors beyond renal capacity likely influence circulating sKl. FGF23 normalisation was observed though a significant proportion of KTRs continued to have high/high-normal values. Longer-term evaluation in transplantation, specifically addressing effects of immunosuppression, is required to understand the pathophysiology of sKl/FGF23 axis and potential for modification.

152 Deborah Hui Fui Wong
Heart rate variability in Fabry disease
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Background: Fabry disease (FD), an X-linked lysosomal storage disease, has significant symptom burden presumed secondary to autonomic nervous system (ANS) dysfunction. Heart rate variability
therapy fails, a rescue anti-emetic protocol is followed. Chewing gum. The patients who receive chewing gum therapy are receive the randomised intervention of either ondansetron 4 mg IV or care unit (PACU), patients who experience nausea and/or vomiting management is similarly protocolised. Once in the post-anaesthesia Methods: We aim to recruit 100 female employed in the treatment of PONV. and this pilot trial explores whether the same mechanism can be an effective treatment for ileus following major gastrointestinal surgery, with side effects, cost, and are variably effective in all patients. Through Reasons for admissions to hospital following planned ambulatory for the treatment of postoperative nausea and vomiting (PONV). Aim: To determine whether chewing gum is non-inferior to ondansetron in 153 Michael Handscombe Chewing gum for the treatment of postoperative nausea and vomiting: a pilot trial Darval J(1), HANDSCOMBE(1) M, Leslie K(1) Department of Anaesthesia and Pain Management, Royal Melbourne Hospital Aim: To determine whether chewing gum is non-inferior to ondansetron for the treatment of postoperative nausea and vomiting (PONV). Background: Nausea and vomiting is a common complication, occurring in up to one third of post-operative patients, and is a leading reason for admissions to hospital following planned ambulatory surgery. While current treatments are available, they are associated with side effects, cost, and are variably effective in all patients. Through the mechanism of “sham feeding,” chewing gum has been utilised as an effective treatment for ileus following major gastrointestinal surgery, and this pilot trial explores whether the same mechanism can be employed in the treatment of PONV. Methods: We aim to recruit 100 female patients ≥ 18 years of age who are undergoing laparoscopic or breast surgery at the Royal Melbourne Hospital. Patients’ risk of developing PONV, as determined via the Apfel score, guides protocolised antemetic prophylaxis. Intra-operative management is similarly protocolised. Once in the post-anaesthesia care unit (PACU), patients who experience nausea and/or vomiting receive the randomised intervention of either ondansetron 4 mg IV or chewing gum. The patients who receive chewing gum therapy are instructed to target a minimum of 15 minutes chewing. Improvement or resolution of symptoms are recorded. If the randomised first line therapy fails, a rescue anti-emetic protocol is followed. Results: Results will be presented once all of the data has been collected and analysed. This trial and sample size are designed as a non-inferiority trial. Conclusion: If chewing gum proves to be non-inferior to ondansetron in the management of PONV in the PACU, this study will form the basis of a future multi-centre randomised controlled trial. 154 Austin Lee Survey of anaesthetists’ practice of sedation for gastrointestinal endoscopy LEE A, Leslie K, Allen M, Hessian E Department of Anaesthesia and Pain Management, Royal Melbourne Hospital Introduction: Australia’s large volume of gastrointestinal endoscopy continues to rise with our ageing population and the advent of a national bowel cancer screening program. In Australia, specialist anaesthetists often facilitate endoscopy by administering intravenous sedation to patients. Sedation practices: Our 2007 survey on the practice of sedation for gastrointestinal endoscopy by specialist anaesthetists yielded valuable information on the trends and variability in procedural sedation. The results of the survey were useful during the revision of the guidelines on procedural sedation by the Australian and New Zealand College of Anaesthetists (ANZCA). The revised procedural sedation guideline strongly supported uniform standards for assessment, monitoring, staffing and recovery of endoscopy patients. The guideline also emphasised the need to modify anaesthesia care in the emergency setting. We therefore decided to repeat this survey, with the inclusion of care in emergency as well as elective patients. This survey facilitated comparison of endoscopic sedation practice in Australia and overseas, and compliance by Australian anaesthetists with the ANZCA guideline. Methodology: A 24-item survey was constructed in Survey Monkey® and emailed to 1,000 randomly selected anaesthetic fellows in August 2015. Questions covered monitoring, airway management, drugs and depth of sedation. A space for free text comments was provided at the end of the survey. Data were summarised as number (%) and were compared using Chi-squared tests. All analyses were performed using Stata 12.0 and a P value <0.05 was considered statistically significant. Results: 409 anaesthetists responded to the survey (response rate = 41%), and responses from 395 anaesthetists analysed. Sub-groups of data (elective and emergency gastroscopy, ERCP and colonoscopy) were assessed for completeness. Propofol is the drug of choice for endoscopy sedation administered by specialist anaesthetists in Australia. Blood pressure is not routinely measured by all respondents, which is not compliant with ANZCA professional document PS59. Prophylactic intravenous fluids were routinely administered in a minority of elective gastroscopy patients, but in a majority of elective ERCP and colonoscopy patients. A maximum depth of sedation commensurate with general anaesthesia is routinely targeted by the majority of respondents for all procedures except for elective gastroscopy.

155 Austin Lee Fluid therapy to prevent hypotension in patients having colonoscopy LEE A, Leslie K, Allen M Department of Anaesthesia and Pain Management, Royal Melbourne Hospital Introduction: This randomised control trial sought to determine the effect of intravenous fluid therapy on the incidence of hypotension during sedation for elective colonoscopy. As one of Australia’s most commonly performed procedures, it is beneficial to optimise patient care and establish an efficient use of medical resources. Significance of Hypotension: Hypotension during colonoscopies is a common occurrence with an incidence of 25-29%. The occurrence of hypotension is significant because of its potentially deleterious effects on patient health. If hypotension is extended beyond an individualised critical threshold, complications such as myocardial ischaemia and other organ damage can result. Fortunately, adverse outcomes can be avoided if the duration of hypotension is brief. Other less extreme but nevertheless significant endpoints include nausea, vomiting,
headaches and dizziness. These consequences impact on patient's readiness for discharge and hence duration of outpatient care.

Methodology: Elective colonoscopy patients who met the eligibility criteria were preloaded with random allocations of either 2 or 20 ml/kg of Plasmalyte. Intravenous access in a forearm vein was established, and the Plasmalyte administered over the course of 20 minutes. Fentanyl and propofol were administered by the anaesthetist until patient were drowsy but remained responsive to command or mild prodding. Vasopressors were utilised at the anaesthetist’s discretion to ameliorate hypotension.

Systolic blood pressure (SBP) was monitored non-invasively, with SBP recorded at 2.5 minute intervals during the intraoperative period, and assessed before and after the procedure. Pre and post-operative questionnaires quantified patient’s level of thirst while a QoR-15 survey assessed patient comfort. Vasopressor usage and time to eligibility for discharge were recorded.

Results: The incidence of our primary outcome, hypotension (decrease in SBP > 25% from baseline during sedation) was not significantly different between the 2 or 20 ml/kg groups (59% vs. 56%; odds ratio 0.90, 95% confidence interval, 0.47 to 1.71; P = 0.74).

The incidence of SBP < 90 mmHg, the lowest SBP during sedation, the duration of hypotension and the use of vasopressors did not differ significantly between the two groups. Postoperatively, the incidences of nausea, headache, drowsiness, dizziness, recall, dreaming, and change in QoR-15 score did not differ significantly between the two groups either.

Implications: Routine administration of intravenous fluid is not indicated in adult elective colonoscopy and increases the cost of care.

156 Kate Leslie

Safety of sedation for endoscopy at University of Melbourne-affiliated hospitals

LESLIE K, Allen M, Hessian E, the Safety of Endoscopy Study Group

Introduction: Gastrointestinal endoscopy is performed in a range of settings and by a variety of health professionals. Specialist anaesthetists commonly administer sedation for endoscopy in Australia, but there is limited literature on the safety of this service model. The aim of this study was to determine the risk profile of presenting patients and the incidence of significant unplanned events in patients having endoscopy at the nine public hospitals affiliated with the University of Melbourne that provide endoscopy services for adult patients.

Methods: The study included all adult elective and emergency patients who presented for upper or lower GI endoscopy (including enteroscopy and ERCP) at the nine University of Melbourne-affiliated hospitals that provide endoscopy services for adult patients. Data were collected during a 28-day period between March and August 2015. Sedation was administered by specialist anaesthetists or trainees. Outcome measures were incidence of significant unplanned events including airway obstruction, cardiovascular deterioration, abandoned procedure, unplanned intubation, advance life support and death within 30 days.

Results: Patients were aged 60 (range: 18-95) years and 42% were ASA status 3-5. The most common procedures were gastroscopy alone (33%), colonoscopy alone (41%) and combined gastroscopy and colonoscopy (18%). Patients were managed by a specialist anaesthetist without the participation of a trainee anaesthetist in 80% of cases. Oxygen saturation, blood pressure, ECG and capnography were monitored in 100%, 99%, 94% and 84% of patients respectively. Most (92%) patients were managed without an airway device. Propofol was used in 98% of cases at a median dose of 200 (IQR: 130-300) mg. Most (82%) patients were discharged home after the procedure with a median post-procedure admission time of 60 (33-82) minutes. Forty-seven patients (7%) required advanced life support. The overall 30-day mortality rate was 1.2% (95% confidence interval: 0.8 to 1.8) with a median time to death of 11 (0-28) days. Emergency patients suffered more intraoperative events (20.6% vs. 14.4%) and 30-day mortality (6.0% vs. 0.2%; P < 0.0001) than elective patients.

Conclusion: This study demonstrated that many patients presenting for endoscopy at University of Melbourne-affiliated hospitals have high pre-procedure risk status. Intra-procedure significant unplanned events were common, especially in emergency patients. The current specialist anaesthetist-based service model provides the greatest flexibility with respect to sedation services for endoscopy at our hospitals.

157 Zoe Milner

Complex regional pain syndrome: A new model of care improving patient outcomes

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1 Melbourne Health

Aim: i) Develop and implement a new model of care to improve the outcomes for patients with Complex Regional Pain Syndrome (CRPS); and ii) Improve the early identification of CRPS within Melbourne Health.

Background: CRPS is a painful and functionally debilitating condition associated with both sensory and motor abnormalities. It is usually associated with trauma of the affected limb and frequently utilises high healthcare utilisation. Literature indicates nearly half the number of patients diagnosed with CRPS will not return to the workforce.

It is widely accepted within clinical opinion and current literature that early recognition of CRPS can improve the outcomes for this clinical population. The Budapest Criteria is clinically utilised for diagnosis of CRPS, however, early recognition is yet to be defined. Establishing early identification guidelines within key areas of the hospital will facilitate this new model of care and ultimately improved outcomes for this cohort.

Methods: Developed strong collaborative relationship with pain services team; Developed and implemented clinician resources including: identification tool and clinical algorithm; Established early and direct referral pathway to assist clinicians in the emergency department and key medical units to identify patients including regular stakeholder education.

Results: Preliminary evaluation indicates patients presenting within Melbourne Health with signs and symptoms of upper limb CRPS are being identified earlier and subsequently being referred for expert multidisciplinary assessment and intervention earlier. Furthermore, these patients are obtaining improved outcomes including returning to daily activities and work.

Discussion: CRPS is a complex condition with historically poor outcomes. Early identification, early intervention and a multi-disciplinary team approach is key to improving the outcomes for this cohort of patients. This new pathway has been well supported by a multi-discipline flexible and innovative team approach. Additionally, this newly implemented pathway is anticipated to reduce healthcare utilisation for patients with CRPS and could be employed in other health networks.

158 Catherine Beard

The experience of a large hereditary diffuse gastric cancer family at the Royal Melbourne Hospital familial cancer centre: examining the counselling and clinical issues

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Background: Hereditary Diffuse Gastric Cancer (HDGC) is an inherited cancer syndrome caused by mutations in the CDH1 gene. National guidelines recommend prophylactic total gastrectomy for CDH1 mutation carriers based on published estimates of 80% lifetime risk of advanced gastric cancer.

Aim: This case study aims to examine genetic counselling and clinical issues arising within a large family with HDGC.

Methods: The pedigree and genetic results are presented, along with a review of clinic database notes, including information about cascade testing, risk management decisions, and cancer diagnoses. Genetic counselling issues were considered collaboratively by the investigative team.

Results: At present, 14 family members are known mutation carriers; 10 are unaffected (34-80y), 2 have died from gastric cancer (41y, 51y), one has had breast cancer (40y) and one has had cancer found on gastrectomy specimen (45y). This family’s experience encompasses the full range of severity of HDGC; early death, as well as mutation carriers unaffected in the ninth decade. Two mutation carriers presented with gastrointestinal co-morbidities.
Conclusion: This family’s experience of CDH1 penetrance does not reflect the published 80% lifetime risk. This experiential risk perception within the family coupled with the life-changing risk management options (total gastrectomy versus “wait and see”) has raised unique counselling issues. These considerations can be used in a broader context as cascade testing continues, as well as in other CDH1 families where the lived experience does not reflect published risk estimates. We suggest a possible extension of the CDH1 phenotype based on gastrointestinal co-morbidities within the family. Finally, data from larger prospective cohorts is needed to produce more robust penetrance figures for CDH1 mutation carriers.

159 Joanne Davis
Natural killer cells: Regulators of allogeneic stem cell engraftment, graft versus host disease and graft-versus-leukaemia

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Aim: Use natural killer cell therapy to improve bone marrow transplant outcomes.

Background: Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is used to treat over 600 patients in Australia and 30,000 patients globally per year for haematological malignancies through the immune mediated graft-versus-leukaemia (GVL) effect. Allo-HSCT is limited by significant toxicity related to conditioning intensity, immunosuppression, opportunistic infections and graft-versus host disease (GVHD). Improved outcomes in allo-HSCT are dependent on reducing these complications, yet modifications of conventional transplant techniques have failed to significantly improve these. Natural killer (NK) cells from allogeneic donors can modify GVHD onset and have significant anti-tumour effects in models and clinical trials of relapsed leukaemia. The role of recipient NK cells in determining T cell engraftment, GVHD and allo-HSCT outcome remains largely unexplored.

Methods: We are exploring different means of modifying donor and/or recipient NK cell functionality (using murine NK cell genetic knock outs) to allow reduced morbidity of organ damaging pre-transplant conditioning, reducing GVHD and maintaining GVL in an AML model.

Results: 1. A radio-resistant perforin expressing population of recipient NK cells is present at the time of donor cell infusion and have significant anti-tumour effects in models and clinical trials of relapsed leukaemia. The role of recipient NK cells in determining T cell engraftment, GVHD and allo-HSCT outcome remains largely unexplored.

Conclusions: Using NK cellular therapy to control donor T cell biology (thus limiting GVHD) whilst promoting GVL effect, with a view to minimising (or potentially avoiding) pre-transplant conditioning intensity, has clear clinical implications for the treatment of patients undergoing allo-HSCT. By understanding and applying the efficacy of NK cell biology as both a means of controlling both recipient immunity and residual tumour, we will design an allo-HSCT regimen that minimizes the need for pre-transplant conditioning and improve transplant outcomes for recipients of this life-saving treatment.

160 Lynette Chee
Pre-transplant ferritin, albumin and haemoglobin are predictive biomarkers of survival outcome adding prognostic value to disease risk index following allogeneic stem cell transplantation

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Background/Aim: We have previously identified pre-allogeneic stem cell transplant (SCT) serum ferritin>1000ug/L, Haemoglobin (Hb)>100g/L and Albumin <30g/L as significant biomarkers predictive of inferior survival outcomes independent of the disease risk index (DRI) (Chee et al, Haematologica, 2015). The applicability of the DRI at our centre has been independently confirmed (Lim et al, Transplantation, 2015). We sought to derive a prognostic scoring system utilising these biomarkers pre-SCT.

Methods: We undertook a retrospective analysis in a single centre of all allogeneic SCT patients for haematological malignancy between 2000-2013. The outcomes of overall survival (OS), relapse free survival (RFS) and non-relapse mortality (NRM) was assessed as a function of pre-SCT ferritin, albumin, Hb and platelets. Co-variates included in multivariate analysis included age, gender, disease risk index (DRI) and graft-versus-host disease (GVHD). Multivariate Cox proportional hazard models were fitted for OS, with RFS and NRM treated as competing risk. The predictive model performance was assessed using Harrell’s C statistics.

Results: 602 patients were identified with a median age of 49 years. Patient characteristics were as follows: male 56%, related donor 61%, myeloablative conditioning 62%, peripheral blood graft source 79%, cytomegalovirus (CMV) recipient positivity 55%, underlying disease acute myeloid leukaemia (AML) 37%, Non-Hodgkin lymphoma (NHL) 16%, acute lymphoblastic leukaemia (ALL) 15% and DRI low 9%, intermediate 62% and high 25%.

Multivariate analysis confirmed that pre-SCT biomarkers predictive of inferior OS were Albumin<30g/L (HR 3.1, 95%CI: 1.6-6.0), ferritin>1000ug/L (HR 1.7, 95%CI: 1.2-2.2) and Hb>100g/L (HR 1.4, 95%CI: 1.0-1.9), with scores of 3, 2 and 1 respectively. DRI level of High/ Very High (HR 3.2, 95%CI: 1.7-6.1) was a significant predictor of increased mortality, with scores of Intermediate 1 and High/Very High 4. Four prognostic groups were derived: Score 0-1 (n=180) HR 1; Score 2-5 (n=298) HR 2.7, 95%CI: 1.8-3.9, p<0.001; Score 6-7 (n=87) HR 4.5, 95% CI: 3.0-6.9, p<0.001 and Score 8-11 (n=9) HR 13.4, 95%CI: 5.9-30.2, p<0.001.

Ferritin>1000ug/L and DRI were associated with RFS, with age=60 and Hb<100g/L predictive of NRM pre-SCT. These pre-SCT biomarkers remain predictive for relapse and survival modelling at the post-SCT timepoints of Day 100, 12 months and 24 months.

Conclusion: Serum ferritin, albumin and Hb are important prognostic biomarkers in allogeneic SCT survival outcomes in combination with DRI and add to risk-stratification pre and post-transplant.

161 Elizabeth Vincan
Frazilled7 functions as a Wnt receptor in intestinal epithelium stem cells: implications for colon cancer growth and progression

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Aim: To understand how Wnt signalling fuels cancer.

Background: Cancer initiation and progression are fuelled by cells with cancer-initiating properties (cancer stem cells). Wnt/β-catenin signalling is crucial for normal Lgr5+ stem cell function, while aberrant transduction pathway plays critical roles in these processes in colon cancer.

Methods: To understand how Wnt governs these properties, we use murine and human models of stem cell function and cancer.

Results and conclusions: The intestinal epithelium is a self-renewing tissue with a high turnover rate that is maintained by stem cells that reside at the base of glands (called crypts) in the epithelium. Lgr5, a Wnt/β-catenin target gene, specifically marks the long-lived crypt based population of colon cancer stem cells (CSCs). Fzd7 expression is enriched in the long-lived crypt based population of colon cancer stem cells (CSCs). Fzd7 expression is enriched in the long-lived crypt based population of colon cancer stem cells (CSCs). Fzd7 expression is enriched in the long-lived crypt based population of colon cancer stem cells (CSCs). Fzd7 expression is enriched in the long-lived crypt based population of colon cancer stem cells (CSCs).
163 Justin Gourlay

The role of invadopodia in the metastatic potential of colorectal cancers

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Aim: To determine the potential role of Invadopodia in the metastatic potential of colorectal cancers. Introducition: In 2015, approximately 18,000 Australians were diagnosed with colorectal cancer (CRC) and over 4,000 mortalities occur each year. With the second highest prevalence and mortality, CRC is prone to invade and metastasize if undetected, creating a wide range of complications. Metastasis is responsible for approximately 90% of cancer mortalities and yet further research is required to fully understand the underlying mechanisms.

Invasion and migration is commonly thought to involve proteolytic processing of the extracellular matrix (ECM) which subsequently allows cancer cells to penetrate through surrounding tissue. It is possible that structures known as invadopodia facilitates this function. Invadopodia have been identified in several types of tumour cells which possess highly invasive or metastatic potential. Invadopodia are dynamic actin-dependent protrusions which proteolytically degrade ECM substrates via the targeted secretion of extracellular proteases (MMPs) and actions of transmembrane proteases. It is possible that invadopodia play a role within CRC cell invasion.

Methods: We systematically compared the mRNA expression levels of a number of invadopodia-related proteins (IRPs) in CRC using the Oncomine database. To investigate protein levels, we performed immunohistochemistry on a commercial microarray of human colon cancer tissue samples of normal colon, adjacent tissue and tumour tissue. Western blot and zymograms were utilised to determine the intracellular levels of IRPs and the secreted MMP profile within 16 colorectal cancer cell lines. An invadopodia assay coupled with confocal microscopy was used to determine the invadopodia-forming ability of each cell line by co-localization of the invadopodial marker, decorin, with actin puncta (Rhodamine Phalloidin) over an area of FITC-labelled gelatine degradation. The effect of IL-6 on invadopodia-forming ability was also determined.

Results: Overexpression of Tks5 and cortactin mRNA was observed in tumour tissue compared to normal tissue, and in metastatic versus primary tumours in the Oncomine datasets. Our laboratory investigations revealed an increase in expression levels of IRPs within tumour tissue and surrounding tissue compared to that of normal tissue. Confocal microscopy confirmed the presence of invadopodia in an array of CRC cells. Also the incubation of CRC cells with IL-6 enhanced their invadopodia formation.

Conclusion: Our results have shown that invadopodia are invasive structures that are utilised by CRC cells. We have also determined that the pro-inflammatory cytokine IL-6, which has been linked to the advanced stage and decreased survival of CRC patients, also enhances invadopodia formation in these cells.

164 Belinda Lee

Use and impact of Selective Internal Radiation Therapy (SIRT) in routine care patients with metastatic colorectal cancer (mCRC)

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Background: The liver is the dominant site of metastasis in patients (pts) with mCRC. Radioembolisation is a potential option in the multidisciplinary management of these patients. Recently initial analysis of a randomised controlled trial (RCT) in the 1st line setting demonstrated no overall progression free survival (PFS) benefit from adding SIRT, but prolongation of liver PFS (HR 0.69, p=0.002) was seen.

Method: Consecutive pts with mCRC enrolled from January 2009 were identified from a prospective multi-site Australian registry. Characteristics and outcomes for pts selected for treatment with SIRT were analysed.
Results: Of 1694 pts with mCRC, 580 (34.2%) had liver only disease at diagnosis, 409/580 (70.5%) with synchronous vs 166/580 (28.6%) with metachronous disease. Of pts with liver only disease, 167 (32.2%) were considered resectable at diagnosis, 100 (17%) as potentially resectable and 293 (51%) were treated with palliative intent. Overall 47 pts received SIRT with 1st line chemotherapy (CT). SIRT treated pts were more likely to have a synchronous presentation (85% vs 68%, \(p=0.01\), liver only disease (83.0% vs 27.3%, \(p=0.01\)), to be ECOG 0 (51.1% vs 34.6%, \(p=0.01\)), to be younger (50.8 years vs. 65.9 years, \(p=0.008\)) and to be enrolled on a RCT (38.3% vs 7.3%, \(p=0.01\)). In the liver only population treated with palliative intent, SIRT treated pts (n=30) vs CT only pts (n=188) had a median PFS of 10.6 months vs 9.9 months (HR 0.87, \(p=0.18\)) and a median OS of 24.3 months vs 19.3 months (HR 0.73, \(p=0.04\)).

Conclusion: SIRT is rarely used in the 1st line treatment of mCRC in routine practice. The available data suggests that OS gains can be seen in the absence of differences in PFS. However, this observed differential effect on survival maybe due to selection biases. SIRT treated patients were significantly younger and fitter than the CT alone group. Future analyses will include a multivariate analysis and examine the impact of the recently presented SIFLOX trial data on the use of SIRT in clinical practice.

165 Belinda Lee
Impact of Anti-VEGF therapy in metastatic colorectal cancer with an intact primary tumour

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Background: In patients with metastatic colorectal cancer (mCRC) presenting with an asymptomatic primary tumour and synchronous unrespectable metastases, debate continues regarding the benefits versus risks of initial surgical resection of the primary tumour. Additionally, while the benefit of the anti-VEGF agent bevacizumab alongside systemic fluoropyrimidine-based chemotherapy first line in mCRC is well established, the effect of bevacizumab in patients with an intact primary tumour (IPT) 1 versus resected primary tumour (RPT) is less well understood.

Methods: Subjects were selected from a prospective multi-site Australian registry of consecutive mCRC patients receiving first-line chemotherapy with or without bevacizumab. Progression free survival (PFS), overall survival (OS), (log-rank and Kaplan-Meier analyses) and key safety endpoints were determined for patients with an IPT versus RPT.

Results: Of 1,204 mCRC patients, 826 (69%) were eligible for inclusion. The frequency of bevacizumab use was similar in the IPT (64%) and RPT (70%) arms. In both groups, compared with chemotherapy alone, the addition of bevacizumab was associated with significantly longer PFS (IPT: 8.5 vs. 4.7 months, \(p=0.017\); RPT: 10.8 vs. 5.8 months, \(p=0.001\)) and OS (IPT: 20 vs. 14.8 months, \(p=0.005\); RPT: 24.4 vs. 17.3 months, \(p=0.004\)). Thus, the impact of bevacizumab was no different in the IPT compared to the RPT group, demonstrating survival gains in both groups.

The use of bevacizumab in an IPT was associated with a greater frequency of GI perforations (4.5% vs. 1.8%, \(p=0.210\)) but less frequent bleeding (1.5% vs. 5.3%, \(p=0.050\)) and thrombosis (1.5% vs. 2.7%, \(p=0.470\)), versus chemotherapy alone. However, the median survival was equivalent between patients that did or did not experience bevacizumab-related adverse events — 20.0 vs 19.9 months, HR 0.98, \(p=0.623\).

Conclusions: In routine clinical practice clinicians appear comfortable with using bevacizumab in patients with an IPT. Bevacizumab therapy improved survival outcomes regardless of primary tumour status. The occurrence of bevacizumab-related adverse events did not have a significant impact on survival outcomes.

166 Caroline MacCallum
Use of administrative data to autopopulate colorectal cancer databases: Facilitating outcomes research at an international level

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Background: Colorectal cancer is the second most common cancer in Australia. Research into colorectal cancer requires the maintenance of cancer databases with complex datasets. There are several cancer databases in Australia and internationally which collect data on colorectal cancer patients. For example, in the United States there is the Surveillance, Epidemiology and End Results Program (SEER), while in Australia there is BioGrid Australia (an RMH affiliated database).

There are several problems associated with maintaining these databases, including the extensive resources required, limited geographical scope, lack of uniformity of data, and delays in information production.

Hospital administrative data are another source of information relating to colorectal cancer patients which could be used to populate a large international colorectal cancer database. Using administrative data oversees some of the problems faced by traditional cancer databases: low cost, broad geographical scope, uniformity of data using the WHO International Classification of Diseases (ICD), and large patient numbers.

Aim: The first aim is to determine if administrative data can be used to develop Australian and international colorectal cancer databases. The second aim is to use the international colorectal cancer database to determine if there is a difference between countries in colorectal cancer treatment and outcomes.

Methods: The administrative data and medical records of all colorectal cancer patients admitted to RMH between 2008 to 2013 were obtained, using BioGrid Australia to obtain patient identities. An accuracy study was performed, to compare administrative data coding with medical records. Algorithms of ICD codes were developed to identify incident colorectal cancer patients using administrative data. The next step will be applying the algorithms to state-wide administrative data to create a Victorian colorectal cancer database, allowing analysis of surgical-related outcomes, followed by an equivalent international study.

Results: 575 new colorectal cancer patients were admitted to RMH between 2008 and 2013. Accuracy between medical charts and administrative data was 89% for location of colorectal cancer, 98% for morphology, and 81% for operations. For the algorithm, we used ICD codes C18 to C20 and excluded cases from 2003 to 2008, which successfully identified 95% of incident cases.

Conclusion: Both the good accuracy of administrative data, and the successful development of algorithms to identify incident cases from administrative data, indicate that administrative data may be used to autopopulate colorectal cancer databases. The next step will be to apply these algorithms to state-wide data, and then study the outcomes from such a database.

167 Fiona Tan
Identifying novel inhibitors to STAT3 mediated tumour progression

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Colorectal cancer is the 4th most common cancer globally and the 2nd most common cancer in Australia. Constitutive activation of Signal Transducer and Activator of Transcription 3 (STAT3) has been observed in over 50% of human colorectal carcinomas and its role in tumour progression has been confirmed in numerous mouse models. Previous data suggests that signalling through the Epidermal Growth Factor Receptor (EGFR) and the Interleukin (IL)-6 family of cytokines, contributes to STAT3 activation leading to continual tumourigenesis. Importantly, we have recently shown that IL-11, a closely related IL-6 family member has a more prominent role than IL-6 during the progression of gastrointestinal cancers, including colorectal tumours. In order to block STAT3 activity with the aim of overcoming STAT3-driven tumourigenicity, we evaluated a panel of 1167 FDA approved agents in
their ability for inhibiting STAT3 activity. This was undertaken in human colorectal cancer cell lines using an adenoviral STAT3 luciferase reporter assay. We identified over 50 FDA approved agents (classified as “positive hits”) that were subsequently assessed in a secondary screen to evaluate which agents could inhibit IL-11, IL-6 and EGFR mediated STAT3 phosphorylation by western blot analyses. Amongst these 19/50 positive agents in our secondary screen was Ponatinib (AP24534) a multi-targeted tyrosine kinase inhibitor, currently approved for the treatment of chronic myeloid leukaemia and Philadelphia chromosome-positive acute lymphoblastic leukaemia. Ponatinib markedly reduced EGFR, IL-6 and IL-11 mediated STAT3 phosphorylation and transcriptional activity (and gene expression of STAT3 regulated genes, including SOCS3). Ponatinib also reduced cell migration. Although our preliminary findings offer proof-of-principle evidence, the potential use of Ponatinib for treating STAT3 driven colorectal cancers requires further investigation.

168 Rowa Aljondi
The relationship of WMH and hippocampal volumes with cognition in normal ageing women: results from the Women’s Healthy Ageing Project (WHAP)

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Aim: To investigate the relationship of White Matter Hypointensities (WMH) and hippocampal volumes with cognitive function in a cohort of healthy aged Australian women.

Background: The presence of WMH lesions and hippocampal atrophy on brain Magnetic Resonance Imaging (MRI) are common findings in older age. Whilst relationships between WMH, hippocampal atrophy and cognitive function have been reported in studies specifically recruiting for Alzheimer’s disease (excluding those with vascular risks), there is a paucity of information that includes specialized measures of volumetric MRI and neuropsychiatric evaluation in healthy epidemiological cohorts. Whilst two thirds of the AD is known to be women, few studies have focused on gender specific research. In this study we present analysis of the relationship between WMH, hippocampal volumes and cognitive function in a cohort of healthy aged Australian women.

Methods: We used data from the Women's Healthy Ageing Project (WHAP), a longitudinal study of Australian women. In 2012, 116 women underwent 3T brain MRI and cognitive assessments, their mean age was 69.1 ± 2.6 years. WMH volume was determined manually using ITK-snap on FLAIR images, visually checked by qualified neuroradiologist, and hippocampal volume was measured by FreeSurfer using the MPRAGE images. To account for differences in head size, both MRI volumetric measures were normalized to intracranial volume (ICV). Cognitive assessment included composite Z-score measures based on 8 individual cognitive tests of four different cognitive domains. Linear regressions analyses were then used to examine the relationships of total WMH and hippocampal volumes with each cognitive domain, adjusted for age, years of education, APOE e4 status and midlife Framingham Cardiovascular Risk Scores (FCRS).

Results: A spearman correlation showed that larger total WMH volume was significantly associated with smaller total hippocampal volumes (r = -0.25, p = 0.007). Increased WMH volume was associated with lower performance in executive function (p < 0.05), but not with verbal episodic memory, visuospatial abilities or semantic memory, after correcting for age, years of education, APOE e4 status and FCRS. Smaller total hippocampal volume was associated with a lower verbal memory performance (p = 0.05), but not with the other cognitive factors.

Conclusion: These findings provide further evidence to support the role for cerebrovascular pathology and hippocampal volume loss in cognitive impairment with normal ageing. As vascular risk factors for the development of WMH are modifiable, our findings suggest intervention strategies to delay or prevent progression of WMH; could be useful in preventing cognitive decline.

169 Grace Florescu
The thalamus as a neural correlate for tremor in MS

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Background: The cerebellum has historically been implicated in MS-related tremor but recent studies suggest that MS-tremor may be dystonic with a multifocal pathogenesis.

Aim: Our aim was to determine the correlation between clinical tremor severity and magnetic resonance imaging (MRI) neural correlates, particularly the thalamus.

Methods: Fourteen patients with predominantly unilateral MS-related tremor were recruited. MRI(T1, T2, FLAIR) and clinical tremor assessment by a movement disorder neurologist were performed. Tremor and dystonia were quantified using the Bain tremor severity score and the Global Dystonia Scale(GDS) adapted for upper limbs. MRI was analysed by 2 observers, including a radiologist. Relevant brain structure volumes were calculated using Freesurfer v5.7. Hemispheric volumes were corrected against total brain volume to reduce variability. Statistical analysis was performed with SPSS v23. Non-parametric two-tailed Spearman correlation tested for relationships between tremor scores and imaging parameters.

Results: Eleven right hand dominant patients were included in analysis. Four patients were male. Mean age was 47.6 years (+/-11.6). Mean thalamic volumes were 6058mm^3 (+/- 916.6 mm^3) (right) 6865mm^3 (+/- 12678.0mm^3) (left). There was significant inter-hemispheric difference between thalamic volumes(= -5.003, p= 0.001). Bain tremor severity score and contralateral thalamic volume demonstrated a strong correlation(r= -0.750, p= 0.008 for left thalamus), with a trend for association with the ipsilateral thalamic volume(r= -0.618, p= 0.043 for right thalamus). The ipsilateral thalamic volume association was no longer significant when thalamic volume was corrected for total intracranial volume(r= -0.471, p= 0.144), however contralateral thalamic volume remained a significant correlate(r= -0.677, p= 0.022). A trend for association between distal arm dystonia with contralateral thalamic volume, when corrected for intracranial volume(r= -0.605, p= 0.048), was observed.

Conclusions: This analysis indicates notable thalamic damage in patients with MS tremor, demonstrated by the significant difference in thalamic volumes. Furthermore, there is a significant correlation between contralateral thalamic volume and tremor severity. These findings support the hypothesis that the thalamus has a central role in MS tremor pathogenesis.

170 Benjamin Sinclair
Effect of physical exercise on brain atrophy in patients at risk of alzheimer’s disease

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Aim and Background: Lack of physical activity (PA) is a known risk factor for Alzheimer's disease (AD). Here we present the results of a randomised controlled trial of an exercise intervention on a sample of elderly subjects with at least one vascular risk factor. We hypothesised that participation in a PA program, and initial physical fitness (PF) would reduce the rate of atrophy throughout the brain, with strongest effects in the hippocampus.

Methods: The sample consisted of 98 elderly subjects. Selection criteria included: aged over 60, diagnosis of mild cognitive impairment (MCI) or subjective memory complaints (SMC), community dwelling, and the presence of at least one vascular risk factor. Subjects were scanned at baseline and again (24.2+-1.9) months later, following an exercise intervention of 150 min/week of moderate PA. Measures of PF were taken at baseline. These included timed up and go (TUG) test for mobility, timed chair stands, hand grip strength and 6 minute walk test. Subjects were scanned with a T1 weighted MRI sequence at each time point. Longitudinal voxel based morphometry was then used to quantify localized changes in brain volume as a result of PA and PF.

Results: Both exercise and control groups showed widespread atrophy over the two year interval. There were no significant differences in rates of brain atrophy anywhere in the brain between exercise and control groups. The only significant association with PF was with TUG times, with longer TUG times associated with faster atrophy rates in the putamen and caudate nucleus.

Conclusions: This work provides no further evidence of neuroprotective effects of PA in those at risk of AD. The results may indicate that PA is less beneficial for MCI and SMC patients compared to healthy individuals. Alternatively, it may be that the relatively mild exercise
intervention of 50 minutes walking three times per week did not reach a floor threshold required to observe volumetric changes. Finally one current limitation of this work is that compliance data is not yet available, so it is not clear whether all those in the exercise group carried out their program, and to what extent. The baseline gait abnormalities are involved in the times up and go test. The increased atrophy with longer TUG times suggest that capacity in this physical task (at baseline) predicts subsequent decline only in certain related motor areas, but has no cross-over effects on higher order cognitive regions often observed in exercise studies.

171 Wayland Wang
Acoustic Radiation Force Impulse (ARFI) Imaging - Can we predict when a second operator is needed?

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Aim: To identify factors that predict when the addition of a second operator will not affect the ARFI fibrosis staging result.

Background: ARFI Imaging is an established ultrasound-based elastography method of assessing liver stiffness as a means of staging liver fibrosis. We have previously shown that the accuracy of ARFI improves when there is concordance between two or more operators and at our institution, we routinely utilise two operators for each study and a third operator when there is more than one fibrosis stage. We have also shown that skin to liver distance (SLD) affects accuracy, and it is generally accepted that an interquartile range (IQR)/median-density ratio ≥0.3 reduces accuracy.

Method: This study included 650 consecutive patients with mixed aetiology chronic liver disease who underwent ARFI as part of routine liver ultrasound. Measurements were independently made by two or more sonographers blinded to the results of other operators. The impact of IQR, IQR/median ratio (IMR), skin-liver distance (SLD) and fibrosis score were assessed in relation to their ability to predict operators’ concordance. Concordance in this study was defined as both operators providing the same fibrosis grading.

Results: When ARFI results were discordant, the average SLD was 2.12 cm (95%- CI 2.09-2.16), which is significantly lower than when the results were discordant (average SLD 2.43 cm, 95%-CI 2.36-2.50, p<0.001). In addition, every 1 cm increase in average SLD leads to a 42.1% increase in IQR. When IMR of any operator was ≥0.3 the ARFI results were discordant in 27.5% compared with 7.9% when <0.3 (p<0.001). For F2 and F3 scores the increase in IMR led to a significant reduction in concordance between 2 operators. For F2 fibrosis there was 68.3% concordance, then IMR<0.3 vs 38.1%, concordance when ≥0.3, p<0.001. For F3 fibrosis these concordance values are 66.7% vs 25%, p=0.002. The IMR had minimal impact in cases of F0/F1 and F4 fibrosis (98.7% and 86% of cases were concordant respectively).

Conclusion: More than one set of ARFI measurements is recommended at least when SLD is ≥2.43 cm and when IQR is ≥0.3 in cases of F2 or F3 fibrosis. An SLD of ≥2.12 cm or fibrosis score of F0/F1 or F4 increases confidence in single operator ARFI result.

172 Shaza Abo
Hospital and home based exercise program to improve functional capacity in people following bone marrow transplant - preliminary report

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Background: Cancer is the greatest contributor to the burden of disease of Australians accounting for 19% of the total national burden. Haematopoietic stem cell transplantation (HSCT) is a highly intensive form of treatment for people with haematological diseases and can result in significant physical and psychological impairments. Exercise therapy has emerged as a key factor in enhancing cancer survivorship outcomes; however is not currently part of standard care. Specifically in the area of HSCT, a small number of randomised controlled trials (RCTs) have been conducted (outside of Australia) and demonstrate promising findings; however large RCTs investigating the benefit of exercise in the allogeneic HSCT population in Australia are urgently needed to assess potential benefits for patients and the health system.

Aims: To (1) determine the feasibility of a scheduled exercise program for people following allogeneic HSCT, (2) maximise physical activity and functional performance of people following allogeneic HSCT with a 3-months exercise program, and at 6-months post completion for analysis of longer-term effects. Measures include compliance (Fitbit® steps per day), exercise diary, strength tests, functional capacity (Incremental Shuttle Walk Test (ISWT)) and questionnaires [social demographics, physical activity levels, exercise motivation, health related quality of life (HRQoL)]. Routinely collected data (such as questionnaires, demographics) from patients who underwent allogeneic HSCT prior to commencement of the exercise program will be used to act as a comparator group to identify trends of improvement in functional exercise capacity compared to normal recovery.

Results: 46 patients were approached, 43 consented (93% consent rate); reasons for non-consent were having too many appointments and being too preoccupied with health concerns to think about exercise.

Conclusion: Whilst this pilot study is not complete, results are a promising to provide strong foundations to implement this service into clinical practice and perform a large RCT within Australia, to bridge the evidence-practice gap and improve survivorship outcomes.

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173 Jacqueline Kay
Specialised physiotherapy for in-patients with diabetes leads to improved outcomes

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Aim: To establish the feasibility of a specialised physiotherapy position for in-patients with Diabetes, and impact on patient outcomes (length of stay, and readmission rates).

Background: The Department of Health and Human Services (Victoria) funded a six-month new position, Advanced Practice Physiotherapy for in-patients with Diabetes, at the Royal Melbourne Hospital (RMH) in Melbourne, Australia. This was following a RMH audit showing increased length of stay and readmission rates for in-patients with diabetes.

Methods: Prospective case series. Patients were included if they were: inpatients with a primary or secondary diagnosis of diabetes, body mass index greater than 30kg/m2, and/or predicted to stay greater than 7 days. Patients were excluded if they refused intervention, were already fulfilling Australian physical activity guidelines, were uncontrollable, readmitted to hospital at six-weeks post-discharge, medically unable to exercise post-discharge, or deceased. Participants were allocated into intervention and non-intervention groups due to the large numbers of referrals. Both groups received standard Physiotherapy care, with the intervention group receiving further intervention of exercises and consultation (establishing goals of exercise, education, and problem-solving through barriers to exercise).

All participants completed an International Physical Activity Questionnaire at baseline and six-weeks post-discharge, and a satisfaction survey.

Results: During the three-month intervention period 56 patients were recruited into the intervention (N=36) and non-intervention (N=20) groups. Demographic data of groups were comparable at baseline. The intervention group had a median length of stay of 4.5 days less, and
Impact on the individual's daily activities and HRQoL. However, lit
following surgery, including bladder, bowel and sexual dysfunction.
Background: People with CRC often experience pelvic floor symptoms
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Aim: To determine the amount and types of physical activity undertaken by
community dwelling lower limb amputees from the Royal Melbourne Hospital
(RMH) Amputee Service.

Methods: A cross sectional observational survey design was employed. All
English speaking community dwelling lower limb amputees who
attend an appointment at the RMH Amputee Service between March and
May 2016 will be invited to participate in the study. Participation is voluntary and includes the completion of the International Physical
Activity Questionnaire and a demographics form.

Results: Recruitment and data collection are currently still in process but will be completed by the time of Melbourne Health Research week. Results will include data regarding the amount and types of physical activity completed by participants.

Conclusion: The results of this study will give clinicians a greater understanding of the physical activity patterns of our Amputee Service clients. This information will be used to further develop our service and assist clinicians in helping future clients to engage in regular physical activity for health benefits.

Pelvic floor symptoms, physical and psychological status of patients following surgery for colorectal cancer

Aim: To assess changes in pelvic floor symptoms, physical activity levels, and anxiety and depression, or HRQoL (p > 0.05). Six months after surgery, patients had less abdominal pain (mean difference = 15.3 ± 31.1, p = 0.02) and clinically less anxiety (mean difference = 11.1 ± 32.1, p = 0.10) compared to pre-operative levels. However, the QLQ-CR29 module revealed that hair loss (mean difference = 20.8 ± 30.8, p = 0.003), faecal incontinence (mean difference = 15.3 ± 32.6, p = 0.03), stool frequency, and symptoms of peri-anal sore skin and bowel embarrassment were significantly and clinically worse (changes greater than the minimal clinically meaningful differences).

Conclusion: Bladder and sexual function, physical activity levels, and anxiety and depression did not deteriorate six months after CRC surgery. However, there was significant worsening of specific bowel symptoms including incontinence. Further investigation in larger studies is warranted.

Home-based Exercise Program versus standard Centre-based Exercise Program in elderly chronic heart failure patients – does location of service delivery matter?

Aim: To compare the outcomes of a home-based exercise program and standard centre-based exercise program on exercise tolerance and QOL in frail and elderly CHF patients.

Methods: Sixty consecutively referred CHF patients were recruited between May 2011 - August 2013, with a median age of 82 and mostly NYHA II-IV symptoms. Forty-five patients met inclusion criteria and were offered participation in either a home-based (n=22) or a centre-based (n = 23) exercise program based on clinical judgement and patient convenience. The home-based cohort was sub-divided according to patient baseline exercise capacity; into either a rehab-in-the-home program (RITH), which mimicked the centre-based program (n=14) or a functional home exercise program (Functional HEP) (n=8). Exercise capacity was measured using the 6-minute walk distance (6MWD) test and QOL by the Minnesota Living with Heart Failure Questionnaire (MLWHFQ). Measurements were recorded at baseline, post exercise program and again at 6 months and 12 months post exercise program completion. Descriptive statistics were prepared (Mean±SD) and linear multivariate analysis conducted to compare the three treatment groups.

Results: After adjusting for baseline scores, age and gender, there was a statistically significant decline in the mean scores for the 6MWD from baseline to 6-months post in the functional HEP compared to centre-based rehab group (-96.6m, 95% CI: -178.4 to -14.7). There was also a statistically significant improvement in mean MLWHFQ scores in the functional HEP compared to centre-based rehab from baseline to post exercise (-23.3, 95% CI: -41.8 to -4.8). These statistically significant differences were not maintained at 6 or 12 month post exercise program completion. There were no statistically significant differences between RITH and centre-based rehab for either 6MWD or MLWHFQ scores at any time point.

Conclusions: RITH appears to produce similar short-term and long-term effects on exercise capacity and QOL compared to centre-based exercise program patients, offering flexibility of patient service delivery. Unfortunately, clinical identification of patients only suitable for a Functional HEP group identifies those who will physically decline over the short to medium term. Unexpectedly, despite this decline, an improvement in QOL was reported and it may be that aspects of the program can be maximised to concentrate on achieving a QOL improvement as the main aim.
Aim: Determining whether providing patients with a copy of their medical correspondence and endoscopy report would lead to a measurable increase in subjective understanding, increased satisfaction and decreased anxiety with respect to their medical care.

Background: Patients do not routinely receive copies of clinic letters and endoscopy reports in Australian public hospitals. The evolution of healthcare and its delivery has placed a greater emphasis on patient autonomy and involvement in matters relating to their own medical care. In the NHS and selected outpatient settings globally, there is a shift towards copying patients into medical correspondence alongside their general practitioners.

Methods: A prospective, randomised study conducted from October 2013 until February 2015 at the evening gastroenterology clinic at The Royal Melbourne Hospital. Patients who were undergoing a category one endoscopic procedure and were able to read/write in English were eligible for the study. Participants were randomised to receiving correspondence or not receiving correspondence, which is the current standard of care. The ‘correspondence’ intervention group received copies of letters by mail from their initial and post-endoscopy consultations, as well as their endoscopy report. Participants completed surveys, including visual analogue scales and the “Hospital Anxiety and Depression Scale” at three time points.

Results: 155 participants were enrolled with 70 participants (45%) followed up. There was no reduction in anxiety levels (10.00 vs 11.50, p=0.52), increase in understanding (8.00 vs 8.15, p=0.73) or increase in satisfaction (8.70 vs 8.50, p=0.33) in participants receiving correspondence. However, 97% of participants (58/60) indicated they wanted to receive correspondence in future and 94% of participants (29/31) in the correspondence group reported receiving correspondence had helped them to better understand their medical condition.

Conclusion: Patients wish to receive copies of their correspondence and feel it improves their understanding of their medical condition. We recommend patients be offered the choice of receiving copies of their correspondence letters and endoscopy reports in future.

Aim: The aim of this study was to develop a comprehensive multidisciplinary diagnostic metric for identifying co-existing morbidities of nocturia beyond the urinary tract.

Background: The causal pathway of nocturia is multi-factorial and underlying individual presentation of nocturia. There is currently no diagnostic metric for identifying co-existing causes of nocturia.

Methods: A Cochrane-style review identified variables carrying a significant risk in proportion to nocturia severity. Discriminating items in robust tools measuring co-morbidities were collected; pertinent clinical measures were added. After removal of item duplication, the self-completed 57 item questionnaire (TANGO) was piloted (n=22), modified, then completed by 300 patients >40 years of age with nocturia who were presenting to the sleep disorder, diabetes, rehabilitation, continence or falls and balance clinics, or in-patients of aged care or rehabilitation wards.

Data was entered into SPSS (V23). Endorsement of items was analysed; those with a high floor effect (i.e. >70% of responses “never” or its equivalent), an inter-relationship >0.8 (i.e. redundant) or >50% missing data were removed. Measures included in their entirety were subject to exploratory factor analysis to identify items with multiple loadings. Psychometric properties were used to reduce the initial TANGO metric to a short form.

Results: Non-urinary tract factors identified on the causal pathway of nocturia included mental health, cardiovascular, metabolic, sleep and inflammatory conditions and use of certain types of medication. List 1 showed the metrics from which TANGO items were drawn. A medication and medical history checklist was added to the questionnaire along with a clinician-completed section of physical measures (height; weight; neck, waist and hip circumferences; heart rate; blood pressure; TUG Test).

List 1: Metrics from which TANGO items were sourced: Overactive Bladder Symptom Score; International Prostate Symptom Score; Epworth Sleepiness Scale; Pittsburg Sleep Quality Index; Insomnia Severity Index; STOP-Bang Obstructive Sleep Apnea Questionnaire; AUSDRISK Diabetes Risk Assessment Tool; Hospital Anxiety and Depression Scale; EQ-5D-3L Health Status Questionnaire; SF-36 Health Status Questionnaire; Brief Pain Inventory (Short Form); Psoriatic Arthritis Screening and Evaluation Questionnaire; General Practitioner Cognitive Screening Test.

Conclusion: We have developed a novel patient-completed all-cause diagnostic metric for identifying co-existing morbidities of clinical relevance to nocturia. This tool has the potential to improve practice across disciplines and medical specialties and to smooth inequalities associated with current care of patients with nocturia.
180 Kathryn Marshall  
nutritionDay Worldwide at Royal Melbourne Hospital  
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Melbourne Health  

Aim: To improve patient safety and quality of care by raising awareness and increasing knowledge about disease-related malnutrition.

Background: Malnutrition is associated with increased complications (including infections, pressure areas and falls) resulting in prolonged length of stay, increased healthcare costs and poorer outcomes for patients. The risk of malnutrition can be best identified by unintentional weight loss and suboptimal food intake. Nutrition Day (nDay) is an annual international benchmarking activity to monitor the nutrition care provided to patients and is conducted under the guidance of European Society for Clinical Nutrition and Metabolism (ESPEN). In 2014, the Royal Melbourne Hospital (RMH) participated for the first time.

Methods: All patients admitted to acute and subacute wards were invited to participate in the one-day cross-sectional audit. Data was collected from consenting participants using simple screening tests for nutritional risk and standardised questionnaire. Data collected directly from patients included weight, weight change, current appetite and the amount of food eaten at lunch; and additional demographic and medical information was collected. The data analysis was conducted centrally by the Medical University of Vienna and a comprehensive report presenting RMH results in comparison with worldwide results provided.

Results: A total of 198 RMH patients consented to participate, this represented 43% of eligible population. Forty-nine percent (49%) of patients reported weight loss in the last 3 months compared to 43% in the worldwide cohort (p=0.06), with 40% reporting greater than 5% weight loss in both groups. Only 36% of patients reported eating normal amounts in the preceding week, this was significantly less than worldwide groups (48%, p=0.01). On the study day, two-thirds (66%) of patients reported eating less than half of their meal, this was significantly more than worldwide groups (56%, p<0.01). The reasons for not eating everything given by RMH patients compared to the worldwide cohort included loss of appetite (33% vs 31%, NS), dislike of the taste or smell of food (28% vs 16%, p<0.001) and fasting (13% vs 9%, NS). Compared to the international benchmark, RMH patients received less nutrition therapy including enteral (2% vs 6%, NS), parenteral (1% vs 3%, NS) and oral (26% vs 67%, p<0.001).

Conclusion: nDay presented a unique opportunity to benchmark nutrition care at RMH. Weight loss and reduced food intake are significant issues contributing to malnutrition for patients at RMH. Opportunity exists for timely identification of malnutrition and enhanced nutrition management for all patients.

181 Zoe Milner  

The wait is over: Early health care delivery for acquired hand conditions  
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1 Melbourne Health  

Aim: To improve the access to healthcare for patients with acquired hand conditions.

Background: Acquired hand conditions such as carpal tunnel syndrome (CTS), trigger finger (TF) and basal joint arthritis (BJ OA) increase public health system demands for assessment and management. Current management of these conditions typically involves a lengthy delay (up to 436 days) between referral and initial surgical outpatient appointment, during which time the condition may progress and the option of non-surgical management is eliminated.

Hand therapists have the knowledge and capability to initiate assessment and management of common hand conditions. Current literature indicates that many patients with acquired hand conditions can be successfully managed by a senior hand therapist. Therefore an advanced practice hand therapy role has been established and can be successfully managed by a senior hand therapist. Therefore an advanced practice grant.

Methods: Scoping review undertaken of existing practices and pathways; Established alternate care pathway for acquired hand conditions – CTS, TF, BJ OA; Developed and implemented credentialing package for advanced hand therapist(s) including work based assessment; Received support from Melbourne Health’s Nursing and Allied Health Scope of Practice Committee; Obtained Melbourne Health low level ethics; Appropriate referrals identified and patients contacted; Hand therapy advanced practice screen established to determined appropriateness for non-surgical management; Criteria-led discharge developed; Patient rated outcome measures utilised to evaluate pathway and intervention effectiveness.

Results: Patient flow and access to care has been greatly improved. Patients with acquired hand conditions are currently accessing expert assessment within 26 days of receiving referral, enabling non-surgical intervention for patients with mild-moderate symptoms. Furthermore, this screening clinic is able to identify patients with severe symptoms who require more urgent medical attention.

Discussion: Advanced practice clinicians can positively influence patient flow and are sufficiently skilled to identify appropriate patients for non-surgical management. This model of care could be implemented for other hand conditions and replicated in other health services.

182 Natasha Smallwood  

Outcomes from an integrated respiratory and palliative care service at an Australian teaching hospital  
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The unaddressed palliative care needs of patients with advanced lung disease highlight the urgent requirement for new models of care. The Royal Melbourne Lung Hospital Advanced Lung Disease Service (ALDS) represents such a model, whereby patients with severe, non-malignant respiratory disease receive multidisciplinary specialist clinic review, and telephone and domiciliary nursing support, with management led by the respiratory team.

Aims: To examine the activity and care provided by the ALDS.

Methods: Demographic and prospective outcome data were collected for 170 consecutive patients (2013-16).

Results: 138 patients were included; 77 (56%) male; median age 75 years and primary diagnosis COPD 117 (85%). Median lung function (n=138): FEV1 0.9L (40%), FVC 2.3L (83%) and DLco 8 (35%). Median PaO2 on ABG 57.5mmHg, and median MMRC dyspnoea score 4. 95 (69%) patients used home oxygen and 115 (83%) had undertaking pulmonary rehabilitation. Active dyspnoea management was discussed with all patients. 50 (43%) patients were prescribed opioids for refractory dyspnoea, with median prescribed and consumed daily doses of 12mg and 10mg oral morphine equivalent respectively. 94 (68%) patients saw a palliative care doctor in the ALDS clinic and 34 (25%) also received community palliative care. All patients were invited to undertake Advance Care Planning (ACP) and 116 (84%) discussed and/or completed an ACP. 42 patients died, with place of death known for 36 patients. Only 11 (26%) patients died in an acute hospital bed, and 25 (60%) died in a palliative care bed, nursing home or at home.

Conclusions: The ALDS, an integrated model of respiratory and palliative care, facilitates access to symptom control measures, communication and planning for patients with advanced lung disease.

183 Nick Ternes  

A new model of care – a pilot study for the implementation and evaluation of the Allied Health Interdisciplinary Professional Practitioner (AHIPP)  
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Royal Melbourne Hospital  

Background: Patients admitted to hospital under general medicine units are presenting with increasingly complex problems and comorbidities requiring significant input and expertise from multiple disciplines. This places larger burdens and pressure on the traditional multidisciplinary team (MDT).

Evaluation has identified various inefficiencies in service delivery within the MDT including delay in allied health (AH) referrals and commencement of intervention with only 41% of all AH referrals being made within 24 hours of admission. Other areas for improvement included; reducing duplication of assessment and management across AH disciplines, streamlining discharge planning and coordination of
**184 Anthea Uдовичич**

Supporting Health Professionals’ Emotional Reactions to Grief and Loss

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**Background:** There is a body of research suggesting that health professionals experience difficulties with managing their own emotional reactions when exposed to patients’/carers’ grief and loss. Staff surveys further indicate there is a lack of resources within the workplace to support them with this. A quality project was implemented at the Royal Melbourne Hospital to investigate if a workshop could assist staff in developing strategies to effectively manage their emotional reactions to grief and loss. In addition, this initiative sought to promote a culture of normalising health professionals’ emotional responses.

**Method:** Benchmarking email to members of OT Australia Oncology/Palliative Care SIG exploring support systems; Literature review; OT staff survey on experiences in dealing with patients’ emotional reactions to grief and loss; Development of written resource; Staff in-service on Managing Emotional Reactions to Grief and Loss; Post-survey to guide future directions.

**Results:** Evidence from the literature highlighted the importance of both self-care and support to assist health professionals’ management of grief and loss. The pre-survey revealed that the majority (91%) of staff are exposed to patient and/or carer grief and loss at least monthly. Staff often debriefed with team members, yet many noted they didn’t have any formal strategies or support in place. SIG members also echoed these findings. A staff in-service was conducted educating clinicians on strategies to assist with managing their emotional health. Clinicians were provided with an opportunity to discuss their emotional reactions with facilitator support. Case-studies were discussed in small groups focusing on strategy implementation. Post-survey results were positive.

**Discussion:** This project demonstrated the effectiveness of an education program to support health professionals’ management of grief and loss. Staff particularly found small group discussions on clinical scenarios useful. Future directions include education for supervisors supporting other staff and students.

**185 Rochelle Wynne**

A non-participant observational audit of hand hygiene in the context of caring for isolated patients with communicable disease

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Department of Nursing, University of Melbourne 1, Department of Infection Prevention and Surveillance Service, Melbourne Health 2, Department of Cardiothoracic Surgery, Royal Melbourne Hospital 3

**Aims:** The aim of this study was to determine compliance with Five Moments for Hand Hygiene (HH) by Health Care Workers (HCW) caring for patients under contact precautions at the RMH. A secondary aim was to identify whether use of PPE affected compliance with handwashing.

**Background:** Healthcare acquired infections lead to prolonged hospital stays and increase financial burden on the health-care system. HH is a key measure in preventing the transmission of these infections. The WHO developed the Five Moments of HH to identify critical points at which a HCW should perform HH to prevent infection. The importance of this campaign is widely recognised, however non-compliance remains prevalent. Isolation precautions, implemented to prevent the spread of communicable disease, have been identified as a potential barrier to HH compliance of HCWs. However, the mechanism and extent to which these precautions affect compliance is not well understood.

**Methods:** A non-participant observational audit was undertaken between December 2015 and January 2016. Wards audited were those with larger populations of patients under contact precautions, including the ICU, oncology ward and seven medical-surgical wards. HH compliance involved washing hands and correct application of gloves.

**Results:** The proportion of HH moments according to HH type was 11.9% by medical staff, 68.9% by Nursing staff, 8.5% by Allied Health Staff, and 10.6% performed by staff classified as “other”. Overall, HH compliance across the areas audited was 57.4% (n = 351). Compliance was lowest in ICU with 56.7% (n = 72) compliant moments observed and highest in oncology with 63.4% (n = 20) compliant moments. In addressing our secondary aim, we found compliance with hand hygiene was 76.3% (n = 286) when correct PPE (gloves and gown) was donned and 53.5% (n = 46) when PPE was used incorrectly.

**Conclusion:** HH compliance of HCWs caring for patients under contact precautions was well below the benchmark of 80% and considerably lower than recent audits of HCWs at RMH. The reduced level of HH compliance by HCWs caring for patients in isolation is consistent with a number of studies previously published in this field. Literature attributes reduction in HH compliance to PPE, in particular application of gloves. Findings of this study show the correct donning of PPE increased likelihood of hand washing. Given the low level of HH compliance found in this study and inconsistent findings regarding HH compliance and isolation precautions, further research is required to determine the barriers to HH compliance.

**186 Rochelle Wynne**

Healthcare associated pneumonia: common characteristics and nurse sensitive indicators in the acute care setting

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**Aim:** The aim of this study was to determine the incidence of Healthcare associated pneumonia (HAP) at the Royal Melbourne Hospital (RMH) and to identify common characteristics and trends in nursing and multidisciplinary care of patients diagnosed with HAP.

**Background:** HAP is a source of significant global morbidity, mortality, and healthcare cost. While there is robust evidence describing risk factors, aetiology, and appropriate care of patients with ventilator associated pneumonia (VAP) in the literature, evidence describing these factors in the context of HAP is variable.

**Methods:** Between July 1, 2014, and June 31, 2015, there were 314 patients with ICD-10 Codes indicative of HAP (J189 and Y95) on their discharge summary. In the same time frame 3540 patients had specimens (sputum, bronchial washings, tracheal aspirate) sent for culture and sensitivity. Of the 314 HAP patients 88 (28%) also had a positive sputum culture. We reviewed the medical records of these 88 patients using an audit tool specifically designed to aid in the correct identification of HAP, to detect risk factors for HAP, to review treatments associated with HAP and to identify nurse sensitive indicators for the prevention of HAP.
Results: Five (5.7%) medical records could not be located for review. Criteria for HAP was not met for 64 (77.1%) patients and 19 (22.9%) patients met HAP criteria. Common characteristics of HAP patients were length of stay greater than 5 days, age greater than 65 years, bone fracture/joint dislocation, surgical procedure during admission, impaired mobility, proton pump inhibitor therapy and poor provision of oral hygiene by nurses. There was very little evidence to substantiate the provision of evidence-based respiratory nursing care in addition to poor documentation of patient characteristics and patient care.

Conclusion: Nursing care of patients in this sample was not consistent with recognised respiratory care recommendations and the general quality of nursing documentation was poor. Findings from this study highlight characteristics associated with HAP that warrant further investigation to substantiate their role in HAP development. Preemptive practice changes that may ameliorate development of HAP, or reduce the severity of symptoms associated with HAP should be tested in future interventional studies in the clinical setting.

187 Rochelle Wynne

Appropriateness of red blood cell and platelet transfusion at the Royal Melbourne Hospital in relation to the National Blood Authority Patient Blood Management Guidelines

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Aim: The aim of this study was to determine appropriateness (in line with the NBA PBM) of RBC and platelet prescription at the RMH. A secondary aim was to assess Medical Officer awareness of the NBA PBM guidelines.

Background: Australia-wide guidelines developed by the National Blood Authority (NBA) designed to assist clinical decision making when prescribing blood components. These patient blood management (PBM) guidelines aim to improve patient outcomes through a more restrictive approach to blood component prescription and therefore reduce the associated risk of morbidity and mortality. An audit conducted at the Royal Melbourne Hospital (RMH) in 2014 reported that 31% of red blood cell (RBC) transfusions were considered inappropriate, however it was unclear if this was due to insufficient documentation or medical officers (MOs) prescribing outside of the

Methods: A retrospective audit of patient medical records in the medical and surgical wards at RMH was conducted at the RMH throughout March 2016. Data collection looked at multiple clinical aspects that would influence the decision to transfuse which included primary diagnosis, comorbidities, surgical procedures, presence of impaired oxygen carrying capacity, bleeding or other risk factors, laboratory findings and the clinical indication documented on the prescription form. Appropriateness of blood component prescription was determined by a haematologist and transfusion nurse. For the secondary aim, an online survey was distributed to MOs prescribing blood components during the same period.

Results: A total of 49 blood transfusion events were audited. Data is currently being analysed. Results will explore current trends inappropriately blood component prescription at the RMH. Audited RBC and platelet transfusions will be deemed appropriate, not appropriate, or unclear due to a lack of documentation in the patient medical file. Key areas will be highlighted where patient blood management can be improved including factors associated with inappropriate prescription, if clinical reassessment occurs between multiple units, and whether documentation in the patient medical file reflects the clinical indication as documented on the Blood Component Prescription form.

Conclusion: The project has the potential to influence changes to Blood Component Prescription form and improving patient safety through better understanding current practice and the need for better decision support tools for MOs.
Hypothesis: The Ambu Auragain intubating-LMA will be associated with greater ease of insertion and ease of intubation. There will be no difference when comparing fibreoptic scores which evaluate the laryngeal alignment according to the standardised scale proposed by Brimacombe. There will be no difference in the number of adverse events from use of either LMA.

Methods: 120 patients having general anaesthetic and requiring orotracheal intubation (standard/reinforced endotracheal tube) were recruited in a single-blinded, randomised controlled trial and were assigned to either LMA Fastrach or the Ambu Auragain. Subjects were English speaking adult patients without known airway pathology or aspiration risk, with an ASA ≤ 4 and weighing ≤ 100kg. The practicality of clinical use between the two devices was assessed.

Analysis Plan: Data will be analysed using unpaired two-tailed t-test or Mann Whitney U-test for time taken for intubation. The x2 test will be used to examine the fibreoptic scores. Fisher-exact test will examine the proportion of successful intubation and SGD insertion in each group, used to examine the fibreoptic scores. Mann Whitney U-test for time taken for intubation. The x2 test will be used to examine the fibreoptic scores. Fisher-exact test will examine the proportion of successful intubation and SGD insertion in each group, and the number of complications which occurred. P < 0.05 considered significant.

190 Wai Hoe Alex Yow

Non-clozapine antipsychotic combinations for treatment resistant schizophrenia: a Cochrane systematic review

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Aim: To evaluate the effectiveness of non-clozapine combination antipsychotic treatment for people with treatment-resistant schizophrenia (TRS) by conducting a Cochrane systematic review and meta-analysis.

Background: More than 40% of patients treated with clozapine (a drug of choice for TRS) fail to respond adequately and treatment options beyond clozapine have not been evaluated well.

Methods: We searched the Cochrane Schizophrenia Group’s (CSG) CENTRAL register using a Cochrane approved strategy and identified trial reports relevant to our review. The results were downloaded to EndNote and duplicates were removed. References were screened at two levels - title and abstract and then the full text if required according to a predefined inclusion criteria. Uncertainty was discussed in detail and results documented. Quality assessment was undertaken using the Cochrane risk of bias tool. We calculated relative risks (RR) and their 95% confidence intervals (CI) for relative risks (RR); dichotomous data, and mean difference (MD) for continuous data, based on the random-effects model. We also contacted the investigators for further clarifications.

Results: 962 references were identified from the search, of which 924 records excluded and 6 RCTs (N=402) included. All trials examined the benefits and harms of the non-clozapine antipsychotic combination versus antipsychotic monotherapy. Five studies were from Chinese publications. All studies were small, inpatient based, short-term (≤ 6 months), incompletely reported, and with unclear risk of bias. All, except one study, defined TRS, but the criterion used varied considerably. No statistical significant difference was found between the two groups on leaving the study (RCT=2, n=114, RR=0.61, CI 0.33 to 1.06). There was also no significant impact of non-clozapine antipsychotic combination on the global or specific mental state at endpoint. No statistical significant difference between two interventions was observed for clinically important global state, as defined by the study (RCT=3, n=286, RR=0.69, CI 0.40 to 1.19). Participants from both interventions experienced similar incidence of adverse effects (RR=0.80, CI 0.54 to 1.17, I² = 23%). The effects of non-clozapine antipsychotic combination on TRS for important outcome measures such as relapses, general behavior, quality of life is unknown.

Conclusion: There is no evidence to support or to refute the use of non-clozapine antipsychotic combination in this difficult to treat group of TRS patients. Current practice is based on clinician preferences and not evidence based. Given the paucity of available evidence, further, large, well-planned trials are imperative to inform the effectiveness and tolerability of non-clozapine antipsychotic combinations.

191 Benjamin Sutu

Exploring the use and uptake of non-pharmacological methods for chronic pain management: from a patient and clinician perspective

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Aim: Chronic pain is a high-prevalence issue that places a significant strain on an already resource-scarce healthcare system. It is a multifactorial biopsychosocial issue that is, anecdotal, poorly managed. Non-pharmacological treatments (NPT), such as Music Therapy, are important adjuncts to standard pain medications. This study is an audit at the Royal Melbourne Hospital, investigating the use and uptake, as well as knowledge and attitudes towards NPT.

Methods: 20 participants were part of this observational audit: 10 patients and 10 clinicians. There were three elements: 1. Patients and their treating clinicians were observed in the outpatient setting. Observations were made about frequency, duration and content of discussion regarding NPT; 2. Patients were interviewed to understand their knowledge and attitudes towards NPT; 3. Clinicians were interviewed to understand their knowledge and attitudes towards NPT.

Results: The qualitative data obtained is currently being analysed using thematic analysis and basic summative content analysis. Preliminary analysis suggests: in observation: • Conversations about NPTs were predominantly driven by patients. When that occurred, further discussions ensued between the patient and their treating clinician. • Not all consultations offered patients NPT options.

Patient interview: • Patients wished they were informed about NPT as early as possible. • Patients expressed desire for comprehensive multidisciplinary care.

Clinician interview: • Clinicians believe that NPT should always be used for chronic pain, but didn’t always prescribe NPTs. • Clinicians were exposed to very minimal formal education about NPT in chronic pain management.

Results are being triangulated in order to derive conclusions. This presentation will focus on the patients’ perspective.

Conclusions: Triangulation of results occurring. Formalised conclusions to follow.

192 Jessica Cassells

Abnormal liver function tests develop despite treatment with a gluten free diet in coeliac disease

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Background: Coeliac disease is an immune-like illness triggered by dietary gluten affecting up to 1.5% of Australians. Abnormal liver function tests (LFTs) at diagnosis of coeliac disease reportedly resolve with treatment on a gluten free diet (GFD), a condition referred to as coeliac hepatitis. Emerging data suggests abnormal LFTs can develop after diagnosis, possibly related to an under-recognized increased risk of non-alcoholic fatty liver disease (NAFLD).

Methods: We conducted a retrospective analysis of patients attending a tertiary hospital coeliac disease clinic from 2013-2016. Data on demographics, histology, liver disease and coeliac serology were recorded. All LFTs available were collected.

Results: Of 330 patients, 202 had diagnosed coeliac disease, 198 were biopsy proven. 157 (77.7%) were female, with a median age of 42 years (18-77). The median age of diagnosis was 35 years old (2-68), with a duration of disease of 6 years (0.8-43); 124/202 (61.4%) had normal liver function throughout, 15/202 (7.4%) had abnormal LFTs at presentation, 21/202 (10.4%) developed at least one episode of abnormal liver function while on a GFD, 42/202 (20.8%) did not have LFTs available.

Conclusions: Triangulation of results occurring. Formalised conclusions to follow.
The majority of patients who developed newly abnormal LFTs on a GFD became negative in their coeliac serology at time of their abnormal LFTs (17/21, 81.0%). 2 patients were diagnosed with drug induced liver injury, 1 with biopsy proven NASI and 1 with choleodocholitis and biliary stricture. 2 patients were diagnosed with NASH via hepaticological assessment. 15 patients had no clear aetiology for their new liver disease, only 33% (5/15) had US and 80% (12/15) had liver screens performed.

Conclusion: Abnormal LFTs at diagnosis of coeliac disease are not uncommon. We identify 10% of patients with coeliac disease develop abnormal LFTs on a GFD with evidence of fatty liver disease in a subset. New abnormal liver function affecting coeliac patients on a GFD in the setting of negative coeliac serology is more prevalent than recognized, and may represent a population at risk of development of NAFLD.

193 Yi Heng Yong
Validation of a low fidelity 3D printed model as a tool for bronchoscopy simulation

YONG Y H
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Abstract: The use of a 3D printed model as an effective simulator in a one-day introductory bronchoscopy session

Background: Traditional bronchoscopy training exposes trainees to highly variable training experience which results in unstandardized evaluation of competency levels. Results in increased risk to patients and induces learner anxiety. Simulators place trainees in safe environments to attain the necessary skills while providing a platform for standardised assessment. The aim of this study was to determine whether the use of a 3D printed model can be used as an effective simulator in a one-day introductory bronchoscopy session.

Methods: We conducted a one-day introductory bronchoscopy session measuring pre-test and post-test results of novices and intermediate operators at the Royal Melbourne Hospital (RMH). The novice group consists of 28 medical students from the University of Melbourne and 3 RMHOs from the RMH. Intermediate operators were 7 ICU registrars from RMH. Measurements of learning gains were obtained from pre- and post-test results from these groups. Initial results comparing between novices, intermediate and experts (6 consultants) were used for the validation of the 3D model as a simulator. A second one-day session was held 2 months later to assess the maintenance of learning gains from the novice group. A modified BSTAT was used to measure participant’s performance.

Results: Mean test scores of novices and ICU registrars improved significantly from 3.798 to 6.898 (p < 0.001) and 5.648/8 to 7.648 (p = 0.006) respectively. All initial results comparing the different groups showed a significant difference. Ability of the model to discriminate proceduralists based on skill was demonstrated, with significant differences in test scores demonstrated, based on experience. Scores for novices and registrars were 3.79 and 5.64, respectively (p = 0.005), between novices and consultants were 3.79 and 7.83, respectively (p < 0.001), and between registrars and consultants were 5.64 and 7.83, respectively (p = 0.004). The 2 month review scores of returning students showed an improvement from pre-test 3.7/8 to 6.7/8 (p = 0.002) but a deterioration of post-test 7.03/8 to 5.67/8 (p = 0.03).

Conclusion: The effectiveness of the 3D model in a one-day introductory bronchoscopy session was demonstrated using pre- and post-test results measuring learning gains. Model validation was demonstrated by comparing results of groups with different skill levels. Furthermore, performance reviews after 2 months showed some retention of endobronchial anatomy and bronchoscopy skills.

194 Douglas Tjandra
A prospective study of the role of colon capsule endoscopy in the assessment of mucosal healing Crohn’s disease

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Aim: To assess the correlation in findings between second-generation colon capsule endoscopy (CCE) and conventional optical colonoscopy (OC) in the assessment of mucosal healing in Crohn’s disease. To compare the tolerability and patient preference between modalities.

Background: Mucosal healing is increasingly a treatment target in the management of Crohn’s disease. OC is the current standard means of assessment; however, many endoscopy services are already overburdened. CCE is a reliable tool for visualising the entire gastrointestinal tract, but its safety and efficacy in the assessment of mucosal healing have not been established.

Methods: Patients with established Crohn’s disease and no suspicion of strictureing small bowel disease, requiring routine mucosal assessment, were enrolled. They underwent CCE followed by OC in a 24-hour period, utilising the one bowel preparation of 2-3L Moviprep in split-dose. Five segments (ileum, right colon, transverse colon, left colon, rectum) were graded using the Simple Endoscopic Score for Crohn’s Disease (SES-CD) by readers blinded to the results of the other modality. Capsule endoscopists were asked to provide an opinion on whether treatment should be changed (intensified versus maintained/reduced) and then actual treatment changes advised by responsible clinicians were recorded. Patients’ overall experiences with CCE and OC were graded on a 10-point scale (0 = poorest, 10 = excellent), and they were asked an overall preference for a future procedure.

Results: CCE and OC were performed on 27 participants (51.9% male, median age 34 years). Completion rate (visualisation up to rectum within battery life) was 56%, with no cases of capsule retention requiring emergent retrieval. Bowel cleanliness was 11% poor, 22% fair, 30% good and 37% excellent. Correlation in overall SES-CD was 0.598 (p=0.014); segment-by-segment, the correlations in terminal ileum, right colon, transverse colon, left colon and rectum were 0.853 (p=0.0001), 0.554 (p=0.005), 0.447 (p=0.037), 0.341 (p=0.05) and 0.095 (p=0.05) respectively. Of 22 participants followed-up thus far, agreement between CCE-recommendation and actual treatment change was 90.9%. Patient tolerability for CCE (median 8.5/10) was better than OC (median 6/10) (p<0.007) and 70% of patients would prefer to have CCE for their next procedure.

Conclusion: CCE is a safe procedure in a select population of patients with Crohn’s disease, and is better tolerated than OC. Correlation in SES-CD is high, and CCE-recommendations showed high agreement with actual management changes. However, larger studies improved methodology to increase completion rates are required before CCE may be recommended as an adequate alternative to OC.

195 Arthur Thevathasan
Haemorrhagic transformation is associated with post-stroke seizures after endovascular therapy

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Aim: To identify the influence of haemorrhagic transformation (HT) on the development of post-stroke seizures in patients with acute ischaemic stroke treated with endovascular therapy.

Background: Currently, seizures are not included in many definitions of a symptomatic intra-cerebral haemorrhage (ICH). Despite this, ICH is a major risk factor for post-stroke seizures. It has been suggested there is an increased risk of HT in patients treated with endovascular therapy compared to intravenous thrombolysis in patients with acute ischaemic stroke. However, there is limited evidence to inform clinicians on the effect of HT on seizure development in an endovascular population.

Methods: Data was prospectively collected from a single comprehensive stroke centre with a maximum seizure follow-up of 2 years. Consecutive patients who underwent endovascular therapy for anterior circulation ischaemic strokes were included. HT was determined by 24-hour imaging. Its association with seizures was determined using uni- and multivariable statistics on Kaplan-Meier methods and Cox regression models.

Results: Sixteen of 205 patients (7.8%) developed post-stroke seizures. HT was associated with significantly increased risk of developing seizures on univariate analysis. (HR, 4.33; P=0.004; 95 CI, 1.81 to 11.65). When adjusted for cortical involvement, baseline National Institutes of Health Stroke Scale, patient age and the use of intravenous tissue Plasminogen Activator and mechanical thrombectomy, HT maintained its significance on seizure development. (HR, 3.61; P=0.019; 95 CI, 1.23 to 10.62). HT on seizure development
had a positive predictive value of 16.67% and negative predictive value of 95.36%.

Conclusion: Haemorrhagic Transformation was significantly associated with increased risk of post-stroke seizures in patients with acute ischaemic stroke treated with endovascular therapy. The findings confirm the need for a review of the definitions of symptomatic ICH, the clinical follow-up periods and management for patients with revascularization-induced HT.

196 Michael Ginevra

Effect of antipsychotic drugs on cognition-related processes in hippocampal microcircuits: an in silico study

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Anti-psychotic drugs (APD) have important effects on cognition, suppressing the positive symptoms of schizophrenia including particularly the associated thought disorder as well as inducing somnolence. These drugs are known to have strong activity at the dopamine type 2 (D2) receptor and this is traditionally considered to be the main therapeutic target. Studies in our lab have revealed a strong suppressive effect of haloperidol and clozapine, a traditional and a newer atypical class of APD, on voltage gated potassium channels (Kv). This could represent a completely different pharmacological target. These potassium currents not only affect the oscillatory properties of individual neurons but also the neural network as a whole seen clinically in EEG. Interestingly, the high frequency “gamma” band (30-80Hz) has been shown to be associated with higher cognitive functions and to be affected in schizophrenia and other psychotic illnesses. Importantly, they have also been shown to be modulated by antipsychotics. We therefore sought to use Hodgkin-Huxley derived computer modelling to explore the potential mechanistic connection between these voltage gated potassium channels and: i) Gamma Frequency Parameters; ii) Efficiency of Memory Encoding and Recall in two biophysically detailed models of CA3 and CA1 hippocampal microcircuits containing: a) Experimentally derived models of the major two biophysically detailed models of CA3 and CA1 hippocampal study processes in hippocampal microcircuits: an in silico

Effect of antipsychotic drugs on cognition-related processes in hippocampal microcircuits: an in silico

198 Judy Savidge

Retinopathy and small vessel calibre in gestational diabetes: a single centre cross-sectional observational study

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Background and Aims: Gestational diabetes affects up to 10% of all pregnancies leading to macrosomia, pregnancy-associated hypertension and prematurity. It is associated with an abnormal placental circulation, which comprises mainly small vessels. This study evaluated the retinal microvasculature in women with gestational diabetes.

Methods: This was a single centre cross-sectional observational study of consecutive subjects diagnosed with gestational diabetes on a glucose-tolerance test and recruited from an antenatal clinic. Subjects completed a medical questionnaire, and underwent BP testing and retinal imaging (CANON non-mydratic camera, Japan). Images were de-identified, and graded for diabetic retinopathy (Airlie House classification) and microvascular retinopathy (Wong and Mitchell classification), and vessel calibre using a semi-automated method based on Knudtson’s modification of the Parr-Hubbard formula. Retinal features were compared with those in normal pregnant women using Fisher’s exact test, the student t test and in linear regression models (Stata software, StataCorp, Texas).

Results: Ninety subjects with gestational diabetes were studied. Diabetic retinopathy was present in 25 (28%). Eight (9%) had microaneurysms suggesting pre-existing diabetes. Sixty-two (69%) had a hypertensive microvascular retinopathy in their third trimester compared with 11 (35%) control pregnancies. This was moderate in 20 (22%). Arteriolar calibre was reduced in gestational diabetes in trimesters 2 (151.7 + 13.7 um and 160.4 +7.4 um, p<0.01) and 3 (147.5 + 13.6 um and 159.7 + 6.7 um, p <0.01) compared with the calibre in normal pregnancies. Three of the four subjects who developed preclampsia had more pronounced arteriolar narrowing than the other gestational diabetics.

Conclusions: Retinal small vessels in gestational diabetes are narrower in calibre from the second trimester suggesting early onset changes in both the systemic circulation and placenta. The retinal vasculature represents a model in which to investigate diabetic effects on the placental small vessels.

199 Jonathan Knott

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: 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, controlled, 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 (control), 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): control group 5 (8), droperidol 11 (17), olanzapine 11 (20). Five minutes after the initial sedative administration, 55.9%, 24.3% and 20.2% of patients were adequately sedated, respectively, (p=0.001). At all other times, significantly more patients in the control group were adequately sedated (p<0.01). Significantly fewer patients in the control group required top-up doses (28.0%, 59.5% and 60.8%, respectively, p<0.001) or other drugs to achieve sedation (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%, 16.2% and 20.0%, respectively, p=0.63).

Conclusion: The midazolam-droperidol combination is superior to the droperidol and olanzapine regimens for IV sedation of the acutely agitated ED patient. These findings will inform best-practice guidelines for the management of this difficult patient group.

200 Jonathan Knott
Eye and tissue donors in an emergency department population, we can do better!

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Aim: Eye and tissue transplantation is an important therapeutic intervention. For many years Emergency Departments (EDs) have been considered a potential source of donors, but no specific evidence to support this was identified in the Australian setting.

Methods: A retrospective audit was undertaken of all patients who died within the Royal Melbourne Hospital ED between 2010 and 2014. ED records, pharmacy records, and electronic medical histories were audited for the presence of eye and tissue donation exclusion criteria and the distribution of these criteria within the target population.

Results: Over the five year period, of 326 deaths, one in three was suitable for eye donation and one in seven for tissue donation. If extrapolated at the national level, an increase of 82% in eye donors and 111% in tissue donors could be seen.

For potential donors, who were ultimately excluded from donation eligibility, five criteria were identified that excluded 85% of those patients. These were: haematological malignancy, neurodegenerative conditions, non-haematological malignancies, chronic renal failure, and eye disease.

Conclusion: This study identified a large pool of potential eye and tissue donors that is unrecognised by emergency clinicians; despite 76% of Australians being supportive of eye and tissue donation, and 1 in 4 registering their intent on the national register.

Whilst an extensive list of exclusion criteria restricts donor potential, only five fundamentally limit donation in the ED population. This will allow the development of clinical triggers that should improve identification of potential donors.

201 James Sgroi
The Incidence of Intravenous Dexamethasone Administration for the Prophylaxis of Postoperative Nausea and Vomiting

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Background: Postoperative nausea and vomiting (PONV) is distressing to patients, and increases length of hospital stay and the costs of care. Dexamethasone is an effective antiemetic drug given for the prophylaxis of postoperative nausea and vomiting (PONV). Although dexamethasone is recommended as a first line agent for PONV prophylaxis, its side effect profile is the subject of current further research, in particular in relation to glycaemic control and wound infection. The purpose of this study is to assess the incidence of intravenous dexamethasone administration for PONV prophylaxis in elective non-cardiac surgery patients at the Royal Melbourne Hospital.

Methods: This study is a combined retrospective and prospective cohort study which will involve a total of 1000 patients. Data will be collected prospectively from 500 consecutive patients having elective non-cardiac surgery in the 12 main operating theatres of the Hospital in 2016 and retrospectively from a further 500 medical records of consecutive patients who had elective non-cardiac surgery in 2013. Information was collected from the available documentation from each patient record for that admission and then subsequently de-identified post data analysis. The information collected included patient demographic information, surgical unit and procedure, PONV risk factors for each patient and pre-, intra- and post-operative anti-emetic therapy.

Analysis: PONV risk scores (Apfel and the modified PONV risk score) will be calculated. Continuous data will be assessed for normality. Normally distributed data will be summarized with mean and standard deviation, and skewed data will be summarized with median and range (interquartile range). Categorical data will be summarized with number and percent. Patients in the two cohorts will compared using unpaired two-tailed t-tests (normally distributed data), Wilcoxon rank-sum tests (skewed data) and chi-squared tests (categorical data).

Conclusion: Knowledge of the pattern of dexamethasone and other anti-emetic use will assist in comparing current practice with past practice and with the most current guidelines for PONV prophylaxis. More importantly, it will give us greater insight into the implications of the future research findings about the side effect profile of perioperative dexamethasone.

Notes