6th December 2018

New Horizons in Medical Research
A Scientific Conference organised by the School of Medicine, Research and Postgraduate Affairs Committee, UCC.

Main Atrium, Western Gate Building, University College Cork
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New Horizons Research Conference 2018
Welcome Message from the Research and Postgraduate Affairs Committee,
School of Medicine, UCC

Dear Friends and Colleagues,

On behalf of the School of Medicine’s Research and Postgraduate Affairs Committee (RPAC) it is with great pleasure that I welcome you all to the New Horizons Research Conference 2018. This research showcase will provide an opportunity to enjoy presentations on a diverse range of clinical and translational medical research projects completed across the School of Medicine. It will enable students and staff to discuss the latest research in medical sciences, with contributions from staff, undergraduate and postgraduate scientists at the forefront of developments in their areas. The program includes a stimulating mixture of oral and poster presentations, in addition to plenary lectures by prominent clinician scientists and academic staff from within the School of Medicine. The event has been awarded five CPD credits from the RCPI*. The meeting presents an opportunity to boost strategic growth of the research lead curriculum development agenda. We hope that all of today’s participants, students and staff enjoy the conference programme, as well as the hospitality of University College Cork during the event.

RPAC would like to extend its deep appreciation to all who presented at the conference. RPAC would also like to express its gratitude to those who participated in judging the oral and poster presentations, in addition, to those who chaired the meeting sessions:

Dr. Barry, Orla  
Dr. Clarke, Gerard  
Dr. Clarkson, Michael  
Dr. Duggan, Eileen  
Dr. Fitzgerald, Patricia  
Dr. Joy, Aislinn

Dr. Kenny-Walsh, Elizabeth  
Dr. MacSharry, John  
Dr. O’Malley, Dervla  
Dr. O’ Tuathaigh, Colm  
Dr. Rizzo, Gabriella  
Dr. Sweeney, Catherine

Yours sincerely,

Liam J. Fanning, Ph.D., D.Sc.
Chair, School of Medicine Research & Postgraduate Affairs Committee, UCC
https://www.ucc.ie/en/medical/research/committee/

*Credits can only awarded to registered attendees who return a completed meeting survey to som.horizons@ucc.ie or School of Medicine Office 2.59. Brookfield Health Sciences Complex, College Road, Cork. T12 K8AF.
**5th New Horizons Research Conference**  
*Sponsored by the School of Medicine*  
Western Gateway Building  
University College Cork  
6th December 2018

**Programme of Events**  
**Session One**

*Chairs: Dr. Gerard Clarke and Dr. Gabriella Rizzo*

08:00am  
Free registration commences

08:00am  
Hanging of posters in the main atrium WGB

08:50am  
*Welcome Address* by Dr. Liam Fanning, Chair of School of Medicine Research and Postgraduate Affairs Committee

09:00am  
Dr. David Clarke  
*Connecting fun with function in the microbiome*

09:25am  
*Short Communications* (three, 10 minutes per talk)

O1. *miR-374a, miR-181b, miR-128 and miR-151a are Early Circulating Biomarkers of Hypoxic Ischemic Brain Injury in a Porcine Model.*  
*Ms. Sophie Casey, et al*  
Department Anatomy and Neuroscience, Paediatrics and Child Health and INFANT

O2. *Gut Bugs and Antidiabetic Drugs: Metformin and DPP-4-inhibitor Differentially Manipulate the Gut Microbiome and Serum Metabolome of Metabolically Dysfunctional Mice.*  
*Mr Paul MacDaragh Ryan, et al.*  
School of Microbiology, APC Microbiome Ireland

O3. *Synaptic expression of interleukin-6 receptors and dystrophin may indicate a role in cognitive deficits associated with loss of dystrophin.*  
*Ms Kim Stephenson, et al.*  
Department of Physiology

09:55am  
Dr. Olivia O’Leary  
The Stressed Brain: From Neurobiology to Behaviour

10:30am  
*Short Communications* (two, 10 minutes per talk)

O4. *FKBP5 pharmacological inhibition as a novel strategy for the treatment of stress-related disorders:*  
in vivo and in vitro approaches.  
*Mr Martin Codagnone, et al*  
Department of Anatomy and Neuroscience and APC Microbiome

O5. *The impact of chronic neuroinflammation on adult and adolescent hippocampal neurogenesis and on the stressed brain.*  
*Ms Lauren Fawley, et al*  
Department of Anatomy and Neuroscience

10:50am  
*COFFEE and Viewing of Posters in the Main Atrium, Western Gateway Building*
Session Two

Chairs: Dr. Michael Clarkson and Dr. Aislinn Joy

11:25am  Dr. Anne Moore Delivery Factors that Influence Vaccine Efficacy: The Message and the Route

11:55am  Short Elevator Pitches (five, 3 minutes each)

06. Three-minute short elevator type pitches:
   i.  An Insight into STIs Commonly Encountered in a University Health Department & Prevalence and Predictive Factors. Mr Aidan Coffey et al School of Medicine and Student health department
   ii. An assessment of UCC student’s knowledge of fatal fetal anomaly and termination of pregnancy for fetal abnormalities. Ms Dervla Devine et al School of Medicine and INFANT
   iii. An Epidemiological Study of Invasive Cutaneous Malignant Melanoma in an Irish Cohort. Ms Barbara Marzario et al School of Medicine, Department of Pathology
   iv. Effects of chronic acetazolamide administration on renal oxygen homeostasis in rats exposed to normoxia or chronic hypoxia. Ms Lisa Palubiski et al Department of Physiology
   v.  Modulation of host serotonin and the microbiota-gut-brain axis by the fermented milk drink, kefir. Mr. Marcel Van de Wouw, Department of Anatomy and Neuroscience, APC Microbiome Ireland

12:10pm  Professor Deirdre Murray Nutrition and Growth from Birth to 5 years: lessons learnt from the Cork BASELINE Birth Cohort Study

12:40pm  Short Communications (two, 10 minutes each)

O7. Parental Attitudes towards Human Papillomavirus Vaccination: A Qualitative Study. Ms. Stephanie Creed et al School of Medicine and Department of General Practice

O8. High-frequency analysis for detecting bursts in the electroencephalogram of preterm infants. Mr Christopher Lundy et al INFANT

1:00pm  LUNCH and viewing of posters. Poster judging.
Session Three

Chairs: Dr. Elizabeth Kenny-Walsh and Dr. John MacSharry

2:00pm  Professor Michael Maher  Computed Tomography and Radiation Exposure – How research can impact everyday practice.

2:30pm  Short Communications (two, 10 minutes per talk)

O9. Application of Continuous Real-time Monitoring to Biological Airborne Particle Source Analysis in the Operating Theatre. Mr. Mehael Fennelly et al Department of Pathology and Environmental Research Institute

O10. An assessment of platelet activation status and platelet reactivity in Multiple Myeloma, Smouldering Myeloma and Monoclonal Gammapathy of Undetermined Significance (MGUS) Patients. Ms Leanne O Sullivan et al School of Biochemistry and Cell Biology

2:50pm  Ms. Roisín McCarthy, Atlantic Corridor Medical Student Research Conference 2018, (a Prize Winner for an Abstract Paper) “Sonographic Features of Resistant Infantile Developmental Dysplasia of the Hip”

3:00pm  Mr. Pat O’ Doherty, MVB MRCVS Veterinary Surgeon Modern Veterinary Medicine

3:40pm  2018 BT Young Scientist Winner Mr. Simon Meehan

“Investigation of the antimicrobial effects of both aerial and root parts of selected plants against Staphylococcus aureus.” Coláiste Choilm, Ballincollig, Cork

3:50pm  Prize Giving and Meeting Close by Professor Paula O’Leary, Dean of School of Medicine UCC
Guest Speaker Profiles

Dr. David Clarke

David Clarke graduated with a BSc in Biotechnology from Dublin City University in 1989. From there he went to the National University of Ireland in Maynooth to undertake a PhD in Microbiology, graduating in 1993. He then travelled to France where he was awarded an International Traveling Prize Fellowship by the Wellcome Trust to undertake post-doctoral research in the laboratory of Professor Barry Holland who was based at the Institut de Genetique et Microbiologie, Universite Paris-Sud. In September 1998 David briefly returned to the Department of Biology at NUI Maynooth as a Lecturer before joining the faculty of the Department of Biology and Biochemistry at the University of Bath, UK in January 2000. He was promoted to Senior Lecturer in September 2004 before finally returning to Ireland in February 2007 to join the School of Microbiology at UCC. Dr Clarke's runs a research laboratory with an active interest in understanding the molecular mechanisms that underpin bacteria-host interactions. Dr Clarke is also Director of the BSc Biotechnology programme and he is a Funded Investigator in APC Microbiome Ireland (http://apc.ucc.ie).

Dr. Olivia O’Leary

Dr. Olivia O’Leary is a lecturer in the Department of Anatomy and Neuroscience, University College Cork. Olivia graduated with a BSc in Biotechnology and MSc in Neuropharmacology from NUI, Galway. She conducted her PhD research at the University of Pennsylvania followed by postdoctoral research at the University of Helsinki. In 2008, Olivia was awarded a prestigious Career Development Award from the Health Research Board to pursue further postdoctoral research at the School of Pharmacy, University College Cork, where she was subsequently appointed as lecturer. In 2012, Olivia joined the Department of Anatomy and Neuroscience.

Olivia's research program is unravelling the neurobiology underlying stress resilience, depression and antidepressant action, and is seeking novel targets for the treatment of stress-related psychiatric disorders. Her research has been published in high-impact journals including PNAS and Science. She has been the recipient of several awards from international professional societies including The Rafaelsen Young Investigator Award from the International College of Neuropsychopharmacology, a Fellowship Award from the European College of Neuropsychopharmacology and most outstanding Junior Faculty Award from the International Behavioural and Neural Genetics Society. Olivia is a
reviewer for >59 international journals and is on the Editorial Board for *Neuropharmacology* and *Acta Neuropsychiatrica*.

**Dr. Anne Moore**

After completing her PhD in HIV vaccine immunology with Professor Kingston Mills. Dr. Anne Moore subsequently embarked upon post-doctoral work on defects in immune responses in HIV-infected individuals in the Wistar Institute in Philadelphia and further work on recombinant vaccines against viruses such as HIV and Ebola virus in Dr. Gary Nabel's lab at the University of Michigan. As a senior immunologist in Professor Adrian Hill's group in the University of Oxford, she developed several T cell inducing vaccine candidates against malaria and TB and was involved in clinical trials of these and other vaccine candidates in Oxford and malaria endemic areas in Africa. In 2016, she worked for 10 months with the vaccine biotech company, Vaxart, San Francisco while on sabbatical. Here she worked on tablet-based oral vaccines for a range of therapeutic and prophylactic vaccines. She lectured in Pharmacology in the School of Pharmacy and in September 2018, she took a position as Senior Lecturer in Biochemistry and Cell Biology.

**Professor Deirdre Murray**

Professor Deirdre Murray is a Professor of Paediatrics and Consultant Paediatrician in the Department of Paediatrics and Child Health, University College Cork. Prof Murray trained in General Paediatrics in Dublin before completing a Specialist Registrar Training and Fellowship training in Paediatric Intensive Care Medicine in the Bristol Royal Children’s Hospital, Bristol and the Royal Children’s Hospital, Melbourne. Prof Murray then returned to Ireland to take up a dedicated Research Fellowship in UCC and complete her PhD in the area of neonatal hypoxic ischaemic encephalopathy, supported by the Denis O’Sullivan Research Fellowship award. Prof Murray has a strong research background in newborn brain injury and developmental assessment. She is a founding member of the Neonatal Brain Research Group (www.nrbg.ucc.ie) and a principal investigator and lead for paediatric research in the INFANT (Irish Centre for Fetal and Neonatal Translational Research (www.infantcentre.ie). She is the principal investigator of the Cork BASELINE Birth Cohort Study and the BiHiVE study. Through large international studies she has been working to develop new ways to predict newborn brain injury using continuous multi-channel EEG, blood based biomarkers and early neurological assessment. In 2012, she was awarded a Health Research Board Clinician Scientist Award to study early blood based biomarkers in hypoxic-ischaemic encephalopathy, the BiHiVE study (www.medscinet.net/bihive). She is the principal investigator of the Cork BASELINE
Birth Cohort study ([www.baselinestudy.net](http://www.baselinestudy.net)) which is a collaborative birth cohort study examining early environmental influences of neurocognitive and behavioural outcome.

**Professor Michael Maher**

Michael Maher graduated from Trinity College Dublin in 1989. After internship in the Meath and Adelaide Hospitals in Dublin, he completed a surgical residency in Cork University Hospital. He received his Fellowship of the Royal College of Surgeons in Ireland in 1993 (FRCSI) and completed a two-year postdoctoral research fellowship at the Department of Surgery, John Hopkins Medical Institutions, Baltimore USA in 1995. The degree Of Doctor of Medicine (MD) by thesis was granted by Trinity College, Dublin in June 1996.

He began radiology residency at Mater Misericordiae Hospital in Dublin in July 1995. He received his Fellowship of the Royal College of Radiologists (UK) (FRCR) in 1999 and Fellowship of the Faculty of Radiologists of Royal College of Surgeons in Ireland (FFR(RCSI)) in the same year. He began a fellowship in Abdominal Imaging and Interventional Radiology at Massachusetts General Hospital (MGH) in Boston in July 2000. In 2002, he was appointed as staff radiologist in Divisions of Abdominal Imaging and Intervention and Thoracic Radiology at MGH and in July 2004 was appointed as Assistant Professor in Radiology at Harvard Medical School. In July 2005, he was certified by American Board of Radiology. In July 2005, he was appointed first Professor of Radiology at UCC and Consultant Radiologist at Cork University and Mercy University Hospitals, Cork. Professor Maher’s research interests have focused on imaging of abdominal and thoracic pathology and on Radiation dose optimization at CT scanning.

**Mr. Pat O ’Doherty**

Patrick O Doherty MVB MRCVS, qualified from the Veterinary University of Ireland in 1984 after some years in mixed practice companion animal practice in Ireland and the UK, he returned to Ireland and Cork in 1990 to become a partner in Gilabbey Veterinary hospital, which was based at 38 Gilabbey St. Cork. The practice has since moved to a purpose built premises, occupying 10,000 sq feet on Vicars road, Cork City. The hospital provides a first opinion on companion animal care, a 24/7 emergency service and over the last 20 years has developed a nationwide reputation for quality and service in the area of referrals and second opinion on multiple veterinary disciplines such as soft tissue surgery, orthopaedics, spinal surgery, oncology, diagnostic imaging, internal medicine and veterinary physiotherapy. Mr O’ Doherty has been a consultant for the Irish Guide Dog Association and Fota Wildlife Park for over 25 years.
### Oral Presentations: G05 Western Gateway Building UCC

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ORAL ABSTRACTS SESSION 1

O1. Ms. Sophie Casey et al, Department of Anatomy and Neuroscience, Paediatrics and Child Health and INFANT

miR-374a, miR-181b, miR-128 and miR-151a are Early Circulating Biomarkers of Hypoxic Ischemic Brain Injury in a Porcine Model

S Casey1,2,3, K Goasdoue4, SM Miller4, GP Brennan5, G Cowin6, C Burke7, B Hallberg8, GB Boylan1, DC Henshall5,9, GW O’Keeffe1,3, C Mooney5, ST Bjorkman4, DM Murray1,2

1Irish Centre for Foetal & Neonatal Translational Research (INFANT), University College Cork, Cork, Ireland 2Paediatrics & Child Health, University College Cork, Cork, Ireland 3Anatomy & Neuroscience, University College Cork, Cork, Ireland 4Perinatal Research Centre, UQ Centre for Clinical Research, University of Queensland, Brisbane, Australia 5Physiology & Medical Physics, Royal College of Surgeons, Dublin, Ireland 6National Imaging Facility, Centre for Advanced Imaging, University of Queensland, Brisbane, Australia 7Pathology, Royal Brisbane & Women's Hospital, Brisbane, Australia 8Neonatology, Karolinska University Hospital, Stockholm, Sweden 9FutureNeuro Research Centre, Royal College of Surgeons, Dublin, Ireland

Background and Aims Hypoxic ischemic encephalopathy (HIE) is an acute brain injury occurring in the perinatal period characterised by a complete or partial disruption to cerebral blood flow. We have previously reported specific microRNAs as potential biomarkers of HIE severity, however, in human cohorts the exact timing of injury and miRNA alteration is unclear. The aim of this study was to examine whether these miRNAs are altered in a piglet model, and if so, the timing of that alteration.

Method A panel of 11 potential biomarkers was selected from RNA sequencing and microarray analysis in human cohorts. Hypoxic injury was induced in a piglet model using 4% FiO2. RNA was isolated from control and HIE whole blood samples and miRNA expression was analysed using qRT-PCR at the 0, 1, 2, 8 and 72 hour time points post-hypoxia.

Results miR-374a (p = 0.043), miR-181b (p = 0.016), miR-151a (p = 0.034) and miR-128 (p = 0.043) were upregulated 1 hour post-hypoxia (n=9) when compared to healthy controls (n=10). Expression of all miRNAs decreased over time and was no longer different from controls by 8 hours post-injury onwards.

Conclusion We have shown that these specific miRNAs are altered immediately post injury in both human and piglet cohorts, with downregulation in umbilical cord blood and upregulation in circulating piglet whole blood. These miRNAs may provide early bridging biomarkers of HI injury in a rapidly evolving condition with corresponding rapidly evolving miRNA alterations.
Gut Bugs and Antidiabetic Drugs: Metformin and DPP-4-inhibitor Differentially Manipulate the Gut Microbiome and Serum Metabolome of Metabolically Dysfunctional Mice

PM Ryan1,2,3, E Patterson1,3, I Carafa4, R Mandal5, DS Wishart5,6,7, TG Dinan3,8, JF Cryan3,9, KM Touhy4, RP Ross1,3, C Stanton1,3

1Teagasc Food Research Centre, Moorepark, Fermoy, Co. Cork, Ireland 2School of Microbiology, University College Cork, Cork, Ireland 3APC Microbiome Ireland, University College Cork, Cork, Ireland 4Fondazione Edmund Mach, Istituto Agrario San Michele All'adige, Fondazione, Italy 5Department of Biological Sciences, University of Alberta, Edmonton, Alberta, Canada 6Department of Computing Science, University of Alberta, Edmonton, Alberta, Canada 7National Institute for Nanotechnology, University of Alberta, Edmonton, Alberta, Canada 8Department of Psychiatry, University College Cork, Cork, Ireland 9Department of Neuroscience, University College Cork, Cork, Ireland

This study assessed the impact of two anti-diabetic therapies on the gut microbiome and markers of cardiometabolic disease risk in mice. We employed a metabolic syndrome model in which C57BL/6 mice were fed a high-fat diet for 25-weeks while receiving one of two anti-diabetic therapeutics, metformin or a dipeptidyl peptidase-4 inhibitor (PKF-275-055), for the final 12 weeks. Animals were monitored for weight gain, as well as glucose/cholesterol metabolism. In addition, adiposity was investigated at dissection, cecal microbiome was analysed by 16S compositional sequencing and serum was analysed by liquid chromatography-tandem mass spectrometry. Both therapeutics significantly improved glucose/cholesterol metabolism, attenuated weight gain and mesenteric adipose accumulation. However, multivariate analyses of microbiome and metabolomics data revealed clear profile separation of the therapeutic groups. While both metformin (0.78; p<0.05) and PKF-275-055 (1.00; p<0.05) mice displayed significantly decreased Firmicutes/Bacteroidetes ratios, only metformin animals harboured metabolic health-promoting Akkermansia (3.4%; p<0.0001). Intriguingly, PKF-275-055 mice displayed elevated levels of the butyrate-producing Rumminococcus (2.0%; p<0.05) and the acetogen Dorea (0.95%; p<0.05). We identified reduced levels of certain sphingomyelin, phosphatidylcholine and lysophosphatidylcholine entities within serum of the PKF-275-055 group when compared to metformin and control. Conversely, metformin mice presented primarily with reduced levels of acylcarnitines, a functional group which has correlated with obesity, insulin resistance and systemic metabolic dysfunction in humans. This study adds weight to the hypothesis that some anti-diabetic therapeutics act in part through manipulation of the gut microbiome. Additionally, we identify several metabolites which may be of central importance in the mechanisms of metformin and PKF-275-055.
Synaptic expression of interleukin-6 receptors and dystrophin may indicate a role in cognitive deficits associated with loss of dystrophin.

KA Stephenson, C Shanahan, MG Rae, D O'Malley

Physiology, University College Cork, Cork, Ireland

Duchenne Muscular Dystrophy (DMD) results in a loss of dystrophin which results in skeletal damage. It can also result in dysfunctional synapses in the brain thereby resulting in significant deficits in cognitive function.

Chronic inflammation in DMD is associated with elevated levels of circulating interleukin-6, a pro-inflammatory cytokine detected in diseased brains with cognitive dysfunction.

The aim of this study was to determine if IL-6 receptors (IL-6Rs) are co-expressed with dystrophin at hippocampal synapses. If so, this may indicate a role for IL-6 in dysregulated synaptic transmission associated with loss of dystrophin.

Dissociated hippocampal neurons (3-5 day old) from C57BL/6 mice were cultured for 10-12 days in culture medium with or without supplemental recombinant IL-6 (1nM). The hippocampal neurons were labelled with antibodies against IL-6 receptors, synaptophysin and dystrophin (n=3 cultures) and visualised. RT- qPCR was used to compare gene expression of IL-6 and IL-6R in WT and mdx hippocampal tissue (n=10 per group).

IL-6R expression was present in cell bodies and processes of cultured hippocampal neurons and co-localised with the pre-synaptic marker, synaptophysin. Incubation with supplemental IL-6 resulted in clustering of IL-6Rs in neuronal processes.

IL-6Rs may interact with dystrophin and contribute to synaptic transmission in hippocampal neurons. We did not detect altered gene expression in WT and mdx tissue for IL-6 and IL-6R using RT-qPCR. However, further studies examining synaptic expression of IL-6Rs in dystrophin-deficient mdx mouse hippocampal neurons may help to elucidate the possible role of this cytokine in cognitive dysfunction in DMD.
**FKBP5 pharmacological inhibition as a novel strategy for the treatment of stress-related disorders: in vivo and in vitro approaches**

MG Codagnone¹², JI Cunningham³, C Sanchez³, JF Cryan¹², OF O’Leary¹²

¹APC Microbiome Ireland, University College Cork, Cork, Ireland
²Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland
³Alkermes Inc., Massachusetts, United States of America

Stress-related psychiatric disorders are among the leading causes of morbidity and mortality. Polymorphisms in the FK506-binding protein 51 (FKBP5), a co-chaperone of the glucocorticoid receptor, have been linked to antidepressant treatment response and susceptibility to psychiatric disorders. Although it’s been more than a decade since FKBP5 inhibition emerged as a potential novel antidepressant strategy, its plasticity and antidepressant-like effects remain largely unexplored. The aim of this work was to evaluate the effect of an FKBP5 pharmacological inhibitor on neurite outgrowth in vitro and on depressive-like behaviour in vivo. In vitro, primary hippocampal neuronal cultures from E18 mice were treated for 48 h with different concentrations of a highly selective FKBP5 inhibitor. Compared to DMSO, the FKBP5 inhibitor (250, 500 and 1000 nM) increased both neurite outgrowth and dendritic branch points. Interestingly, treatment with 500 nM of the FKBP5 inhibitor produced greater increases in neurite outgrowth and dendritic branching than treatment with brain-derived growth factor (BDNF; 40 ng/mL). In vivo, the FKBP5 inhibitor (20 mg/kg) was administered to C57BL/6 male mice 16 h or 1 h prior to the forced swimming test and blood was collected for corticosterone measurement. Remarkably, the inhibitor decreased the immobility time of the mice when administered 16 h prior to the behavioural testing but not 1 h before and none of these changes were accompanied by alterations in corticosterone levels. Taken together, this data suggest that pharmacological inhibition of FKBP5 may be a novel strategy for the treatment of stress-related disorders and warrants further exploration.
The impact of chronic neuroinflammation on adult and adolescent hippocampal neurogenesis and on the stressed brain

LC Pawley, JD O'Leary, CM Hueston, JF Cryan, OF O'Leary, YM Nolan

Department of Anatomy and Neuroscience, University College Cork, Cork, Ireland

The hippocampus is particularly susceptible to altered concentrations of the pro-inflammatory cytokine interleukin-1β (IL-1β), with elevated levels implicated in neurodegenerative and stress-related disorders. Acutely elevated levels of hippocampal IL-1β have been shown to reduce adult hippocampal neurogenesis. However, the effect of chronic exposure hasn’t been fully interrogated, nor have potential differences in the effect of inflammation during adulthood and adolescence, a time of increased vulnerability. Further, chronic stress has a detrimental impact on neurogenesis, but the interactions between chronic hippocampal IL-1β overexpression and chronic stress on hippocampal neurogenesis are not yet fully understood. In this study, we utilized a lentivirus to induce chronic overexpression of IL-1β in the dorsal hippocampus of adult and adolescent male Sprague Dawley rats for at least six weeks.

Six weeks after lentiviral-IL-1b injection in adulthood, there was a reduction in the number and complexity of newly-born neurons in the hippocampus. When the same lentiviral-IL-1b was injected to adolescent rats, a reduction in neurogenesis and neurite branching was also observed six weeks later. A reduction in the number of newly-born neurons were observed nine weeks after lentiviral-IL-1b in adulthood, but neuronal complexity was not impacted. Chronic stress also decreased newly-born neurons in this group.

These findings indicate that chronically increased levels of IL-1β in the hippocampus impairs neurogenesis in both adulthood and adolescence but has differential effects on neuronal complexity between these timepoints and that chronic stress during adulthood has a detrimental effect on adult hippocampal neurogenesis.
Elevator Pitches

O6. (i) Mr. Aidan Coffey et al, School of Medicine and Student Health Department

An Insight Into STIs Commonly Encountered In A University Health Department – Prevalence And Predictive Factors
AJ Coffey¹, J Dwyer²
¹School of Medicine, University College Cork, Cork, Ireland ²Student Health Department, University College Cork, Cork, Ireland

Introduction: Third-level students are a demographic at high risk of contracting sexually transmitted infections (STIs). Commonly encountered STIs, such as chlamydia and gonorrhoea, are highly infectious, often asymptomatic and can be associated with significant morbidity. Literature examining STIs in the Irish student population is relatively sparse.

Aims: Assess the prevalence of chlamydia and gonorrhoea in the population of UCC students who underwent STI testing in UCC Student Health Department (UCC SHD) between March 2012 and October 2016. Identify potential protective or predictive factors that affect likelihood of contracting an STI.

Method: Retrospective descriptive population study of laboratory results and associated patient demographic data collected by UCCSHD.

Outcomes: 3619 test results were included in the study. 30% were male (N=1084); 70% female (N=2522). 7.8% of tests indicated the presence of chlamydia (N=282), while 1% of tests indicated the presence of gonorrhoea (N=36). Although a majority of tests were conducted on patients aged 20 – 22 years of age, patients aged between 17 – 19 carried a proportionally higher burden of disease. Detailed analysis of a sample of this population (n=30) did not show statistically significant correlations between STIs and perceived risk factors such as alcohol, cigarette and substance use, sexuality, age at first intercourse and recent morning-after-pill use.

Conclusions: Chlamydia is a relatively common STI in both male and female patients who undergo STI testing in UCC. Fewer males than females undergo testing for STIs, despite similar disease prevalence amongst both genders. Disease burden is higher in younger students than older students.
Title: An assessment of UCC student’s knowledge of fatal fetal anomaly and termination of pregnancy for fetal abnormalities.

Objective: The objective of this study is to assess UCC student’s knowledge of fatal fetal anomaly (FFA) and termination of pregnancy for fetal abnormality (TOPFA).

Design: This descriptive study was conducted with UCC students. Data were collected using an online questionnaire. The survey consisted of fact based questions with a view to ascertaining knowledge level of students around FFA and TOPFA.

Participants: UCC students registered for the academic year 2017-2018. 20,106 students received the survey. 520 answered the survey, 478 of which were completed responses.

Results: 99.62% (519/521) were comfortable with the topic, while only 0.38% (2/521) were uncomfortable with the topic and terminated the survey. Almost half (48%; 232/479) correctly defined FFA with a lack of knowledge demonstrated around the incidence of FFA in Ireland. A small number, (6%; 28/476) of students thought Down Syndrome is a FFA while only 24% (117/478) could identify Patau Syndrome as a FFA. 8% of students considered Cerebral Palsy to be a FFA and 16% thought Spina Bifida is a FFA. Major disparity was obvious around survivability with a diagnosis of FFA; 13% thought a baby will not survive once born, while 16% believed a baby can survive for years.

Conclusion: Deficits in knowledge were identified in accurately defining FFA, survivability, services made available to couples and classification of FFAs. This gap in student knowledge stresses the need for more readily available and accurate public health and college education campaigns, especially now with legislation about to be introduced to allow TOPFA in Ireland for the first time.
AN EPIDEMIOLOGICAL STUDY OF INVASIVE CUTANEOUS MALIGNANT MELANOMA IN AN IRISH COHORT

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Cutaneous melanoma (CM) was the fifth most reported invasive cancer in the Republic of Ireland (ROI) between 2010 and 2012 according to the National Cancer Registry of Ireland. Between 2005 and 2014, County Cork had a significantly higher than statistically expected incidence of CM compared to other counties. An investigation of the epidemiological trends of CM in this population is warranted and timely.

We conducted a retrospective pathology report review of primary CM diagnosed in 2012 at Cork University Hospital, with a 5 year follow-up to December 31 2017.

In our cohort of 127 CMs (126 patients), the mean age at diagnosis was 59.6 years and 61 (48.0%) patients were male. Superficial spreading melanoma was the most prevalent subtype (63.0%), followed by lentigo maligna melanoma (16.1%). Most CMs occurred on the upper extremity (27.6%), lower extremity (24.4%), and head and neck (24.0%). Ulceration was noted in 17 (13.6%) cases. The majority of CMs were staged at pT1 (57.6%) and pT2 (24.8%) while 9.1% of cases were pT4. CM was documented to have metastasized in 16 (13.0%) patients over a 5-year period.

In comparison to international data, our rates of early CM appear to be higher, with lower numbers of pT4 melanoma (9.1% v 12% in a particular Spanish study). In addition, higher numbers of our CMs occur on the extremities than the trunk, which is noted to be a worse prognostic feature. In conclusion, this research contributes to the growing body of knowledge regarding CM epidemiology in our Munster cohort.
Effects of chronic acetazolamide administration on renal oxygen homeostasis in rats exposed to normoxia or chronic hypoxia

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Carbonic anhydrase inhibition (CAI) is used to prevent acute mountain sickness at high altitude. However, acute CAI reportedly increases renal oxygen consumption (QO2), which could have a detrimental effect on the kidney. We aimed to investigate the effect of acetazolamide (AZE), a carbonic anhydrase inhibitor, on renal oxygen homeostasis under normal conditions and following a sustained decrease in environmental oxygen. Male Sprague Dawley rats were exposed to hypoxia (10% O2, CH; n=5) or room air (21% O2, sham; n=7) for 7 days. Daily AZE (44mg/kg; n=7) or vehicle (saline, VEH; n=7) was administered into the peritoneum (ip). Animals were anaesthetized with euthatal (55mg/kg ip) and surgically prepared for the measurement of renal QO2 and cortical (C) tissue oxygen tension (PO2) (fluorescence quenching oximetry). Data were analyzed and compared using 2X2 ANOVA. In sham animals, AZE increased QO2 but had no effect on this variable in the CH group (Interaction: P=0.0576). There was a trend for AZE to decrease CPO2 in sham animals (Drug: P=0.1313). AZE was without effect on CPO2 in CH animals but tended to have opposing effects on TNa/QO2 in both groups, decreasing it in sham animals and increasing it in CH animals (Interaction: P=0.0753). The present data raise the possibility that chronic AZE administration negatively impacts upon renal oxygen homeostasis by decreasing the efficiency of sodium transport in sham animals. Interestingly, this is not evident in the CH group, potentially due to a hypoxia-induced shift towards anaerobic metabolism. Further experiments are warranted to fully delineate these issues.
Modulation of host serotonin and the microbiota-gut-brain axis by the fermented milk drink, kefir

O6. (v) Mr. Marcel Van de Wouw et al, Department of Anatomy and Neuroscience, APC Microbiome Ireland

Mounting evidence suggests a role for the gut microbiota in modulating brain physiology and behaviour. The gut microbiota represents a therapeutic target for influencing centrally-mediated events and host behaviour. The fermented milk drink kefir has recently been shown to modulate gut microbiota composition in mice. In this study, we sought to investigate the potential role of kefir in modulating host reward-seeking behaviour through the microbiota-gut-brain axis in mice. Two distinct kefirs (UK4 and Fr1) or milk control were administered to male adult mice for 15 weeks and reward-seeking behaviour was assessed using the saccharin preference test and female urine sniffing test. In addition, caecal microbiota composition and function were assessed by shotgun metagenomics, gut serotonergic signaling by HPLC and systemic immunity by flow cytometry. Both kefirs increased reward-seeking behaviour in the female urine sniffing test, while kefir Fr1 also increased reward-seeking behaviour in the saccharin preference test. Furthermore, kefir Fr1 increased the 5HIAA/5-HT ratio in the colon, indicating increased serotonergic activity, and additionally reduced circulating neutrophil levels, a marker of inflammation. Interestingly, only kefir UK4 significantly increased caecal microbiota alpha diversity; whereas both kefirs were able to affect caecal microbiota function. Altogether, these data show that kefir can signal through the microbiota-gut-brain axis and modulate reward-seeking behaviour, potentially through local serotonergic signaling and systemic immunity. Overall, these results indicate that kefir could play a beneficial role on the microbiota-gut-brain axis in health and support the recent broadening of the definition of psychobiotic to include fermented foods such as kefir.
Parental Attitudes towards Human Papillomavirus Vaccination: A Qualitative Study
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Introduction

The Human Papillomavirus (HPV) vaccine protects against cervical cancer, reducing the risk by over 70%. Over the past 3 years the vaccination rate in Ireland has dropped considerably. Despite a renewed campaign, current figures indicate a 61% uptake, which is still below the target uptake of 80%. While anti-HPV vaccination groups have been postulated as the cause for poor uptake, the specific reasons remain unclear.

The aim of this study is to explore current parental attitudes towards HPV vaccination and to gain an understanding regarding why parents consent or decline vaccination.

Methods

A qualitative study using face-to-face interviews with parents of girls aged 11-13 years, who had not yet received the HPV vaccine. Interviews, all in Co. Cork, were audio-recorded, transcribed verbatim and analysed for emergent themes, using a grounded theory approach.

Results

18 interviews were performed with 19 participants (14 female and 5 male), average age 45.5 years (range 39-55 years) and average interview duration was 42 minutes (range 24-56 minutes). Reasons parents agree to HPV vaccination include the desire to protect and trust in medical opinion, while barriers included fear of side effects, lack of information, peer-pressure, and concern regarding possible promiscuity. The greatest sources of influence on parents were the local GP and the media.

Conclusion

Notwithstanding improved HPV vaccination rates recently, significant parental concerns remain, resulting in continued suboptimal rates of vaccination. Clinicians need to be aware of the impact of negative HPV reports by the media. Specific concerns raised by parents need to be addressed in detail and disseminated to this important target audience.
O8. Mr. Christopher Lundy et al, INFANT

High-frequency analysis for detecting bursts in the electroencephalogram of preterm infants
CT Lundy, GB Boylan, JM O'Toole
INFANT Centre, UCC, Cork, Ireland

Aims: Clinical utility of electroencephalography (EEG) for preterm infants is limited by the necessary complex visual interpretation of the EEG by a specialist. Automation of quantitative EEG analysis for preterm infants could improve efficiency, objectivity, and scalability leading to continuous intensive care monitoring with real-time diagnosis. Standard practice is to calculate features in frequency bandwidths (FBs) <50Hz, and mostly in FBs <30Hz. This study aims to evaluate a set of 34 EEG features at FBs >50Hz, compared to the regular FBs <50Hz, to determine performance at detecting bursts in the EEG.

Methods: Ten minute epochs were extracted from the EEG of 36 preterm infants (gestational age <30 weeks), recorded within 72 hours of birth. Using a previously defined EEG feature set for detecting bursts, we generated amplitude and spectral features at 3 high-FBs: 30-48Hz; 52-99Hz; 107-127Hz, in addition to the standard 4 FBs <30Hz. Detection performance was calculated using the area-under the receiver operator characteristic (AUC).

Results: Spectral power was small at the high-FBs compared to power at the low-FB: median (IQR) spectral power of bursts was 4897 (3643) µV² within the 0.5-3 Hz low-FB in contrast to 8 (4) µV², 6 (4) µV², and 1 (1) µV² at the 3 high-FBs, respectively. AUC values for detecting bursts using spectral power, from low-FBs to high-FBs, were 0.95, 0.94, 0.93, 0.91, 0.86, 0.78 and 0.81 respectively.

Conclusions: This pilot study of EEG features at high-FBs highlights promising detection accuracy and justifies further investigation.
ORAL ABSTRACTS SESSION 3

O9. Mr. Mehael Fennelly et al, Department of Pathology and Environmental Research Institute

Application of Continuous Real-time Monitoring to Biological Airborne Particle Source Analysis in the Operating Theatre
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Conventional microbial sampling of air in operating theatres is usually carried out on commissioning after construction or structural modification. Cultures of settle plates or impaction air samples provide little information about the source of any contamination. Substandard operating theatre air quality usually relates to theatre practice or engineering faults whereas in-service monitoring of operating theatre air quality mainly relies on review of engineering parameters such as air-change rates and direct inspection of procedures. Limited data is available on the efficacy of continuous air particle monitoring with laser particle detectors. Portable instruments such as the Wideband Integrated Bioaerosol Sensor (WIBS) combine laser particle size and shape detection with signals indicating biological origin (fluorescence from amino acids and NAD(P)H) characteristic of viable bioaerosols. We present evidence of the utility of WIBS analysis in identifying sources of air contamination in operating theatres. In one example, unsatisfactory conventional culture counts (50 cfu/m3) were obtained from an operating theatre. WIBS detected regular spikes of spherical, fluorescent airborne particles of 0.5-2 microns over the operating table. These coincided with automatic flushing of sensor-operated taps in an insufficiently recessed scrub area. Another example concerns heater cooler units (HCU) in cardiothoracic surgery. WIBS analysis in operating theatres found no change in ambient airborne particles with operation of the Maquet HCU30, but a significant increase during operation of the Sorin 3T heater cooler device. WIBS thus provides a rapid method for detection of airborne particles in operating theatres facilitating source attribution and enabling appropriate response measures for source elimination.
An assessment of platelet activation status and platelet reactivity in Multiple Myeloma, Smouldering Myeloma and Monoclonal Gammopathy of Undetermined Significance (MGUS) Patients.

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Thrombotic events are a major cause of death and morbidity in haematological cancer patients, being reported in up to 10% of patients with Multiple Myeloma (MM), Smouldering Myeloma (SM) and the premalignant disorder, monoclonal gammopathy of undetermined significance (MGUS). Platelet dysfunction, arising from the disease state or associated treatment regimes, is a key modulation of thrombotic risk reported in these patients which is incompletely characterised. In addition, recent evidence has pointed towards a relationship between platelets and tumour cells in MM patients via P-Selectin Glycoprotein Ligand and IL-1β mechanisms, highlighting the need to characterise platelet dysregulation in these patients.

Platelet hyperactivity and the influence of circulating paraprotein levels on platelet activity are investigated in MM, SM and MGUS patients and healthy controls in this study. Fibrinogen receptor activation (PAC-1), platelet degranulation (CD62P, CD63), Phosphatidylserine exposure (Annexin V) and Platelet-Leucocyte Aggregates (CD61/CD45) were assessed by flow cytometry at baseline and following treatment. Changes in platelet activation markers in response to ADP and TRAP-6 were also assessed by flow cytometry. Reticulated platelet quantification, platelet function testing under shear flow and platelet-immunoglobulin complex assessment was also used to assess platelet dysregulation.

Results indicate that platelets are hyperactivated and platelet reactivity is altered in patient groups. Identifying activated pathways in these patients will also allow further study of the role of key regulators in these pathways, including cytoskeletal proteins, and may highlight alternative therapeutic targets in the prevention of myeloma associated thrombosis.
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P001

Nurses’ Knowledge and Practices Regarding the Early Detection and Prevention of Venous Thromboprophylaxis: An Integrative Review
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Background: Venous thromboembolism (VTE) involves two serious and life-threatening conditions: deep vein thrombosis and pulmonary embolism. High rates of VTE are reported among hospitalised patients and those discharged from acute care settings. VTE prophylaxis is known to reduce mortality, which highlights the importance of educating healthcare professionals in general and nurses in particular about the prevention and early detection of this condition.

Aim: To review the literature on nurses’ knowledge and practices regarding VTE prevention and early detection regarding VTE thromboprophylaxis.

Methods: An integrative review of the literature was conducted. Five electronic databases (CINAHL, ERIC, PsycINFO, PubMed and Web of science electronic) were searched in April 2017 to identify papers published in English or Arabic between the year 2007 and 2017. The quality of the reviewed studies was appraised using different tools.

Results: A total of nine studies were included. Nurses’ knowledge and practices regarding VTE prevention and early detection were lacking. Factors affecting knowledge were nurses’ age, qualification, years of experience and type of the institution they graduated from. Examples of factors influencing practices included the language barrier, lack of knowledge and confidence, lack of time and lack of standardized tools for VTE prophylaxis. Two brief educational interventions helped improve nurses’ VTE preventive practices, VTE risk assessment and pharmacological thromboprophylaxis.

Conclusion: Findings from this review highlight the need to educate nurses about the importance of VTE thromboprophylaxis in improving patient outcomes. This could be achieved by designing and implementing well-structured educational and training programmes targeted towards nurses working in acute care settings.

This is the first review that gathered evidence from studies that addressed nurses’ knowledge and practices regarding VTE prevention and early detection.
Older inpatients experience and insights into fear of falling
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Background: Fear of falling (FOF) is often reported post-hospitalization and has been associated with functional decline. Identifying the determinants of FOF during hospitalization and patients’ perception of FOF can help guide their management. To inform a planned future intervention study, this study aimed to evaluate the effects of acute hospitalization on FOF among older adults, older adults’ perception of risk factors, intervention and coping strategies for FOF.

Methods: Thirty-two older inpatients were recruited in an acute teaching hospital. Mixed methods were used to collect data. FOF was measured quantitatively using the Single-item question “Are you afraid of falling?” and Fall-Efficacy Scale-International (FES-I), self-reported retrospectively for premorbid status, currently on admission and again at discharge. Patients with FOF completed a questionnaire exploring their perception of FOF, possible coping strategies and interventions they believed may help.

Results: No significant changes in FES-I scores were detected over time, suggesting acute hospitalization did not change FOF in this cohort. A change in FOF (FES-I) score was associated with the history of falls in previous year. Perceived risk factors included balance problems (n=10), breathlessness (n=5), reduced lower limb muscle strength (n=5) and history of falls (n=4). To cope with FOF, most would avoid activity, seek help and slow their pace. Exercises and education were perceived as effective interventions to reduce FOF.

Conclusions: Fear of falling did not appear to develop, or change during hospitalization. Patients had faith in education and exercise prescription as effective treatments for FOF post-hospitalization.
A systematic review of the quantitative analysis of suicide and self-harm clustering

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Introduction: Suicide clustering has reportedly been on the rise in recent years, owing to factors such as contemporary communication technology. While suicide clusters are relatively uncommon, they are a cause for great community concern due to the potential impact of contagion associated with such phenomena. The detection and surveillance of clusters can potentially avert subsequent suicide and self-harm by implementation of early intervention in at-risk populations and geographic locations.

Aim: The aim of the current research is to determine whether scientific analysis of suicide and self-harm clustering has progressed as a result of advances in statistical methods of verification and geospatial analytical techniques in recent years.

Methods: A systematic search of relevant databases is being conducted to identify studies that have statistically analysed the presence of suicide and self-harm clustering within a population. The review synthesises existing evidence on the quantitative analysis of suicide and self-harm clustering and examines the accuracy of cluster determination, based on specific criteria.

Results: The limited number of studies addressing self-harm clustering are mostly narrative reports of possible clusters that have not been statistically verified. Recent studies testing for the presence of suicide clusters have utilised spatial mapping techniques to detect temporal-spatial clusters, most commonly applying the Poisson mixture model to determine the statistical significance of the clustering phenomena.

Discussion: Current research demonstrates the efficacy of geospatial analysis methods in accurately detecting suicide clusters with populations and settings, with less evidence of the accurate detection of self-harm clusters. Future studies of self-harm clustering should employ geospatial methodology to determine the statistical evidence of such phenomena.
N-Acetyl cysteine improves dystrophic (mdx) mouse diaphragm muscle quality and strength

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Respiratory muscle weakness occurs as a consequence of dystrophin deficiency in Duchenne muscular dystrophy (DMD), with implications for breathing and airway protective behaviours. The mdx mouse model of DMD shows evidence of impaired respiratory muscle performance with attendant inflammation and oxidative stress. N-Acetyl cysteine (NAC) is a dietary antioxidant used in the treatment of respiratory disease. We examined the effects of NAC intervention on respiratory system performance in the mdx mouse.

Young adult male wild-type and mdx mice were studied; a subset of mdx received 1% NAC in the drinking water for 14 days. Ventilation was assessed in conscious mice using plethysmography. Inspiratory pressure and respiratory muscle EMG activity were assessed in anaesthetised mice. Diaphragm ex vivo force-generating capacity, muscle structure, cytokine concentrations and mRNA expression were determined.

Diaphragm force was severely depressed in mdx mice, with evidence of fibre damage, fibrosis, immune cell filtration and elevated pro-inflammatory cytokine concentrations. Diaphragm force was increased in mdx following NAC supplementation. Collagen deposition and infiltration of inflammatory cells in mdx diaphragm was decreased following NAC. Mdx diaphragm and plasma IL-1b and IL-6 concentrations were significantly decreased by NAC. mRNA expression of Nrf2 (antioxidant response element) was increased in mdx diaphragm and increased further with NAC supplementation. No adverse effects of NAC were observed on ventilation, inspiratory pressure and EMG, and growth measures.

We reveal that NAC treatment improved mdx diaphragm force-generating capacity by way of beneficial anti-inflammatory and anti-fibrotic effects. These data support the potential use of NAC as an adjunctive therapy in the dystrophinopathies.
Impact of the 2004 Irish Workplace Smoking Ban on Lung Cancer Incidence and Mortality

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**Background:** In 2004, Ireland became the first country worldwide to institute a comprehensive workplace smoking ban. Previous research has found that smoking bans are associated with major public health benefits, including reductions in cardiovascular and respiratory disease. However, the effect of smoking bans on lung cancer has not been well explored.

**Methods:** Annual, age- and sex-specific incidence and mortality of lung cancer were calculated. A one-sample, Poisson-based, interrupted time series analysis, adjusted for the confounding of smoking prevalence, was used to quasi-experimentally compare lung cancer incidence and mortality before and after a modelled interruption. The effect was measured by sex and gender and in absolute terms.

**Results:** Each year following the modelled interruptions, lung cancer incidence decreased 3% (95%CI 2-5, p<0.01) and lung cancer mortality decreased 1% (95%CI 0-2, p=0.01) relative to the modelled counterfactual. In absolute terms, the 2004 Irish Workplace Smoking Ban was associated with an estimated 209 (95%CI 155-274) fewer incident cases of lung cancer per year and 122 (95%CI 104-143) fewer mortalities due to lung cancer per year. These reduction estimates correspond to approximately 7.4% of incident cases of lung cancer and 6.3% of mortalities due to lung cancer.

**Discussion:** The 2004 Irish Workplace Smoking Ban averted over 1,000 incident lung cancer cases and 1,000 lung cancer mortalities. This is among the first studies to examine the effect of smoking bans on lung cancer. These results give policy-makers, tobacco control practitioners, and advocates one additional reason to institute (or preserve) smoking bans.
Effects of Chronic Intermittent Hypoxia on Renal Functional Response to Volume Expansion in Anesthetized Rats

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Aim:
Obstructive sleep apnoea is characterized by repetitive cycles of upper airway obstruction during sleep, which leads to intermittent hypoxia (IH) and hypoxaemia. However, the impact of IH on kidney function and its ability to respond to physiological challenges is unclear. We aimed to determine whether chronic exposure to IH (CIH) impairs the natriuretic and diuretic response to an acute volume expansion (VE).

Methods:
Male Wistar rats were exposed to CIH for two weeks (90s exposure to hypoxia reaching 5% O₂ at the nadir followed by 210s exposure to 21% O₂, 12 cycles/hr, 8 hr/day). Following anaesthesia, baseline urine and plasma samples were collected, as well as during and after saline VE (0.25% body mass/min for 30 min) in the presence of intrarenal infusion of either saline or transient receptor potential vanilloid type 1 (TRPV1) antagonist, capsazepine.

Results:
Basal urine flow rate, absolute and fractional excretion of Na⁺ and GFR were similar in control and CIH groups (UFR 0.007±0.002 vs. 0.012±0.003mL·min⁻¹; UNa⁺ 1.5±0.6 vs. 0.7±0.2 mmol.min⁻¹; FNa⁺ 0.51±0.15 vs. 0.76±0.24%; GFR 4.9±1.0 vs. 5.1±1.4 mL·min⁻¹·g⁻¹). There was a significant increase in UFR, UNa⁺, FNa⁺ and GFR during VE in both control and CIH. CIH blunted the VE-induced increase in UFR and UNa⁺ by almost 57% (p<0.05) but did not affect FNa⁺ or GFR. Intrarenal capsazepine did not change renal functional parameters during VE in CIH or control.

Conclusion:
These findings suggest that exposure to CIH blunts the diuretic and natriuretic response to VE, which was not dependent on renal TRPV1 signalling.
Title: Antibody associated bacteriophage profiling in the gut
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Background: The mucosal immune system acts as the first line of defense and maintains a tolerance towards non harmful commensal intestinal flora. The aim of our study is to investigate whether specific components of the enteric virome consistently generate an IgA response in healthy individuals.

Methods: Virome fraction was isolated from faecal samples of self-declared healthy individuals (n=8). Magnetic beads were used to isolate viruses using an anti-sera. Shotgun metagenomic sequencing was performed on the Illumina MiSeq platform. Using an in-house bioinformatics pipeline, contigs or putative viral genomes, were assembled with the metaSPAdes assembler. PVOG scores were used to assess the viral probability, where the score ranges from 0 to 1, with 0 being the least probable score for a virus.

Results: IgA endogenously (in the gut) labelled phage were isolated successfully and found within the Next Generation Sequencing dataset. 509 putative viral genomes were identified as being IgA positive, with contig sizes ranging from 1232 – 149793 bp and coverage ranging from 2.81242 – 1128.67. The known viral families identified were Microviridae, Poovirus and Gokushovirus. Many putative viruses could not be assigned to any viral family.

Conclusion: This study demonstrates that IgA endogenously labelled virome fraction is present in the faecal virome. This provides the first evidence of the mucosal immune response elicited against certain member of the gut virome. The sequences that had no homology with the viral database are representative of the “dark matter” and currently cannot be assigned to any viral family.
Peripheral immune-biome profiling of the enteric virome
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Background: The humoral immune system represents a historical record of immune exposure. Immunoglobulin class G (IgG) comprises the dominant peripheral circulating immunoglobulin. The aim of our study is to investigate whether specific components of the enteric virome consistently generate an IgG response in healthy individuals and to identify IgG associated phage.

Methods: The virome fractions were isolated from faecal samples of self-declared healthy individuals (n=8). IgG (n=8) from matching serum samples was isolated. IgG exogenously labelled phage were isolated. Shotgun metagenomic sequencing was performed on the Illumina MiSeq platform. Using an in-house bioinformatics pipeline, contigs or putative viral genomes, were assembled with the metaSPAdes assembler. PVOG scores were used to assess the viral probability, where the score ranges from 0 to 1, with 0 being the least probable score for a virus.

Results: Exogenously labelled phage with IgG (from serum) was isolated successfully and was identified within the Next Generation Sequencing dataset. 450 putative viral genomes were identified as being the exogenously labelled IgG positive fraction, with contig sizes ranging from 1116 – 149793 bp and coverage ranging from 3.00866 – 1319.27. The known viral families identified were Microviridae, Poovirus and Gokushovirus. Many putative viruses could not be assigned to any viral family.

Conclusion: This study demonstrates that a humoral immune response is elicited against some of the gut virome. The sequences that had no homology with the viral database are representative of the “dark matter” and currently cannot be assigned to any viral family.
Physical comorbidities and pharmacological treatment of major self-harm repeaters presenting to emergency departments in Ireland

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Data from the IMPRESS study (Improving Prediction and Risk Assessment of Self-harm and Suicide) have indicated that there are 2 main subgroups among self-harm patients presenting to emergency department in Ireland: high risk self-harm patients and major repeater patients (MR). MR are defined as patients with a history of 5 or more previous self-harm episodes.

The aim of this study is to investigate predictive risk factors associated with repeated self-harm. Results presented in this abstract include first findings from baseline interviews conducted with MR. Consecutive patients presenting to three emergency departments in Ireland following a repeated self-harm episode were invited to participate in semi-structured interviews.

Data on physical health and pharmacotherapy were analysed. From 133 patients identified as MR, 31 engaged in an interview. The average age of the patients was 34 years, mainly female (60%) and the most common methods of self-harm were intentional drug overdose (IDO-70%) and self-cutting (22%). The most common physical comorbidities were asthma (20%), metabolic diseases (20%), gut related disorder (23.33%) and orthopaedic related problems (16.6%). Nearly half of the patients (46.6%), reported suffering from pain. When looked at the pharmacological treatment, 50% of the patients were prescribed antipsychotics, 50% antidepressants and 26.6% anxiolytics. The majority of participants were prescribed more than one psychotropic drug (73.33%).

Our results highlight the need for a better understanding of the physical comorbidities among self-harm patients since they represent common biological pathways. Moreover, the high rates of IDO combined with the high rates of psychotropic drugs prescribed to MR imply the need for improved monitoring of prescribing them to this specific group of patients.
Method of self-harm and risk of self-harm repetition: findings from a national self-harm registry

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Background: Risk of self-harm repetition has consistently been shown to be higher following self-cutting compared to intentional drug overdose (IDO) and other self-harm methods. The utility of previous evidence is limited due to the large heterogeneous method categories studied. This study examined risk of hospital presented self-harm repetition according to specific characteristics of self-harm methods.

Methods: Data on consecutive self-harm presentations to hospital emergency departments (2010-2016) were obtained from the National Self-Harm Registry Ireland. Associations between self-harm method and repetition were analysed using survival analyses.

Results: Overall, 65,690 self-harm presentations were made involving 46,661 individuals. Self-harm methods associated with increased repetition risk included minor self-cutting, severe self-cutting, multiple drug IDOs involving psychotropic drugs and self-harm by blunt object. Minor self-cutting was the method associated with highest repetition risk (adjusted hazard ratio (AHR) 1.38, 95% CI 1.31-1.45). Risk of repetition was comparable following IDOs of four or more drugs involving psychotropic drugs (AHR=1.29, 95% CI 1.20-1.39), severe self-cutting (AHR 1.25, 95% CI 1.16-1.34) and blunt object (AHR=1.23, 95% CI 1.07-1.42).

Limitations: Information was not available on suicide or other causes of mortality.

Conclusions: Self-harm method and the associated risk of repetition should form a core part of biopsychosocial assessments and should inform follow-up care for self-harm patients. The observed differences in repetition associated with specific characteristics of IDO underline the importance of safety planning and monitoring prescribing for people who have engaged in IDO.
Multiple drug intentional overdose: An examination of national self-harm surveillance data.

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Introduction: Non-fatal Intentional Drug Overdose (IDO) is the most common form of hospital treated self-harm. IDO commonly involves more than one drug type, with significant implications for patient treatment and outcome.

Aim: To examine the characteristics of multiple drug IDO and the drugs involved.

Methods: We included emergency department IDO presentations recorded by the National Self-Harm Registry Ireland between 2007-2015. Multiple drug use involves the ingestion of two more drugs, excluding alcohol.

Results: Of 72,383 IDOs recorded, approximately half (48%) featured multiple drug use. Multiple drug IDOs were most often made by females (60%) and persons aged 25-54 (63%). Compared to single drug presentations, multiple drug IDOs involved the consumption of a greater quantity of tablets (mean 36 vs. 24, p<0.001), and more often resulted in hospital admission (45% vs. 38%, p<0.001). The majority (52%) of multiple drug IDOs involved the consumption of a benzodiazepine and 39% involved an analgesic. In one third of multiple drug presentations an antidepressant was taken and 12% involved an antiepileptic. The most common drug combination identified were benzodiazepines and antidepressants, recorded in 18% of presentations. Alcohol featured in 43% of multiple drug IDOs.

Conclusion: The results show that multiple drug IDO is common, and associated with particular drug types. These findings underline the need for monitoring of prescribing practices, particularly when multiple drugs are involved. The specialised care needs of patients with alcohol consumed requires consideration and emphasis should be placed on prevention measures given the resources required to treat these patients.
The BMI adjusted weight loss grading system is associated with poorer quality of life and reduced survival in patients with incurable cancer: results of an international prospective study.

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Background: The body mass index (BMI) adjusted weight loss grading system (WLGS) has been shown to associated with reduced survival. However, its impact on quality of life (QoL) has not been established. The aim of this study was to validate the prognostic ability of the WLGS in patients with advanced cancer and determine its relationship with QoL.

Methods: A prospective study of adult patients with advanced cancer was conducted at two international sites between 2012-2016. Data collected included information on patient demographics, performance status, inflammatory markers and nutritional parameters [BMI, %weight loss (WL)]. Patients were categorised according to the WLGS into one of five distinct WL grades (grades 0-4). QoL data were collected using the EORTC QoL Questionnaire.

Results: 1027 patients were included in the study [51% male, median age: 66 years]. Gastrointestinal cancer was most prevalent (40%) and 87% of patients had metastatic disease. Half (56%) of patients had a WL grade 0-1, while 15%, 19% and 11% had WL grades of 2, 3 and 4, respectively. Increasing WL grades were associated with deteriorating QoL. High grade WL (≥2) was independently associated with a QoL summary score below the median (<77.7) [OR:1.97 (95% CI:1.40-2.75)]. Median OS decreased from 16.6 months (95% CI:13.6-19.6) in WL grade 0 to 5.4 months (95% CI:3.9-6.8) in WL grade 4 (p<0.001). On multivariate analysis, WL grade 3 and 4 remained independently associated with reduced survival [HR:1.46 (95% CI:1.14-1.89) and HR:2.04 (95% CI:1.51-2.74), respectively].

Conclusion: The WLGS was independently associated with reduced survival and poorer QoL. WL grade 4 carries a particularly poor prognosis and increased symptom burden. Patients with WL grade 4 may benefit from early referral to palliative care services.
Determinants of quality of life in patients with incurable cancer: a prospective international study

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Background: Optimising quality of life (QoL) remains the central tenet of care in patients with incurable cancer, however determinants of QoL are not clear. The aim of this study was to examine which factors influence QoL in patients with incurable cancer.

Methods: A prospective study of adult patients with advanced cancer was conducted in both Cork and Glasgow. Data collected included: patient demographics, performance status (ECOG-PS), nutritional parameters [% weight loss (%WL) and body composition assessed using computed tomography images (skeletal muscle index (SMI) and skeletal muscle attenuation (MA)], inflammatory markers [modified Glasgow Prognostic Score (mGPS)] and QoL (EORTC QLQ-C30). The relationship between these parameters and QoL was assessed using the Spearman rank correlation coefficient (ρ) and multivariate logistic regression.

Results: 1027 patients were included in the study (51% male, median age: 66 years). Gastrointestinal cancer was most prevalent (40%) and 87% of had metastatic disease. ECOG-PS, systemic inflammation and %WL were significantly correlated with deteriorating QoL functional and symptom scales (all p<0.001). On multivariate regression analysis, ECOG-PS stage 3-4 [OR 10.14 (95% CI:4.76-21.63)], mGPS score 2 [OR 1.55 (95% CI:1.07-2.24)], >10% WL [OR 3.71 (95% CI:2.17-6.35)] and cancer site lung [OR 1.92 (95% CI:1.28-2.89)] were independently associated with reduced overall summary QoL score. Muscle parameters correlated with domains of QoL functional and symptom scales to a small effect (ρ<.29), but on multivariate analysis, neither sarcopenia nor low MA predicted QoL.

Conclusion: ECOG-PS, systemic inflammation and %WL are independent predictors of poorer QoL in patients with advanced cancer. Determining early predictors of poor QoL may allow the identification of patients who may benefit from early referral to palliative and supportive care, which has been shown to improve QoL.
Baseline demographics of cow’s milk allergic infants recruited to a randomised trial of single-dose food challenge with cow’s milk.
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Background:
Single dose challenges are a new method of assessing reactivity in food allergic children that have shown to be safe. We report the clinical features of cow’s milk (CM) allergic infants prospectively recruited to a randomised, controlled trial of single dose exposure to CM, using the estimated dose of CM milk that would elicit reactions in 5% of CM allergic (CMA) subjects - the ED05.

Methods:
Infants were recruited from new referrals to 2 tertiary allergy centres. Inclusion criteria were infants less than 12 months old with a CM allergic reaction within previous 2 months and positive skin prick test (SPT) +/- raised spIgE to milk. Children were randomised 2:1 to a single dose of the ED05 for CM (0.5mg mil protein). SPT to peanut and egg were also performed and advice re dietary introduction given accordingly.

Results:
20 children were recruited. The mean age of recruited infants was 7.4 months. 13 of 20 (65%) were male, 12 (60%) were first born. 1 was bottle fed from birth, 19 were breast fed, of which 12 (60%) had formula supplements. Thirteen (65%) had eczema. 15 (75%) were sensitised to egg and 6 (30%) to peanut of which all were also sensitised to egg. None of 11 children randomised to the intervention of CM ED05 consumption reacted.

Conclusion:
A single low dose of cow’s milk, using the ED05, is well tolerated. Irish children with CMA have rates of egg and peanut sensitisation comparable to international rates. Irish breastfed infants frequently receive formula supplementation which may contribute to development of CMA.
Is heart rate variability (HRV) a predictor of intraventricular haemorrhage (IVH) in preterm infants?
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Introduction-IVH occurs in up to 30% of babies born before 28 weeks gestation, causing significant short and long term problems. HRV is a measure of autonomic function controlled by cardiorespiratory reflexes. Recent literature has suggested that depressions in HRV and decelerations are sometimes witnessed clinically if an acute central nervous system injury occurs, such as haemorrhage.

Aim-This study aims to describe HRV as a prognostic tool in diagnosing IVH.

Methods-This project analysed ECG data from 28 preterm infants who have been enrolled in the CUPID trial in CUMH.
1) An epoch of ECG free from major artefacts was extracted from the long-duration recordings. ECG was pruned and transformed into EDF.
2) The ECG R-peaks were identified by visual inspection using a UCC HRV Analysis software.
3) The HRV was computed from the R-R interval as in 1).

Results-6 of the 28 babies developed IVH. Aged 6 hours, a number of HRV features were associated with the development of IVH. These included sd of RR interval (45.3 vs 272 milisecs, p value 0.046) and HF power (275 vs 104, p value 0.046).

Discussion-Some features of HRV are associated with the development of an IVH in a preterm’s first 6 hours of life. A larger cohort of infants is needed to validate these features which may be a useful early biomarker for infants at risk of IVH.
Baseline Scores on Food Allergy Quality of Life Questionnaire (FAQLQ) and State/Trait Anxiety Inventory in Mothers and cows milk allergic Infants recruited to a randomised controlled trial of single low dose challenges.

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Rationale: The Food Allergy Quality of Life Parent Form (FAQLQ-PF) questionnaire has proven a valid and reliable measure of change in randomised control trials (RCT). Single dose challenges are a novel method of assessing low dose reactivity in food allergic children. We report the baseline scores on the FAQLQ-PF, the Food Allergy Independent Measure (FAIM) and the State/Trait Anxiety Inventory (STAI) scores in an ongoing RCT of single dose challenges in cows milk allergic infants.

Methods: Twenty mothers completed the questionnaires at randomisation. The total STAI score (on a scale of 20 to 80) was categorised as severe anxiety ≥ 75th percentile; moderate anxiety 75th to 25th percentiles; and mild anxiety < 25th percentile.

Results: Mothers (mean age 37, 3.2) of 20 infants (mean age months 7.4, 1.9) completed all measures. Mean scores for FAQLQ (3.0, 1.6) and FAIM (3.9, 1.6) were above norms for age. 25% of mothers scored in the top percentile on STAI indicating severe State anxiety with 25% in the lowest, indicating mild anxiety. State anxiety was normally distributed (Shapiro-Wilk>0.05) and was positively associated with FAQLQ (r=0.4, p=0.04), FAIM (r=0.63, p=0.001), and Trait anxiety (r=0.66, p=0.001).

Conclusions: The small standard deviations and normal distributions on all measures suggest an homogenous sample. There were significant associations found between anxiety, expectation of adverse outcome if an accident occurs for child, and parentally perceived quality of life in infants at randomisation in an RCT of treating cows milk allergy in young infants.
An examination of Quality of Life and General Anxiety Disorder in Parents, Children and Teens in Russia.

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\textbf{Rationale:} Research with Food Allergy Quality of Life (FAQQLQ) questionnaires has raised awareness of patient issues and has impacted provision of resources and policy. No auto-injectors are registered in Russia, which may result in anxiety. We examined 1) the performance of the FAQQLQ and 2) associations between FAQQLQ in children/teens and anxiety in parents.

\textbf{Methods:} FAQQLQ (parent proxy-report, child/teen self-report) and Food Allergy Independent measures (FAIM) were translated and completed by patients (8-18 years) and/or their parents (0-12 years). Parents completed the General Anxiety Disorder (GAD) measure. Data were collected in The Research and Clinical Institute for Pediatrics Moscow. Analysis included Cronbach’s alpha, analysis of co-variance (ANCOVA), and linear regression (LR).

\textbf{Results:} N=142 completed FAQQLQ and FAIM and N=89 parents (93% mothers) completed GAD. All FAQQLQ had alpha > 0.94, and discriminated between number of allergies, number of foods avoided, FAIM and GAD scores ($\eta^2$ 0.40 p<0.001). Relationship strength between GAD and FAQQLQ increased according to age (p =0.004); with< 2 years (r=0.4), 6 to 12 years (r=0.5) and >13 years (r=0.7). Eighteen percent had GAD score >10 indicating moderate to severe anxiety. In LR, GAD score predicted FAQQLQ PF score (t=2.7, p=0.01), controlling for age, sex, number of allergies, reaction severity and recency.

\textbf{Conclusions:} The FAQQLQ questionnaires are valid and reliable for use in Russia. The findings will contribute to the development of online manual of normed scores for FAQQLQ. The significant association found between general anxiety in parents and quality of life in children and teens has practice, screening and resource implications.
Sugar sweetened food consumption and the association with weight status in Irish children.
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Objective:
To explore the situation between dietary sugar intake and overweight and obesity among children aged 8-11 in the Republic of Ireland.

Design:
A secondary cross-sectional analysis of data from the Cork Children’s lifestyle Study (CCLaS) from April 2012 to June 2013. A three-day food diary was completed by participating children aided by their parents to provide estimates of nutrient intake. High sugar consumers were defined as consuming >87.12g/day when including beverages, and >58.72g/day when beverages were not included. The exposure (overweight/obesity) was defined as a Body Mass Index (BMI) equal to or over the 95th percentile for the same age and sex.

Setting:
27 Primary schools across Cork City and County (Mitchelstown)

Subjects:
Fourth class pupils aged 8-11 years. (n=1075)

Results:
Sugar consumption including beverages was associated with increased BMI in children aged 8-11 years. (Crude B= .006; 95% CI= .002 .010; P=.006) This effect was independent of Age, Sex, Frequency of takeaways, Parents’ Education, Family type, Parent reported TV viewing, Child reported TV viewing and moderate to vigorous physical activity. (Adjusted B=.006; 95% CI=.001 .010; P= 0.012). Non-Milk Extrinsic Sugars were also independently significant in increasing BMI (Adjusted B=.007; 95% CI=.001 .013; P=.022). Sugar excluding beverages was not significantly associated with Body Mass Index. Under reporters were not included in the study.

Conclusion:
Overall daily sugar consumption including beverages and Non-milk extrinsic Sugars were independently associated with a lower Body Mass Index among children aged 8-11 in the Republic of Ireland.
Antibody associated allergens in asthmatic patients
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Background Asthma is a common chronic inflammatory disease with a substantial disease burden on patients. Worldwide the incidence of asthma is increasing; Ireland has the 4th highest prevalence in the world. Increasing evidence suggests a key role for dysregulation of the immune system response to environmental and microbial components in asthmatic airway inflammation. Previously, we have identified fungi and large pollen structures in asthmatic patient lung washes. However, it is currently unclear whether microbes, pollens etc., are triggering allergic immune responses or merely bystander bodies.

Study approved by CREC and patient participation was voluntary. Patients attended Dr. Des Murphy, Cork University Hospital. Sample type: Bronchiolar lavage (n=8):


Results Defined immunoglobulin profiles from BALs from asthmatic patients. We will discuss the success of using a protein G based antibody-antigen capture as an immune biome profiling technique in conjunction with MinION sequence analysis. We will present antibody associated biome data present in BALs with some preliminary correlations with clinical characteristics already collected.

Conclusion Importantly, our data when completed will enable us to determine microbial and allergic insult at the lung mucosa asthmatic patients. It is anticipated that our findings may provide patients with improved understanding of their disease, inform the use of individual therapeutic regimes and further optimise lifestyles to enhance quality of life.
Continuous Real-time Monitoring of Biological Airborne Particles on a Hospital Ward and the Effect of Plasma Air Disinfection
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Conventional sampling methods for airborne organisms in hospitals are limited in sample time intervals (minutes to hours) and conventional culture requirements, restricting organism detection and only allowing retrospective analysis (days). This limits their usefulness in analysing air quality and risks of airborne transmission of infection. They provide limited data for standard setting and assessing the effect of interventions designed to increase air quality and decrease airborne infection risks. Direct continuous bioaerosol sampling is an established technology used to characterise ambient external air. Portable instruments such as the Wideband Integrated Bioaerosol Sensor (WIBS) combine laser particle size and shape detection with signals of biological origin (fluorescence from amino acids and NAD(P)H) characteristic of viable bioaerosols. This campaign used WIBS to characterise airborne biological particles in a 4-bedded hospital bay over four weeks spanning a control period followed by a two-week intervention with plasma air disinfection. Conventional impaction plates, settle plates and surface swabs were taken in parallel. No significant difference was detected between conventional culture counts before and during intervention. Continuous monitoring found regular diurnal fluorescent particle peaks, most of which coincided with nebuliser therapy and/or ward traffic. Both filtered WIBS data (excluding signatures of nebulised drug particles) and raw WIBS data showed a significant reduction in airborne fluorescent particles 0.8-5 μm in diameter (P<0.05), during operation of the plasma units. The clinical significance of this requires further study. WIBS continuous real-time monitoring of the hospital environment provided information on air quality which was not revealed by conventional culture-based sampling.
What do key stakeholders consider to be important in a model of dementia palliative care?

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Background: The Model for Dementia Palliative Care Project aims to develop a service delivery model for the HSE for community-based dementia palliative care. A number of dementia palliative care services exist internationally, however not much is known about what the people who provide these services want included in these services and what they would deem to be the most important aspects in the provision of dementia palliative care. The aim of this study was to identify what key stakeholders consider to be important in a model of dementia palliative care.

Methods: A survey was developed, piloted (n=5), and revised. It was distributed electronically within five healthcare jurisdictions, i.e. Republic of Ireland, Northern Ireland, England, Scotland, and Wales. The target population included academics, healthcare professionals, and policy-makers with an interest in dementia and/or palliative care.

Results: In total, 121 complete responses were received. 74% of respondents were male. The results showed that the three most essential general aspects of a good model of palliative care for dementia were ‘Care for People at all Stages of Illness’ (77% considered ‘essential’), ‘Information Continuity’ (75%) and ‘Defined Pathways for Specialist Service Input’ (58%). People felt that good communication and between palliative care and dementia care teams was essential. A key worker is needed to facilitated this communication, and to support families e.g. around care transitions.

Conclusion: Consistent aspects of a ‘good’ model were identified. This research complements other studies ongoing within The Project, to develop a useable and acceptable model for dementia palliative care.
Sex differences in the actions of corticosterone on hippocampal neural progenitor cells

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Stress, particularly during early life, is a major risk factor for the development of major depression. Depression is twice as prevalent in women compared to men, which suggests that biological sex is also a risk factor. In animal models, stress during early life can induce depressive-like behaviours and negatively impact neurogenesis in the hippocampus, a brain area important in the regulation of the stress response. Evidence suggests that sex may modulate the impact of stress on adult hippocampal neurogenesis, but it is unknown whether these differences are cell-intrinsic or depend on the actions of sex hormones. We aimed to determine whether sex differences in response to the stress hormone corticosterone are apparent in the absence of sex hormones prior to the onset of puberty. To this end, we evaluated the impact of corticosterone on proliferation and differentiation of hippocampal neural progenitor cells (NPCs) derived from pre-pubertal males and female Sprague-Dawley rats in vitro. NPCs were exposed to corticosterone and cultured in media promoting either cell proliferation or neuronal differentiation. Corticosterone significantly decreased both cell proliferation and neuronal differentiation compared to control. However, the effect of corticosterone was more pronounced in cells derived from males than females. The results suggest a sexually dimorphic response of hippocampal NPCs to corticosterone in the absence of circulating sex hormones in vitro. It will be important to determine how these results relate to behavioural responses to stress in males and females and may contribute to risk for developing stress-related psychiatric disorders.
PARROT Ireland: Placental growth factor in Assessment of women with suspected pre-eclampsia to Reduce maternal morbidity: a Stepped Wedge Cluster Randomised Control Trial

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Pre-eclampsia complicates 2-8% of pregnancies and is associated with significant maternal and neonatal morbidity and mortality. Placental Growth Factor (PIGF) is a protein involved in placental angiogenesis and in women with pre-eclampsia levels of PIGF can be abnormally low. Previous studies suggest that PIGF testing may be an important and innovative adjunct to the management of women with suspected pre-term pre-eclampsia. NICE has recently highlighted the need for further research on PIGF based testing in routine clinical care in women presenting with suspected pre-eclampsia.

Our primary aim is to establish the effectiveness of plasma PIGF measurement in reducing maternal morbidity, without increasing neonatal morbidity, in women presenting with suspected pre-eclampsia prior to 37 weeks' gestation. The long term aim is to determine if knowledge of PIGF measurement enables appropriate stratification of antenatal management of women presenting with suspected pre-eclampsia.

PARROT Ireland is a prospective, multi-centre, stepped wedge cluster randomised controlled trial of women presenting with suspected pre-eclampsia from 20 to 36+6 weeks’ gestation inclusive. It is being conducted in the seven largest maternity hospitals in Ireland. It commenced recruitment in June 2017 and will continue until April 2019 with a recruitment target of 4000 women.

The study has two co-primary outcomes; maternal morbidity and early neonatal morbidity, as both are equally important. Each will be assessed by use of composite scores. Using trial evidence, a health economic evaluation will assess the intervention's economic impacts.

If this trial shows PIGF testing to be beneficial, it will influence healthcare guidelines at both a national and international level.
Title The Impact Of An Early Mobilisation Initiative Evidence From An Acute Care Setting
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Unnecessary bed rest results in a loss of mobility and an increased length of hospital stay. Despite, mobilising regularly being acknowledged as an important preventative measure for deconditioning, inpatient functional decline continues to pose a significant challenge in hospital settings. Hospital-based mobility initiatives offer the potential to address issues of functional decline, improve patient outcomes and hospital length of stay. The aim of this research is to examine the impact of an early mobilisation initiative called “End PJ Paralysis”.

The research design comprises of three elements: (i) an examination of a period that promoted mobility to all patients on one acute unit (ii) an analysis of the reported number of falls during the study period and (iii) an exploration of perceptions and attitudes of nurses, nurse managers, and patients involved with the initiative. Our study demonstrates that following a 10-week promotion of the initiative from April 17th-June 26th 2018 in an acute care setting in South of Ireland, an increase of 15% of patients were mobilising and a decrease in the number of reported falls. In addition, staff participation was found to increase and self-reported patient satisfaction improved. Factors identified as influencing the impact of the initiative included patient and staff behaviour, nurse management leadership, and effective communication.

The study provides evidence to suggest that early mobilisation initiatives can prevent deconditioning and improve patient outcomes. Each day a patient spends in hospital should contribute towards their recovery and discharge and mobilising patients while in hospital has a profound impact on their functional status.
Assessment of a Stress-Reduction Intervention for Pregnancy-Related Pelvic Girdle Pain: a Pilot Study.
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Background: Pregnancy-related pelvic girdle pain (PPGP) is a condition which refers to pain in the lumbosacral, sacroiliac and/or symphysis pubis joints. It occurs in approximately 20% of pregnancies and can persist post-partum. While the aetiology of PPGP is poorly understood, stress during pregnancy is predictive for persistent post-partum pelvic pain. Evidence for the efficacy of current treatments has been limiting and conflicting, with treatment often unsuccessful.

Aim: To assess the effectiveness of a stress-reducing intervention on pain and stress symptoms associated with PPGP.

Methods: 15 women with PPGP were recruited from Cork University Maternity Hospital (CUMH). Participants received two, one-hour sessions, where they received information on the stress response, alongside gentle exercises and confidence-building counselling. Before and after each session, salivary cortisol samples were obtained and later quantified with ELISA. Before each session, participants completed the Roland Morris Disability Questionnaire, Cohen Perceived Stress Scale, Stait Trait Anxiety Questionnaire, and the average number of steps possible in 60 seconds was recorded.

Results: 15 participants completed the first intervention session, of which 7 completed both intervention sessions. The questionnaire results and steps per minute indicated the intervention led to a significant improvement in anxiety, pain, stress and mobility. A significant decrease in salivary cortisol was measured after the two sessions, compared to the initial baseline measurement.

Conclusions: This study illustrates the potential benefit of a stress-reducing intervention for women experiencing PPGP, through reducing anxiety, pain and stress while concurrently improving mobility. This data will support a feasibility trial study, followed by a multi-centre clinical trial.
Serial cell free DNA (cfDNA) monitoring in melanoma patients correlates with tumour burden and therapeutic response as assessed by CT scan

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Background:

The assessment of tumour burden and therapeutic response in melanoma patients is currently undertaken by way of serial lactate dehydrogenase (LDH) level measurements and radiological imaging by CT or PET scan. While both assessment strategies are frequently successful at monitoring disease burden and treatment response, the problems of pseudoprogression and pseudoresponse increasingly render these methods crude measures of underlying disease status in affected patients. In these contexts, complementary strategies are needed to assess alterations at the molecular level, and to detect the event of genomic evolution as it relates to therapeutic resistance. Cell free DNA (cfDNA) has emerged as an easily accessible biomarker to assess tumour burden and therapeutic response in several malignancies including melanoma.

Patients and Methods:

We extracted and quantified plasma derived cfDNA from nine patients with melanoma. Four patients had stage I disease, and cfDNA was obtained prior to surgical excision of their moles. The other five patients had stage IV disease, and serial assessment of cfDNA levels was undertaken in the course of treatment with pembrolizumab.

Results:

Patients with stage IV disease had significantly higher plasma cfDNA levels than patients with stage I melanoma (6500 ± 1000 versus 3125 ± 625. P< 0.05). Positive correlation was found between malignant tumour burden and cfDNA levels in stage IV melanoma patients receiving immunotherapy (N=6) (r= 0.8241, P= 0.0437).

Conclusion:

We postulate that a quantitative measure of cfDNA may complement current methods of assessing tumour burden and therapeutic response in stage IV melanoma patients undergoing immunotherapy.
Neuroanatomy of the spinal pathways: Evaluation of an interactive multimedia e-learning resource
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Medical students and practitioners interlink the difficulty in managing neurology patients with their impaired understanding of neuroanatomical concepts and associated clinical correlates. Due to the limitation of traditional pedagogies, intelligently designed e-resources could be instrumental in helping students learn neuroanatomy. This study describes the design and evaluation of a novel, interactive, neuroanatomy learning e-resource developed at University College Cork (UCC), whose instructional design has been informed by students’ and educators’ opinions acquired in our earlier work (Javaid et al., 2018b).

Medical, clinical-therapies and neuroscience-students voluntary participated in the study. They were randomized into experimental and control groups and were provided online access for 2 weeks, to the novel online tool and the previously identified best-ranked resource, respectively. Participants’ knowledge of neuroanatomy of spinal pathways was assessed using neuroanatomy quizzes, before and after exposure to the online tools. Participants’ opinion regarding the usefulness of various components of the tools was gauged using a Likert scale-questionnaire.

Participants in both control and experimental groups showed a significant increase in their knowledge of neuroanatomy following exposure to the online tools, however, the Likert scale ratings revealed a significantly higher median rank-scores for the experimental tool (v. the control tool) for learning the clinical neurological correlates. Moreover, stronger and significant correlations between the students’ perceptual opinion and their quiz 2 scores imply that students intuitively favored the instructional design of the UCC e-tool. The e-resource shows promising results in the context of breaking the perceived nexus between the neuroanatomy-phobia and the neurophobia.
In-Hospital Adverse Drug Reactions (ADRs) in Hospitalised Older Adults - A Systematic Review

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Background: Recent studies indicate 1 in 4 older people experience an ADR in hospital. This systematic review aims to evaluate the incidence, commonly involved drug classes, severity, and consequences of in-hospital ADRs in hospitalised older adults.

Methods: Conducted following PRISMA-methodology [PROSPERO-registration-CRD42018079095]

Search terms: aged, ADRs, hospitalized, multi-morbid, polypharmacy, hospital-acquired.

Databases: PubMed, Embase and Ebsco-CINAHL, Cochrane-Library, library hosted academic sources, Google® scholar, ‘grey’ literature, hand search of bibliography lists from relevant editorials and systematic reviews.

All languages and dates up to and including the date of the final search [15/01/2018], reporting ADRs either as a primary or secondary outcome in patients aged ≥ 65 years hospitalised at time of ADR occurrence were included. Two researchers screened all papers for inclusion, risk of bias and data extraction.

Results: 1930 abstracts (228 full-texts) were screened, 23 papers (22 studies, n = 21,306) were included; 11 studies reported ADRs in all ages, 11 reported ADRs in ≥ 65 years; 74% [15,769] ≥ 65 years.

ADRs occurred in 19.77% median [IQR 10.44 – 25.35%]; 70% were preventable (672 ADRs, 5 studies); 72% of ADRs were moderate to life threatening severity (n = 1720, 14 studies). 5 papers reported post-ADR outcomes. Frequency of culprit drug-groups [1528 drugs 15 papers]; 22% [339] diuretics, 14% [209] antithrombotics, 12% [184] anti-infectives, 11% [169] opioids, 6% [87] psycholeptics.

Conclusion: One-in-five ≥ 65 years experience a clinically significant ADR during hospitalisation, one-third being severe, 11 commonly prescribed drugs account for 80% of ADRs. Clinical outcomes associated with ADRs are poorly described in the literature.
Characterising post-operative pain following peripheral nerve block regression in patients who have undergone open reduction and internal fixation of ankle fractures.

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Introduction: Peripheral nerve blocks (PNBs) are a common and effective analgesic modality in orthopaedic surgery. Following ankle fracture surgery, rebound pain has been reported on block regression. Defined as a quantifiable increase in acute pain after PNB resolution(1), rebound pain is poorly understood.

Methods: We conducted a prospective, observational cohort study of patients undergoing ankle fracture open reduction and internal fixation (ORIF). Prior to surgery patients received ultrasound guided popliteal and saphenous blocks. Multimodal oral analgesics were prescribed. Patients were assessed at 6, 12, 18 and 24 hours after block administration, for the presence of the PNB and pain score on the numerical rating scale. Analgesics administered throughout these time periods were recorded.

Results: Eleven consecutive patients were included. PNB offset was seen in 2 patients at 12 hours and in a further 7 patients at 18 hours with reported median pain scores of 8[7-9] and 5[0-10], respectively. Increases in pain resulted in reciprocal increased opioid rescue analgesia requests. 3 patients remained pain-free throughout the study period.

Discussion: Rebound pain is a real and clinically important problem upon resolution of PNBs in patients following ankle fracture ORIF. The findings presented are consistent with other reports of rebound pain. This data will inform clinical practice development.

An Assessment of Buccal Oestrogen Receptor Expression in Patients Diagnosed with Oestrogen Receptor Positive Breast Cancer as a Potential Non-Invasive Marker of Response to Tamoxifen Therapy

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Background: Adjuvant anti-oestrogen therapy reduces mortality in Oestrogen Receptor (ER) positive breast cancer by up to 50%. However, therapeutic efficacy is heterogeneous which can negatively impact on individual outcomes. Currently, it is not possible to assess response to hormonal therapy non-invasively. Previous studies have postulated that the buccal mucosa expresses both ERα and ERβ. This pilot study sought to verify the expression of these receptors and assess their utility in breast cancer care.

Methods: Buccal mucosal swabs were obtained from a sample of ER+ breast cancer patients attending the Regional Breast Cancer Centre in Cork University Hospital. Patients receiving adjuvant tamoxifen, aromatase inhibitor and no hormone therapy were equally represented. Following standard cytological procedures for sampling and cell extraction, immunohistochemistry was performed to quantify the ERα and ERβ expression from each sample. These results were to be correlated with the magnitude of ER expression in the corresponding breast tissue.

Results: 9 patients were analysed in total. Mean age was 62 for tamoxifen subjects (n=3), 59 for aromatase inhibitor subjects (n=3) and 57 for non-hormonally manipulated subjects (n=3). 9/9 breast tissue samples were strongly ER+, 8/9 were PR+ and only 1/9 was HER2+. Tumour size, grade and nodal status were variable. Despite adequate cell yields, ER expression was not identified on buccal mucosal samples from any cohort.

Conclusion: It is unlikely that buccal mucosal ER expression is a non-invasive marker for assessing response to tamoxifen therapy. Further research will be required to identify, evaluate and enable the utilisation of alternative surrogates.
Title: Expert Delphi (e-Delphi) Educational Needs Assessment for Advance Care Planning in COPD.

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Introduction:
Advance Care planning (ACP) is desirable in Chronic Obstructive Pulmonary Disease (COPD). Studies have shown that ACP has a significant impact on place of death and patient satisfaction with care. To facilitate ACP in COPD, healthcare professionals (HCPs) need knowledge, confidence and competence. The CONCORDAT (inCOrporatiNg ACP intO Routine COPD mAnagemenT) group aims to design, deliver and evaluate an evidence based educational guidance document and workshops for HCPs. To ensure these address the educational needs of HCPs, an educational needs assessment (ENA) was required. A modified e-Delphi method was proposed.

Aim:
To use expert consensus to inform the focus of the CONCORDAT guidance document and educational workshop.

Methods:
The modified e-Delphi method had 2 rounds. An expert panel prepared 40 statements divided into 3 themes informed by a scoping of the literature. HCPs were invited by email to participate in rating statement on a 5 point Likert scale. Consensus on each statement was established by 80% participant agreement.

Results:
Thirty eight individuals were surveyed. Response rate (Round 1) was 45% .Round 1: 32 out of 40 statements reached consensus. Round 2: 8 statements were re-rated with 2 additional statements formed from Round 1 feedback. Five of these statements reached consensus. The final number of accepted statement was 37.

Conclusion:
The e-Delphi ENA affirmed the findings from the scoping review and provided information from HCPs regarding their priority learning needs for ACP in COPD. The 37 accepted statements will inform the guidance document and educational workshops.
A Multidisciplinary Approach to Clinical Supervision: Charter of Best Practice in Medicine, Dentistry, and Pharmacy.

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Introduction:

Clinical Supervision is integral to training of healthcare professionals. The Irish Medical Council guidelines outline “A Doctors’ Duty to Educate”. Other healthcare professionals’ roles in education are not clearly defined by their respective governing bodies. The aim of this project is to improve student experience of clinical supervision, thus ensuring competent, confident, healthcare professionals upon graduation. The objective of this project was to gain knowledge of the student experience in a number of different healthcare disciplines.

Methods:

Representatives from University College Cork Schools of Medicine, Dentistry and Pharmacy convened to share multidisciplinary student perspectives. Each school then presented the student experience of clinical supervision outlining both positive and negative aspects and acknowledging inherent challenges faced. Key points were discussed and common themes were identified. Using the Model United Nations Resolutions, a Charter of Best Practice was produced to provide a framework for an ideal form of clinical supervision.

Results:

All schools recognised the importance of Clinical Placement to gain exposure, experience, and develop skills. The Charter focuses on three key areas: the responsibility of the School, the responsibility of the Supervisor, and the responsibility of the Student.

Discussion:

The Charter wishes to open dialogue around the area of clinical supervision and inform strategies for best practice. It is intended that universities will engage with and implement this Charter of Best Practice in order to achieve an ideal model of clinical supervision. This Charter intends to further empower the student community to deliver high quality healthcare in the future.
Analysis Of 100 Consecutive Cases In The Rapid Access Seizure Clinic At Cork University Hospital
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Introduction: The Rapid Access Seizure Clinic (RASC) was set up in Cork University Hospital (CUH) in 2012, as part of the National Epilepsy Care Programme in Ireland. The purpose of the clinic is to provide a clinical care pathway for appropriate evaluation of patients presenting with seizures and seizure-mimics. Since the RASC was established in CUH, more than 800 patients have attended. Misdiagnosis of epilepsy is common (up to 25%) potentially leading to inappropriate prescribing of anti-epileptic drugs (AEDs) and restrictions on driving and employment. This study evaluates the role of the RASC in the management of patients presenting with seizures.

Aims: To assess the value of the RASC, particularly by determining the rate of misdiagnosis of epilepsy.

Methods: A retrospective chart review was conducted on 100 consecutive patients in the RASC. The data was analysed in SPSS v 23.

Results: Ninety-eight patients (2 outliers) were included in the analysis (M=43, F=54 with a mean age of 38.44 years). The mean duration of waiting time from referral to clinic appointment was 4 weeks. Evaluation in the RASC resulted in a change of diagnosis in 19.39% of patients, discontinuation of AED therapy in 26.32% and return to driving in 26.32%. The working diagnosis of epileptic seizure was upheld in 60.2% of referred patients.

Conclusions: The RASC pathway provides a valuable clinical service, mainly by significantly altering the working diagnosis of epileptic seizures in one-fifth of referred patients.
Neurovascular Coupling Remains Intact During Incremental Ascent to High Altitude (4240m) in Acclimatized Healthy Volunteers.

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Neurovascular coupling (NVC) is the temporal link between neuronal metabolic activity and regional cerebral blood flow. Exposure to high altitude (HA) imposes several stressors, including hypoxia and hypocapnia, which modulate vessel tone. Whether these contrasting stressors affect NVC during incremental ascent to HA is unclear. The aim of this study was to assess whether incremental ascent to HA influences the NVC response. Given that cerebral blood flow (CBF) is sensitive to changes in arterial blood gases, in particular PaCO\textsubscript{2}, we hypothesized that the vasoconstrictive effect of hypocapnia during ascent would decrease the NVC response. 10 healthy study participants (21.7±1.3yrs, 23.57±2.00kg/m\textsuperscript{2}, mean±SD) were recruited as part of a research expedition to HA. Resting posterior cerebral artery velocity (PCAv), arterial blood gases (PaO\textsubscript{2}, SaO\textsubscript{2}, PaCO\textsubscript{2}, bicarbonate [HCO\textsubscript{3}\textsuperscript{-}], base excess and arterial blood pH) and the NVC response of the PCA were measured at four pre-determined locations: Calgary/Kathmandu (1045/1400m, control), Namche (3440m), Deboche (3820m) and Pheriche (4240m). NVC was determined in response to visual stimulation (VS; Strobe light; 6Hz; 30sec on/off x 3 trials). PaO\textsubscript{2}, SaO\textsubscript{2} and PaCO\textsubscript{2} were each significantly decreased at 3440m, 3820m and 4240m. No significant differences were found for pH at HA (P>0.05) due to significant reductions in [HCO\textsubscript{3}\textsuperscript{-}] (P<0.043). As expected, incremental ascent to HA induced a state of hypoxic hypocapnia, whereas arterial pH was maintained normal due to renal compensation. No significant differences were found for NVC response magnitude between locations (P>0.05). We conclude that NVC remains remarkably intact during incremental ascent to HA in acclimatized individuals.
Physician knowledge and perception of technology use and screen time in children

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Background:
Technology use in the home by children and their families has become common place. Although there are potential benefits from screen use in children, there are risks that must be considered regarding developmental, psychological, and physical health. General practice physicians and paediatricians can play an important part in educating parents and caregivers on the impact of screen use. They can also advise parents on the correct duration of screen use, setting limits, effects on health and well-being, and appropriate content. Currently there are no national Irish guidelines regarding media use in children, and there is a lack of knowledge regarding Irish doctors’ knowledge and attitudes towards screen use by children.

Methods:
This study was a quantitative, cross-sectional study, where questionnaires were distributed among General Practitioners and Paediatric Consultant and Specialists Registrars in the Munster region. The principal aim was to evaluate physicians’ level of knowledge based on recommendations for media and technology use in children. The secondary aim was to assess physicians’ personal experience in initiating these discussions with parents and how they perceive their role as an educator on screen use in their practice.

Results & Conclusion:
It is expected that the present study will provide a snapshot of Irish medical practitioners’ knowledge and attitudes regarding appropriate screen use in children, as well as whether (and how) screen use should be discussed with parents during clinic visits. These results may contribute to the development of formal guidelines to educate healthcare providers regarding health use of technology by children.
The association between sarcopenia and overall survival and cancer recurrence in breast cancer: A Systematic review and meta-analysis

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Background:

Sarcopenia has been associated with chemotoxicity, tumour recurrence and mortality in many forms of cancer. The prevalence of sarcopenia in breast cancer, as well as its effects on breast cancer outcomes, however, is not well-studied. Thus, we aimed to establish the prevalence of sarcopenia in breast cancer patients and investigate its effect on overall survival and disease-free survival in female breast cancer patients.

Methods:

We conducted an independent review of five databases - PubMed, Medline, Embase, Cinahl and Cochrane from January 1998 to July 2018 using relevant filters and keywords related to breast cancer, sarcopenia and prognosis. A random-effects meta-analysis was generated to estimate the pooled hazard ratios for overall survival, 95% confidence intervals and P-values. Quality assessment was performed using validated systems.

Results:

Our initial search yielded 446 results. After screening for eligibility, 5 articles were included, of which, four used CT scans and one used DEXA scan to assess sarcopenia. Across the 5 studies (n=4037), the prevalence of sarcopenia ranged from 15.9% to 66.9% in the target population. Sarcopenia was found to be associated with worse overall survival (HR=1.73, 95% CI=1.17-2.56, p=0.006, I²=64%). The association between sarcopenia and recurrence was inconclusive. Heterogeneity was observed across the 5 studies.

Conclusion:

This study illustrates a relatively high prevalence of sarcopenia in breast cancer patients. In addition, sarcopenia was a prognostic factor for overall survival in these patients. Future prospective studies are required to carry out a more thorough evaluation of the association between sarcopenia and breast cancer outcomes.
Time to Find the Evidence: Does Fostering Connections, an evidence-informed intervention, improve outcomes for children in Foster Care?

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This poster reports the findings of an early-stage process evaluation of a trauma-informed foster care training intervention. The intervention seeks to develop the capacities of foster carers to relate with and respond to a child in their care in trauma-informed ways and thus, to promote placement stability.

Using a mixed-method research design was used. Firstly, a pretest-posttest non-randomised quasi-experimental study design with a control group was completed. Quantitative data was collected over three-time points to measure the degree of change occurring because of the intervention on pre-defined outcomes. Both intervention and control groups were pre-tested (Time 1, before), post-tested (Time 2, on completion) and post-tested (Time 3, at 16 weeks post intervention) using validated measures. Secondly, qualitative data was collected post intervention through focus groups (n=21).

Both quantitative and qualitative data strongly suggest that this intervention can significantly improve the capacities of foster carers to respond to children in trauma-informed ways. Foster carers that received the intervention reported significantly higher scores than the control group post intervention (Time 2) and at 16 weeks follow-up (Time 3) in KBS scales of parenting, tolerance of misbehaviour and efficacy. Qualitative data (n= 27) illuminated how foster carers applied the principles and strategies of trauma-informed care in their care of the children.

This study provides the first empirical evidence to support that Fostering Connections is a successful foster carer training intervention and could play a significant role in supporting foster carers in caring for children who have experienced trauma.
Title Time to Find the Evidence: Does Fostering Connections, an evidence-informed intervention, improve outcomes for children in who have experienced trauma who are in Foster Care?

MG Lotty

School of Applied Social Studies, UCC, Cork, Ireland  
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This article seeks to report the findings of an early-stage process evaluation of a trauma-informed foster care training intervention. The intervention seeks to develop the capacities of foster carers to relate with and respond to a child in their care in trauma informed ways and thus, to promote placement stability.

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This study provides the first empirical evidence to support that Fostering Connections is a successful foster carer training intervention and could play a significant role in supporting foster carers in caring for children who have experienced trauma.
**β1-adrenoceptor dependent augmentation of left ventricular contractility develops after three days of chronic intermittent hypoxia exposure**

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Modest durations of chronic intermittent Hypoxia (CIH) exposure increases cardiac output, which may contribute to the development of CIH-induced hypertension. We sought to determine if increases in cardiac work manifest before CIH-induced hypertensive develops.

Male Wistar rats were exposed to repetitive hypoxic cycles (FiO₂=0.05 nadir; 90 seconds) and normoxia (FiO₂=0.21; 210 seconds) for 8hr.day⁻¹ for three days (n=6). Sham animals (n=7) were exposed to room air. Cardiovascular assessments were performed under urethane anesthesia (1.5g/kg i.p.). Data are presented as mean±SD (sham vs CIH) and were analysed using unpaired Student’s t-tests.

Systolic blood pressure (p=0.439), heart rate (p=0.149), plasma adrenaline (p=0.294) and plasma noradrenaline (p=0.155) concentrations were unaffected by three days of CIH exposure compared with sham controls. Basal left ventricular (LV) contractility (dP/dtMAX) was significantly increased in CIH-exposed animals compared with sham animals (12320±2725 vs 15300±2002mmHg/s; p=0.025). β1-adrenoceptor inhibition with atenolol (5mg/kg; i.v.) reduced LV dP/dtMAX in CIH animals to levels equivalent with sham animals (-4747±2080 vs -7604±1298mmHg/s; p=0.014). Sympathetic ganglion blockade with hexamethonium (25mg/kg; i.v.) produced equivalent responses in CIH and sham animals for measured cardiovascular parameters (p>0.05). Gene expression of the β1-adrenoceptor signaling pathway was unchanged in CIH-exposed LV cardiomyocytes compared to sham.

This study suggests that global sympathetic hyperactivity has not developed in this three-day model of CIH, as evidenced by equivalent catecholamine concentrations, blood pressure and heart rate in sham animals. Nevertheless, three days of CIH exposure is sufficient to increase cardiac work. We hypothesise that the heart drives the development of CIH-induced hypertension through elevated β1-adrenoceptor tone.
The Development of Key Performance Indicators using the Delphi Technique for a Regional Lymphoedema Service in Ireland

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Background:  
A Classic Delphi Technique was used to develop Key Performance Indicators (KPIs), relevant to the HSE Mid-Western Lymphoedema Service at University Hospital Limerick. This specialist Lymphoedema Service provides care to patients from the symptomatic breast cancer services and other services.

Aim:  
To develop relevant KPIs as an essential tool for an LE service and as a means of quantitatively measuring quality for service improvement and future service delivery. The KPIs centred around equity of access to the service; efficiency, patient education and evidence of effectiveness of service delivery.

Methods:  
A classic two round Delphi Technique was used to achieve consensus among lymphoedema specialists and service referees working nationally and internationally. This included feedback from an Expert Panel of national and international clinical leads. The KPIs consultation process used a Balanced Scorecard™ as prescribed by Kaplan and Norton. An 80% consensus of ‘important’ or ‘very important’ was used as the acceptable cut off and deciding factor for study iterations. Every effort was made to ensure the KPIs are easy to understand, objective, reliable, quantifiable and relevant to patient outcomes.

Results:  
The Delphi Panel response rate was 93.33%. Following Expert Panel feedback, more than 80% (96.3%-100%) of Delphi Panellists agreed on a Suite of 7 proposed KPIs allowing the KPIs to be accepted.

Conclusion:  
This is the first Irish study to identify KPIs for lymphoedema services. The Suite of 7 KPIs will play an important part for setting standards and will prove invaluable for the quality of care in Lymphoedema Services.
The influence of object distinctiveness on reach-to-grasp signals at the human anterior intraparietal sulcus.

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The implementation of movement kinematics is supposed to be associated with dorsal parietal structures, which should not be sensitive to object features that are not relevant for the implementation and control of movement. Particularly, the anterior intraparietal sulcus (aIPS) has been associated with the adjustment of reach-to-grasp movements to objects, of different sizes and orientations, independent of non-spatial features (i.e. colour or surface patterns). However, neurophysiological data from monkeys showed that neurons in the dorsal parietal cortex do encode an object’s colour if information has relevance for a task. Since everyday objects provide a lot of task-relevant information, we examined whether aIPS shows different signals when grasping recognisable everyday objects in comparison to grasping simple cuboids.

27 participants grasped different sized objects in an fMRI experiment. Objects were either distinguishable everyday objects or monochrome cuboids (similar spatial dimensions). In a control experiment the same participants saw the same objects but did not grasp them.

The contrast between grasping well-known objects and simple cuboids revealed significant signal differences at the aIPS, the vPMC, and the lateral occipito-temporal cortex. Regions of interest analyses of the visual presentation data at these locations showed that differences at the occipital-temporal cortex could also be found without movement execution. In contrast, no signal differences between object categories were found at the vPMC and aIPS without movements.

The aIPS not only receives and processes spatial parameters necessary for action implementation, but also considers non-spatial features that primarily might have been associated with a specific action parameters.
ORAL HEALTH LITERACY, ATTITUDES AND BEHAVIOURS AMONGST THIRD LEVEL STUDENTS IN CORK
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BACKGROUND:
Health literacy is considered a social determinant of population health, but also relates to making informed health decisions. Approximately 40% of the general population in Ireland has inadequate or problematic health literacy. However, little information is available of oral health literacy (OHL) among young adults. It is crucial to inform targeted interventions on oral health and care.

OBJECTIVES:
This study i). Estimates the prevalence of OHL amongst the third-level students in Cork; ii). Identifies determinants of OHL by exploring potential correlates of OHL; iii). Examines students’ oral health behaviours.

METHODS:
All students in UCC were sent out a previously validated questionnaire through the online Lime Survey in April 2018 (n = 1487). Both descriptive and inferential statistics (Chi-squared/correlation) were undertaken.

MAIN RESULTS:
Adequate OHL prevalence was 23%. OHL was significantly correlated with age (r = 0.10), school of study (r = -0.13), dental visits (r = -0.08) and dental-communications (r = -0.41). Male gender, younger age-group, and those in non-medical schools had significantly higher inadequate OHL. However, 84.2% students brushed at least twice daily and 69.2% used other oral hygiene aids. Overall, female students reported better oral health behaviours.

CONCLUSION
Approximately, only one-in-four third-level students in Cork have adequate OHL, which is worrying. Significantly higher proportions of students with inadequate OHL visited dentists. Targeted interventions in the form of tailored health promotional oral health campaigns and awareness in higher educational institutions are warranted to reduce the burden on oral health care and health.
Prenatal maternal stress and childhood obesity: A systematic review
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Background: Maternal prenatal stress and childhood overweight and obesity are important global public health challenges. Up to 30% of women experience some form of stress during pregnancy. Currently approximately 1 in 5 children worldwide are overweight or obese. Prenatal stress may impact on obesity but research to date has been inconsistent. The aim of this study was to systematically examine effects of prenatal maternal stress on childhood obesity.

Methods: This examination formed part of a larger review on the effects of maternal stress. The Cochrane Library, MEDLINE, PsycINFO, EMBASE, CINAHL, and Maternity and Infant Care were searched from inception to June 2018. Studies were required to examine stress during pregnancy and child anthropometric outcomes measured from birth to 12 years of age.

Findings: Eleven studies were identified that met inclusion criteria for prenatal stress exposure and child anthropometric outcome. Eight of these studies found significant positive associations between prenatal stress and child weight outcomes. All studies examining hormonal stress markers demonstrated associations with child weight outcomes, while examinations of perceived psychological stress demonstrated inconsistencies. Differences in conceptualisations of stress and timing of stress measurement were observed across studies.

Discussion: Stress experienced during pregnancy appears to be associated with increased risk of childhood obesity. This most likely occurs through psychophysiological pathways; however exactly how this occurs is unknown due to methodological limitations of existing studies. Future comprehensive, longitudinal research is needed to fully examine effects of prenatal stress on childhood obesity.
Are We Measuring Modifiable Risk Factors in Acute Stroke Patients?
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Stroke is a leading cause of death and disability. Control of modifiable risk factors is the most effective approach to decreasing the burden of stroke. The purpose of this study was to examine the frequency of measurement of modifiable risk factors in acute stroke patients admitted to Cork University Hospital (CUH).

A retrospective review was conducted of the records of stroke patients admitted to CUH from December 2016 to March 2017. HbA1C, fasting glucose (FG), total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglycerides (TG) measurements during admission were recorded.

Among 117 strokes admitted to CUH in this period, 98 (83.7%) were ischaemic. 68% of acute stroke patients had both a measurement of cholesterol, and a test for diabetes mellitus (DM) performed. Current stroke guidelines recommend measurement of both LDL and HDL, which was performed in only 63% of our cohort. There are two lipid profiles on available on the CUH ordering system, one of which only includes HDL and not LDL. This is an issue that needs to be evaluated. This is a re-audit to compare with findings from March 2014-2015, which showed 80% of acute strokes having tests for both cholesterol and DM, but only 34% had both LDL and HDL measured. In April 2018 a standardised investigations form was introduced, which is completed by the Stroke CNS. It is hoped that this will ensure all appropriate risk factors are assessed, and this will be audited again for the period of March 2017-2019.
Detecting Diabetes Mellitus and Pre-Diabetes in Patients with Acute Stroke
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Stroke is a leading cause of death and disability. Control of modifiable risk factors is the most effective approach to decreasing the burden of stroke. The purpose of this study was to determine the prevalence of diabetes mellitus (DM) and pre-diabetes (pre-DM) in acute stroke patients in an Irish population.

A retrospective review of the records of stroke patients admitted to Cork University Hospital was conducted from December 2016 to March 2017. HbA1c and fasting glucose measurements during admission were recorded. DM and pre-DM prevalence levels were determined using both HbA1c and fasting glucose level.

Among 98 ischaemic strokes admitted to CUH, 72 (73.5%) had a test for diabetes performed. 64 (65.3%) had a HbA1c check, while 43 (43.8%) had a measurement of fasting glucose performed. 36.7% had both tests performed. 9 (13.8%) of those who had a HbA1c checked had a level >47 mmol/L. 19 (29.7%) of those checked had a level between 42-47 mmol/L. 10 (23.3%) had a fasting glucose greater than 7 mmol/L. The rate of Impaired Fasting Glucose varied from 9.3 – 27.9% dependant on range used (ADA versus WHO ranges).

In this audit 13.8-23.3% of acute strokes had either a fasting glucose or HbA1c consistent with DM, while 9.3-29.7% had pre-DM. The rate of detection of DM and pre-DM varies with diagnostic test performed, suggesting that both HbA1c and fasting glucose should be performed in cases of acute stroke.
Title Effect of milk storage processes on physicochemical properties of breast milk

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Text

Donated breast milk from human milk banks is provided to term or pre-term infants when the mother’s own milk is not available, and milk may also be stored at home or in hospitals after expression. Such milk experiences many processes, possibly including cold storage, freezing, thawing, and pasteurization, which may influence the quality of the milk and therefore the benefits to neonates. In recent years, high pressure processing (HPP) of human milk has been proposed as a faster and convenient alternative to thermal pasteurization. The objective of this work is to evaluate the influence of these treatments on human milk from the point of view of its physicochemical properties. The milk from 27 mothers with recorded lactation time was studied. The influences of temperature, freezing and thawing, heat treatment and HPP on creaming properties, which reflects the instability of the milk, were investigated. HPP treatments were also compared with pasteurization in case of color, fat globule size, and protein properties of the samples. The results showed body temperature (37°C) facilitates the separation of fat in human milk, while there was no effect of freezing and thawing on creaming. HPP changes the shape of milk proteins and may influence its stability. These results may help to understand and improve the human milk storage method and thus the health of newborns.
Predicting Type 2 Diabetes Development Among Patients in General Practice – A Prospective Analysis Comparing Diabetes Risk Scores and Components
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Background and Objectives: Various diabetes risk assessment tools have been developed. However, no diabetes risk score has been validated or derived in an Irish population. The aim of this study was to compare the ability of nine proposed diabetes risk scores to discriminate incident type 2 diabetes cases in general practice to determine which tool more accurately identifies individuals at increased risk.

Materials and Methods: This was a prospective study involving a random sample of 1,754 men and women aged 46–73 years. Receiver operating characteristic curve and net reclassification improvement analyses were used to evaluate the ability of diabetes risk scores and components to accurately classify high-risk subjects.

Results: Risk scores incorporating biological variables demonstrated the highest area under the curve (AUC) values, with the Kahn ENHANCED score showing the greatest predictive ability (AUC=0.89). With regard to non-invasive risk scores, the Kahn BASIC score (AUC=0.74), German Diabetes Risk Score (AUC=0.73) and Leicester Practice Risk Score (AUC=0.73) displayed the largest AUCs as continuous variables and at optimal cut-offs. The positive predictive values for a two-step screening method using risk score thresholds corresponding to 80% sensitivity and a subsequent fasting glucose test ranged from 17%–20%.

Conclusions: Although non-invasive scores provide little information beyond that measured by fasting glucose, a two-step screening method using risk score cut-offs at a high sensitivity, followed by a glucose test, may be an effective procedure for predicting diabetes progression. Non-glucose biological components could be employed in diabetes prediction tools after prior stratification by non-invasive methods.
Predicting Type 2 Diabetes Development Among Patients in General Practice – A Prospective Analysis Comparing Metabolic Syndrome Definitions and Components  
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Background and Objectives: A definition of metabolic syndrome (MetS) has been recommended as a tool to help identify individuals at risk of developing type 2 diabetes. However, an agreed protocol for defining MetS does not exist and some studies have shown MetS definitions to be inferior at predicting diabetes compared to a single measurement of fasting glucose. In this study we examined the ability of five proposed MetS definitions to discriminate incident cases in order to determine whether MetS more accurately predicts type 2 diabetes.

Materials and Methods: This was a prospective study involving a random sample of 1,754 men and women aged 46–73 years. Receiver operating characteristic curve and net reclassification improvement (NRI) analyses were used to evaluate the ability of MetS definitions and components to accurately classify high-risk subjects.

Results: A model including proposed MetS components displayed a significantly (P=0.02) higher area under the curve (AUC) to discriminate diabetes (AUC=0.90, 95% CI: 0.87–0.93) compared to fasting glucose alone (AUC=0.88, 95% CI: 0.83–0.92). Models using the European Group for the Study of Insulin Resistance MetS criterion, and which included glucose as a mandatory component, demonstrated significant overall NRI when compared to recommended and optimal fasting glucose cut-offs. A final model had a sensitivity of 0.91 and a specificity of 0.73.

Conclusions: In this population there is evidence that a combination of MetS components may help predict diabetes beyond that which is measured by glucose alone. Proposed MetS definitions should include fasting glucose as a mandatory component.
Predicting Type 2 Diabetes Development Among Patients in General Practice – A Prospective Analysis Comparing HbA1c with Fasting Plasma Glucose

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Background and Objectives: Evidence suggests discordance between glycated haemoglobin A1c (HbA1c) and fasting plasma glucose (FPG) for the diagnosis of pre-diabetes. In this study we compared the ability of HbA1c and FPG to discriminate incident diabetes cases in order to determine which marker more accurately predicts type 2 diabetes development.

Materials and Methods: This was a prospective study involving a random sample of 1,754 men and women aged 46–73 years. Receiver operating characteristic curve, integrated discrimination improvement and net reclassification improvement (NRI) analyses were used to evaluate the ability of HbA1c and FPG to accurately classify high-risk subjects.

Results: Joint measurement, using both HbA1c and FPG together, displayed the highest area under the curve (AUC) to discriminate incident diabetes (AUC=0.91, 95% CI: 0.87–0.94) followed by FPG alone (AUC=0.88, 95% CI: 0.83–0.92) and HbA1c alone (AUC=0.80, 95% CI: 0.73–0.86). When using both markers together, an optimal cut-off had a sensitivity of 0.85, a specificity of 0.83 and demonstrated significant overall NRI when compared to recommended and optimal HbA1c and FPG pre-diabetes cut-offs.

Conclusions: FPG is superior to HbA1c as an indicator of diabetes risk. Using HbA1c and FPG together may improve accuracy for detecting high-risk patients. As diagnostic performance can vary, external validation in the population to be tested should be undertaken to evaluate each marker’s performance and determine optimal pre-diabetes threshold values.
Neprilysin degrades murine Aβ more efficiently than human Aβ: Further implication for species-specific amyloid accumulation

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For over a century, aggregated forms of amyloid-β protein (Aβ) have been viewed as a key hallmark of brains affected by Alzheimer’s disease (AD). Today, it remains unknown whether Aβ aggregates (oligomers, fibrils or plaques) originate from increased production or decreased catabolism of Aβ. Neprilysin (NEP) is a ubiquitously distributed peptidase, known to degrade Aβ, amongst other peptides. In this study, we identified differences in NEP-mediated catabolism of murine and human forms of Aβ, using recombinant NEP, membrane-bound NEP from cells overexpressing the murine peptidase or from human organ preparations with high NEP activity, and purified soluble NEP. NEP degraded murine Aβ (mAβ) faster than human Aβ (hAβ). These findings were observed with full-length Aβ containing 40 or 42 amino acids (Aβ₁₋₄₀ and Aβ₁₋₄₂) and a truncated form (Aβ₄₋₁₅), which (i) contains one of the main NEP cleavage sites for Aβ (between positions 9 and 10), (ii) harbours all three amino acid differences between murine and human Aβ sequences, and (iii) is less prone to aggregation and thus might be a simpler model to investigate Aβ biochemistry. While it has previously been shown that mAβ has a far lower propensity to aggregate than hAβ, evidence from this study suggests that a more favourable NEP-mediated turnover of mAβ may provide additional protection against Aβ aggregation in murine species.
Determining a fingerprint of peptidase activity to develop medications to counteract resistance to Sunitinib in Renal Cell Carcinoma

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Renal cell carcinoma is one of the top ten most common cancers in both men and women. Beside programmed death-1 pathway (PD-1) inhibitors, agents targeting vascular endothelial growth factor (VEGF) receptors, such as Sunitinib, are the main treatment options. Unfortunately, about 70% of the patients on VEGF targeted therapies develop hypertension. Furthermore, treatment success is limited, since resistance to VEGF inhibitors ultimately develops at a median within one year of therapy. Thus, the development of novel targets to sustain the efficacy of VEGF inhibitors could improve the treatment.

It is well-known that the renin-angiotensin system (RAS) plays a key role in cardiovascular health including regulating hypertension. In particular, the angiotensin (Ang)-(1-7)/Ang II ratio is one of the most important metrics within the RAS. In this study, we aimed to measure the activity of several peptidases generating or truncating Ang peptides (such as ACE, ACE2, APA, NEP, etc.) in RCC tumours collected from mice with and without Sunitinib.

Sunitinib treatment led to faster degradation of Ang-(1-7) and the increased degradation was related to both an increase in amino peptidase activity and ACE. Analyses of Ang II degradation discovered less ACE2-like activity and confirmed an increase in amino peptidase activity.

Taken together, our experiments show that Sunitinib reduces the amount of Ang-(1-7) present in the tumours by upregulating Ang-(1-7) degrading peptidases and downregulating peptidases generating the heptapeptide. The results open the avenue to specific pharmacological interventions to be used alongside the VEGF receptor inhibitors to develop powerful new treatment options.
Age-related hearing loss (presbycusis) is a multifactorial, degenerative condition which worsens with advancing age and results in impaired comprehension of speech during conversation. Since this population are more likely to experience greater healthcare requirements, presbycusis may contribute significantly to interactions with healthcare providers. Although verbal communication remains a cornerstone of clinical practice, the impact of presbycusis on the comprehension of information conveyed during doctor-patient interactions has yet to be elucidated.

To investigate the potential impact presbycusis may have on the comprehension of clinical information conveyed in a healthcare environment.

1. Whether presbycusis results in impaired comprehension of clinical information

2. Whether there is increased difficulty comprehending information conveyed at higher frequencies in presbycusis

3. Whether removing levels of background noise during clinical consultations increases comprehension in presbycusis.

During this double-blinded experiment, participants were played a simulated clinical consultation. Whilst the consultation contained identical information, sound quality of was manipulated into six groups. These varied according to clinician gender, whether the information was manipulated to simulate presbycusis and the presence of background noise. Responses to a standardised set of questions, pertaining to the information in the consultation, was assessed to establish comprehension.
Methodological and Ethical challenges in including community-dwelling people with dementia in qualitative interview research
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Background: Meaningfully including the voices of people with dementia is now becoming a priority in dementia research, but researchers face many challenges related to this endeavour across the research process.

Method: Six interviews with people with dementia were conducted as part of a larger qualitative study; the researcher documented the methodological challenges in relation to including people with dementia throughout.

Results: The methodological issues identified here fall into the following five categories, which will be illustrated through case examples: 1) Applying for and receiving ethical approval; this involved demonstrating not only ethical soundness, but making a case for the right of the person with dementia to not be excluded on the basis of their ‘vulnerability’. 2) The recruitment of participants with dementia; the primary recruitment challenge related to complex gatekeeper issues. 3) The process of obtaining consent/assent; taking a process approach is described in relation to consent and assent. 4) Conducting the interviews; here communication strategies/tools were tailored to the communication challenges faced by each individual participant. Location, and the situatedness of the person with dementia in relation to the topic of interest, was another vital factor which influenced engagement. 5) Interpreting the data collected; triangulating the data with the person with dementia themselves after the fact, and/or carers is central to a meaningful interpretation of the data.

Conclusion: Useful insights into the challenges associated with including people with dementia in qualitative interview research are discussed, using six illustrative cases.
Chronic Intermittent hypoxia augments IL-6 expression and decreases ZO-1 expression in renal tubules.

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Obstructive sleep apnoea is characterised by chronic intermittent hypoxia (CIH) owing to recurrent episodes of upper airway obstruction exclusively during sleep. Consequential blood deoxygenation/reoxygenation cycles are associated with systemic inflammation and impaired renal oxygen homeostasis. The present study investigated the impact of a 2-week CIH exposure on inflammation and epithelial barrier integrity in the kidney. Male Sprague Dawley rats were exposed to CIH (n=4); 90 seconds of hypoxia (6.5% O₂ nadir) and 270 seconds normoxia (21% O₂) for 8 hrs/day for 2 weeks. Sham animals (n=3) were constantly exposed to room air (21% O₂) under similar environmental conditions. Animals were euthanised via pentobarbitone overdose and both kidneys harvested, fixed, and cryosectioned (20µm slices). Slices were permeabilised, blocked and incubated with primary antibodies against interleukin-6 (IL-6), IL-6 receptor (IL-6R), claudin and zonoccludin-1 (ZO-1) and complementary secondary fluorophores. IL-6 expression was amplified in the renal tubules of CIH-exposed rats (P<0.05), while CIH had no impact on IL-6R expression. Detection of ZO-1, evident at epithelial tight junctions, was lower in CIH-exposed animals and diffuse across the tubules compared to sham animals (P<0.05). CIH causes IL-6 accumulation in the renal tubules with no evidence of alterations to IL6R abundance, raising the question as to whether there was an increase in IL6/IL6R signalling. ZO-1 expression was lower in kidney tubules of animals exposed to CIH, indicating disruption of the junctions between epithelial cells. This could potentially have detrimental effects upon epithelial cell polarization, vectorial NaCl transport and ultimately the efficiency of renal oxygen utilization.
Cost Minimisation Analysis of Intravenous or Subcutaneous Trastuzumab Treatment in Patients with HER2-Positive Breast Cancer in Ireland
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Background Two large acute Irish University teaching hospitals changed the manner in which they treated human epidermal growth factor receptor (HER)2-positive breast cancer patients by implementing the administration of trastuzumab via the subcutaneous (SC) route into their clinical practice. The objective of this study is to compare the trastuzumab SC and trastuzuamb intravenous (IV) treatment pathways in both hospitals and assess which route is more cost-effective and time saving in relation to active healthcare professional (HCP) time.

Methods A prospective observational study in the form of cost minimisation analysis. Active HCP time for trastuzumab SC and IV-related tasks were recorded. Staff costs were calculated using fully loaded salary costs. Loss of productivity costs for patients were calculated using the human capital method.

Results On average, the total HCP time saved per trastuzumab SC treatment cycle relative to trastuzumab IV treatment cycle was 59.21 minutes. Time savings in favour of trastuzumab SC resulted from quicker drug reconstitution, no IV catheter installation and removal, and less HCP monitoring. Over a full treatment course of 17 cycles, average HCP time saved accumulates to 16.78 hours with an estimated direct cost saving of €1,609.99. Loss of productivity for patients receiving trastuzumab IV (2.15 days) was greater than that of trastuzumab SC (0.60 days) for a full treatment course.

Conclusion Trastuzumab SC treatment has proven to be a more cost-effective option than trastuzumab IV that generates greater HCP time savings. Healthcare policymakers should consider replacing trastuzumab IV with trastuzumab SC treatment in all eligible patients.
A Cost Saving Measure from the Utilisation of Biosimilar Infliximab in the Irish Secondary Care Setting

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OBJECTIVES: The main rationale for using biosimilar medicines is one of cost saving. The aim of this study is to demonstrate the potential cost savings accrued by switching patients from the originator brand, Remicade® to biosimilar infliximab CT-P13 in the treatment of inflammatory bowel disease in a large acute Irish teaching hospital.

METHODS: Throughout September 2016 to May 2017, data were collected on 20 patients that were switched from Remicade® to biosimilar infliximab CT-P13. Cost data for these medicines were obtained using ex-factory prices available from a national pharmaceutical database. Hypothetical biosimilar pricing scenarios using discount rates of 15%, 30% and 45% were applied to the biosimilar infliximab CT-P13 price. These rates are believed to mimic national current commercially sensitive transactions offered by pharmaceutical manufacturers on biosimilar medicines to Irish Hospitals and are corroborated by the literature. The viewpoint of the study was that of the Irish healthcare payer.

RESULTS: With respect to the various hypothetical biosimilar pricing scenarios outlined, potential cost savings from switching these 20 patients can range from €76,638 to €180,099. In addition, assuming no applied discount rate to the publically available ex-factory price, switching this cohort of patients to biosimilar infliximab CT-P13 can result in an immediate cost saving of 25% to the Irish healthcare payer.

CONCLUSIONS: Cost savings accrued from biosimilar medicine usage is of benefit to all stakeholders: increased access to medicines for patients, more treatment options for prescribers, sustainable healthcare budgets for payers and more business opportunities for manufacturers. Healthcare policymakers are one body that need to do more to increase biosimilar medicine uptake.
Uptake of the Seasonal Influenza Vaccination amongst a Cohort of Pharmacists in Ireland

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OBJECTIVES: Influenza is responsible for between 200 and 500 deaths each year in Ireland. Immunisation is a crucial component in infection control. Vaccinating priority groups such as healthcare workers is a vital focus of infection prevention efforts. In late 2017, the Irish Health Service Executive (HSE) recommended that 40% of all healthcare workers receive the influenza vaccination in order to maximise protection of at-risk patients. The aim of this research was to ascertain the uptake of the seasonal influenza vaccination in a cohort of pharmacists.

METHODS: An online survey was distributed using LimeSurvey® version 2.6.6 across 84 pharmacies within an Irish community pharmacy chain in January 2018. Quantitative data was managed and analysed in IBM SPSS Statistics® version 22.

RESULTS: A total of 109/238 pharmacists (45.8%) completed the survey. One-hundred and six of the respondents (97.2%) were trained to administer the influenza vaccine. The majority of respondents (79.8%) received the seasonal influenza vaccine during the 2017/18 influenza season. Prior to being trained in influenza vaccine administration, 29/106 pharmacists (27.4%) received the vaccine. There were no statistically significant differences in the vaccination uptake rates between younger and older pharmacists (p= 0.509) and between newly qualified and more experienced pharmacists (p= 0.875).

CONCLUSIONS: Uptake of the seasonal influenza vaccination among a cohort of pharmacists exceeded standards recommended by the Irish HSE for the vaccination of healthcare workers. Allocation of vaccination appointments, incentives, and promotion of influenza vaccination benefits are strategies that should be implemented to enhance vaccination service usage.
Incidents and Risk Factors of Chronic Post-Total Knee Arthroplasty Pain in an Irish Population

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Introduction:

Chronic post-surgical pain (CPSP) is a well-known complication postoperatively. However, there is little data to be found on CPSP post total knee arthroplasty (TKA). The aim of this study was to determine the risk factors for development of CPSP when undergoing TKA in an Irish population.

Materials and Methods:

A retrospective random sample was carried out on a population of 502 patients who attended SIVUH for TKA between January 2015 and July 2016. A confidence interval of 95% was obtained through review of 218 patient charts. SPSS and Microsoft Excel were utilised to analyse the data gathered. Outcomes of CPSP were measured at 6 months post-TKA by standard interview using the Oxford Knee Score.

Results:

Women are more likely to undergo TKA, 61% of the randomised sample was female. Women are also significantly more likely to suffer from CPSP (44%) versus their male counterparts (25%). An ASA score of 1 was linked with greater incidence of CPSP (55%) compared with ASA scores of 2 and 3 (34% and 36% respectively). Use of an Attune implant was shown to have a decreased incidence of CPSP (33%) versus the use of Triathlon implant (39%). The anteromedial approach was superior to that of the medial parapatellar approach in improving patient outcomes (31.5% vs 36.5% incidence of CPSP).

Neither age nor knee operated on affected the incidence of CPSP.

Conclusion:

This retrospective study has demonstrated that healthy (ASA 1) women having a TKA using the Triathlon implant via a medial parapatellar approach have a higher incidence of CPSP after TKA. Overall the incidence of CPSP was 36.5%. Future research is required to determine if some of these risk factors are modifiable.
A qualitative multi-country analysis of the process of implementing system-wide frameworks on self-management support for chronic disease.
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Background: Frameworks have been developed in national and state health systems to improve self-management support (SMS) for chronic disease. These are large-scale frameworks which involve changes at patient, provider, organisational and system levels. Little is currently known about the process of implementing such frameworks.

Methods: Participants were key informants responsible for directing the implementation of a system-wide framework for SMS of chronic disease. Semi-structured interviews were used to explore the process of implementation and were analysed thematically. Theoretical literature was incorporated into development of themes, drawing on a multiple streams approach to policy implementation.

Results: Six participants across three health systems in different countries participated in the study. Implementation involved a process of continued prioritising and adapting framework plans. Challenges for implementation included ambiguity in the definition and operationalisation of SMS; resistance from healthcare professionals; the crisis driven nature of health systems; and changing political contexts which alter health system structures and priorities.

Conclusions: Implementation of SMS frameworks was progressing in a complex adaptive manner. Challenges included ambiguity in the definition of SMS and resistance to implementation, both of which may be overcome through greater consultation with people at the centre of SMS, including people with chronic disease. Long-term reliable mechanisms of communication across the health service are needed to maintain support for implementing SMS over a long time period. Despite contextual variation, similar challenges and enablers across countries suggest global learning may help to advance implementation of SMS for chronic disease.
Chronic intermittent hypoxia related cardiorespiratory dysfunction in adult rats

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Obstructive sleep apnoea syndrome is characterised by exposure to chronic intermittent hypoxia (CIH) and has maladaptive outcomes for whole-body health. We sought to explore the effects of exposure to CIH on homeostatic control systems with a focus on cardiorespiratory physiology and the microbiota. We hypothesise that host-microbe interactions contribute to the development of aberrant cardiorespiratory plasticity evident in CIH-exposed rats.

Sprague Dawley rats were exposed to intermittent hypoxia for 12-cycles per hour, 8 hours per day for 2 weeks, or room air. Ventilation and metabolism were recorded in unanaesthetised animals during quiet rest. Under anaesthesia, cardiorespiratory challenges were performed. Brainstem monoamines and metabolites, plasma corticosterone and pro-inflammatory cytokines were measured. Data are presented as mean±SD and were analysed using unpaired Student t-tests or Mann-Whitney unpaired t-tests.

CIH exposure increased respiratory pauses (apnoea) during normoxia and hypercapnia. Alterations in sigh frequency during hypercapnia were also noted in CIH-exposed animals. Mean arterial blood pressure was increased in CIH-exposed animals. β-adrenoceptor blockade elicited an enhanced bradycardic response in CIH-exposed animals. Moreover, sympathetic ganglion block produced a significant bradycardia in CIH-exposed animals compared with shams. Corticosterone and pro-inflammatory cytokine levels were equivalent in CIH-exposed animals and shams. Brainstem neuromodulators were decreased in CIH-exposed animals.

Our study employing a CIH-exposed rat model of sleep apnoea reveals dysregulated cardiorespiratory control. We hypothesise that CIH disrupts microbial composition, associated with impaired cardiorespiratory homeostasis. Investigation into the association between host-microbiome and cardiorespiratory homeostasis is underway in our laboratory. Manipulating the microbiota may function as an adjunct therapy for the treatment of sleep apnoea.
Falls amongst the elderly: How much will it cost the State?
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Aim
The Irish population aged over 65 is expected to grow from 0.63 million in 2016 to 1.45m in 2046. Research suggests 30% of this population can expect to have a fall. Falls can have a large impact on both an individual’s health and wellbeing. Not only the fall but also not being able to get up and thus lying on the floor for a long period of time after the fall (a long lie) has further clinical consequences for the elderly faller, as well as an economic impact on the national health service. This research attempts to estimate the future cost of falls to the State.

Method
A systematic literature review was conducted from which a probability of adverse events from falls were determined. Monetary values were assigned to falls using the Irish evidence on the economic impact of falls extracted from the literature review on cost of falls.

Results
The literature review reveals that falls are estimated to cost €13,809 per person. Applying this cost estimate to expected increasing aging population estimates indicates that the expected cost of falls is expected to increase from €2.6b in 2016 to €6b in 2046.

Conclusions
As the aging population is expected to rise so too are the cost of falls. While clinical evidence on fall prevention and fall detection programmes are emerging, little is known about the cost of implementing such programmes and their potential to be cost effective.
Biochemical confirmation of protein-protein interactions and the phosphorylation status of the human RNA-binding protein, SMAUG1.

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RNA-binding proteins are involved regulating every step of gene expression and their dysfunction, abnormal expression and/or mislocalisation have frequently been implicated in human diseases, including neurodegeneration. This study focuses on SMAUG1, one of two human paralogs of the well-characterised Drosophila Smaug RNA-binding protein. While its role as a transcriptional repressor in Drosophila is well-established, its role in humans remains largely under characterised. Yet, changes in SMAUG1 gene expression have been reported in Alzheimer’s disease. In this study, candidate SMAUG1 interactors were identified using a GFP-TRAP experiment followed by mass spectrometry. Of the interacting proteins identified, four members of the 14-3-3 protein family, β/α, γ, η and ζ, as well as the RNA-binding protein, TDP-43, were of particular interest. Co-immunoprecipitation with Myc-tagged 14-3-3 and TDP-43 proteins successfully confirmed an interaction with SMAUG1 in vitro. Supporting our biochemical evidence, we identified three putative 14-3-3 binding sites in SMAUG1, where the key residue for 14-3-3 binding is a phosphorylated serine, using a 14-3-3 interactome database. Phos-tag electrophoretic mobility shift was used to determine that SMAUG1 is phosphorylated in vitro. Site-directed mutagenesis, followed by Myc co-immunoprecipitation, were conducted to determine key phosphorylated serine residues necessary for 14-3-3 binding to SMAUG1. SMAUG1 protein levels were also examined in Alzheimer’s disease and healthy control whole brain samples where no substantial difference in total protein concentration was observed. Taken together, our data provide an important groundwork for understanding the role of SMAUG1 in humans and its link to neurodegenerative disease.
An Investigation into the Role of Gut Microbiota in Rebound Pain

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Background

Rebound pain (RP) may occur following resolution of peripheral nerve blockade. Reasons for why some people develop RP are not clear. Yet the role of gut microbiota (GM) in pain is starting to emerge. We aimed to determine if there was an association between RP in patients undergoing upper limb trauma surgery and the GM.

Methods

Ethical approval and informed consent were obtained. Patients (n=20; 7 males, 13 females) undergoing surgical fixation of distal radius fracture under axillary brachial plexus block were enrolled. Fecal samples were analysed for GM and we chose pain level acceptable to the patient in the first 24 hours, gender and a verbal rating scale of \textless{} 4 in the first 24 hours as well as max pain score as are variables.

Results

There was a significant impact of gender on beta-diversity. There were also significant differences at the genus level with respect to pain not being acceptable at 24 hours including \textit{Lachnospira}. Interesting, \textit{Porphyromonas} was noted to be more abundant in the group reporting an acceptable pain level at 24 hours. A correlation was also noted between \textit{Collinsella} and max pain score with movement.

Conclusion

While the main factor driving differences in gut microbiota in our study appeared to be gender there are still some changes that are worth investigating further. This includes the correlation of pain score with the abundance of \textit{Collinsella}. \textit{This} bacterium is associated with the production of the pro-inflammatory cytokine IL-17A and experimental arthritis.
Tuft cell hyperplasia in diarrhoea-predominant Irritable Bowel Syndrome colonic biopsies.

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Tuft cells are a rare subtype of gastrointestinal epithelial cell, which are thought to be activated by parasites and allergic reactions. Irritable bowel syndrome (IBS), a heterogeneous functional bowel disorder, characterised by abdominal pain and altered bowel habit, exhibits altered circulating cytokine profiles. Gastroenteritis, which could stimulate tuft cell hyperplasia, is a strong predictor of developing IBS. The aim of this study was to investigate if the number of colonic tuft cells was altered in human IBS or in a stress-sensitive animal model of IBS. The number of DCLK1 immuno-labelled tuft cells was compared between mucosal biopsies from diarrhoea- and constipation-predominant IBS patients and healthy controls (n=6 per group) and also in stress-sensitive Wister Kyoto and control Sprague Dawley rats (n=3 per group). As compared to healthy controls, colonic tuft cell hyperplasia was detected in diarrhoea-predominant IBS mucosal biopsies (p<0.05) only. Mucosal secretion of interleukin-25 was also elevated. Increased numbers of tuft cells were also detected in the colonic mucosa of Wister Kyoto rats (p<0.05) as compared to Sprague Dawley controls. Activation of the stress response and its exacerbating actions in IBS pathophysiology may be important in colonic tuft cell hyperplasia. However, no change in tuft cell numbers were observed in chronically stressed mice (p>0.05, n=5). These findings illustrate a previously unreported change in IBS colonic morphology. As no patient was diagnosed with post-infectious IBS and clean rodent-housing excludes stimulation by protozoans or helminths in Wister Kyoto rats, another stimulus must be involved. This may be a luminal microbial product.
As funding agencies increasingly require adoption of open science practices in the research that they fund, there is a pressing onus on researchers to respond. For many, awareness of the tools, skillsets and resources available to achieve this is lacking. University subscriptions to statistical analysis software, such as (but not limited to) SPSS, restricts the end user to a defined suite of operations and functions, that may not be accessible at a later stage in the research project or the researchers career. Furthermore, such programmes do not allow for reproducible research to be faithfully applied.

Conversely, the R programming language is free to download, install and use. Together with the graphic user interface, RStudio, it is now the favoured data analysis tool across a variety of fields, including statistics. Advances in R software development, namely the reorganisation of popular R packages under the umbrella banner of the “tidyverse”, has made R accessible to a wider audience. This has numerous benefits, chief amongst them being that R, as a programming language, has become more human readable, intuitive and accessible. Data importation, cleaning, exploration, visualisation, analysis and reporting can be enacted through R. Combined, R allows for reproducible workflows to be enacted, packaged and published.

We propose that senior academics and programme coordinators adopt R modules as a core element of academic programmes aligned with research activities. We suggest that this be implemented through structured PhD training modules or as part of early career researcher continuing professional development.
Physiotherapists’ perspectives of rehabilitation for patients with dementia post-hip fracture surgery
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Background: Hip fractures in older adults with dementia are prevalent in Ireland. Currently there is lack of evidence in post-operative physiotherapy management of these patients. Hence the purpose of this study is to investigate the challenges physiotherapists in Ireland face and strategies undertaken when providing rehabilitation for patients with dementia after hip fracture surgery. Another aim is to establish the availability of community rehabilitation services in Ireland.

Methods: A survey with mixed methods design was used to explore the experiences of the physiotherapists in Ireland who had previously worked with patients with dementia post-hip fracture surgery.

Results: Nineteen responses were received from 543 surveys sent out. Common challenges physiotherapists faced were the patients’ inability to comprehend instructions, lack of knowledge to guide rehabilitation approach and lack of time and resources. Common strategies used were involving family members and adopting person-centred care approaches. Physiotherapists also believed there were inadequate community rehabilitation for patients with dementia post-hip fracture surgery in Ireland.

Conclusion: Physiotherapists should adopt the person-centred care approach during rehabilitation for patients with dementia post-hip fracture surgery. There is also a need to enhance community rehabilitation services in Ireland for these patients for further rehabilitation.
Seldom heard: Evaluating the impact of involving patients and the public in a consensus process to inform intervention development.

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Background

Intervention development is a critical step when conducting large-scale trials. Emerging evidence suggests that Patient and Public Involvement (PPI) in intervention development increases the likelihood of developing interventions which are acceptable, feasible and effective. However, very little evidence exists supporting these claims. The aim of this Study Within A Trial (SWAT) is to evaluate the impact of involving patients and the public in the development of an intervention to improve uptake of eye-screening for people with diabetes.

Methods

This is a concurrent mixed methods design. Three consensus meetings will be held to establish the intervention content and delivery. Meeting 1 will involve PPI contributors. Meeting 2 will involve health professionals and policy makers. Meeting 3 will involve both of these groups. Meetings will be audio-recorded, field notes will be taken and participants will be asked to complete an experience survey assessing individual experiences of group dynamics and decision-making processes. Each meeting will be compared to assess the impact of PPI on (1) feasibility of the proposed intervention and (2) group dynamics and processes. The recommendations made by each group will be compared using the APEASE criteria (Acceptability, Practicability, Effectiveness/cost-effectiveness, Affordability, Safety/side-effects, Equity). Quantitative data will be analysed using SPSS V24 software. Each survey item will be compared across groups using one-way ANOVA’s with post-hoc testing.

Results

The study is ongoing. The meetings will take place in October 2018. Preliminary results will be available in November 2018.

Conclusions

The results of the study will contribute to the evolving literature on the potential impact of PPI on intervention development.
Process evaluation of an osteoarthritis disease management programme for older people with knee and hip osteoarthritis
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Introduction: Exercise plays a crucial role in osteoarthritis management in older people. Group-based interventions are effective at reducing pain and improving physical function and quality of life. Health professionals frequently encounter difficulties implementing such programmes, particularly ensuring high levels of patient attendance and participation.

Objective: To conduct a process evaluation alongside the implementation of a new disease management programme for older people with knee and hip osteoarthritis to examine programme uptake, fidelity, barriers and facilitators to implementation.

Methods: A mixed method design was used. Quantitative data were collected through routine monitoring of the service, including attendance records and outcome assessments. A fidelity checklist was used during site-visit observations. Interviews were conducted with the intervention staff and purposefully sampled programme participants.

Results: Fifteen participant interviews, four physiotherapist interviews and three site-visits were conducted. Facilitators of attendance included the development of a physiotherapist-patient rapport, participants’ positive perception of exercise and previous experience of physiotherapy. Barriers to implementation included the intervention’s vague structure and staff turnover.

Conclusions: A group-based osteoarthritis intervention should consist of a well-structured and scheduled programme with emphasis on education aimed at improving participants’ perception of exercise and developing a physiotherapist-patient rapport. This may help to maximise participation in osteoarthritis patients and ensure greater implementation success.
Investigating the association between long non-coding RNAs and ductal carcinoma in situ (DCIS)

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Breast cancer is the most common cancer in women worldwide with incidence rates increasing and survival rates varying widely depending on early detection and access to treatment. In Ireland, the number of diagnoses is increasing with 89% of new cases being invasive breast cancer. To reduce the number of individuals with invasive cancer, there is an urgent need for specific and sensitive diagnostic biomarkers for the earliest stages of breast cancer. Ductal carcinoma in situ (DCIS) is a non-obligate precursor to invasive ductal carcinoma. With an increasing number of studies linking long, non-coding RNAs (lncRNAs) to various cancers, we have specifically selected to examine lncRNAs as novel DCIS biomarkers and to characterise their biological roles.

Here, we present RNA sequencing (RNAseq) results from a small patient cohort (n=5) of DCIS-affected and normal-matched tissue, two DCIS patient-derived cell lines and one DCIS cell line model. From the cell lines, we identified several lncRNAs with altered expression that are associated with adverse breast cancer patient outcomes (The Cancer Genome Atlas). In parallel, we compared the overlap between this dataset and RNAseq data from our cohort of DCIS patients to confirm those candidates and identify novel, DCIS-associated lncRNAs. Ultimately, our work aims to identify and characterise lncRNAs in DCIS in an effort to enhance earlier diagnoses and to improve patient outcomes.
The information needs of patients with breast cancer at years one, three & five post diagnosis
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Introduction

According to the National Cancer Registry of Ireland, eighty three percent of patients with invasive breast cancer are surviving five years after a cancer diagnosis. Therefore, there exists a need to investigate the information needs of patients who have had a diagnosis of breast cancer over time.

Aim

To examine the overall information needs of patients with breast cancer post diagnosis & to examine for a change in the type of information sought over time.

Method

The Toronto Information Needs Questionnaire for Breast Cancer (TINQ-BC) was selected as the tool with which to measure patient’s information needs. This was completed by one hundred & five patients presenting for follow-up appointments in the breast cancer clinic in Cork University Hospital. Patients who were diagnosed in the years 2012, 2014 & 2016 (five, three & one year post-diagnosis) were chosen for inclusion in the study.

Results

The overall median score was 4.15, on a five point Likert scale, indicating a high level of information need overall. There existed a small, statistically insignificant difference between the 2012, 2014 & 2016 cohorts (p = 0.15). Information pertaining to the disease process scored highest overall (median score: 4.50), while information regarding the psychosocial aspect was ranked lowest (median score: 3.75). There was a small, statistically insignificant, negative correlation (-0.12, p = 0.21) between age & information need.

Conclusion

The information needs of patients with breast cancer are high throughout the follow-up period post-diagnosis. Age was not found to be significant predictor of information need.
Loss of adipose tissue mass during systemic chemotherapy predicts poor survival in patients with colorectal cancer

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Background: Obesity is an established risk factor for colorectal cancer (CRC), however little is known about changes in adiposity during chemotherapy and its impact on survival.

Methods: A prospective study of adult CRC patients undergoing chemotherapy between 2012-2016 was conducted. Longitudinal changes in body composition were examined using computed tomography (CT) images at two timepoints (interval 7 months IQR:4-9 months) using paired t-tests. Sarcopenia and low muscle attenuation (MA) were defined using published cut-points. Cox proportional-hazards models were used to estimate mortality hazard ratios.

Results: 227 patients were recruited (67% male, mean age 63 years) and 53% were treated with curative intent. At baseline, 4% were underweight (BMI<20kg/m²) and 60% were overweight/obese. However, 47% had cancer cachexia, 45% were sarcopenic and 43% had low MA. Neither baseline BMI, sarcopenia, sarcopenic obesity, low MA nor cachexia predicted survival. Longitudinal analysis (over 200 days) revealed significant muscle loss (2.8%, p=0.01) in patients treated with palliative intent, while the curative group lost 1.9% muscle mass (p=0.018) and gained total and subcutaneous fat (4.4%, p=0.038 and 6.3%, p=0.009 respectively). Adjusting for known prognostic covariates, loss of subcutaneous fat (Q1) was independently associated with poorer survival compared to those who remained stable or gained subcutaneous fat (Q2-Q4) [HR:2.04 (95%CI:1.31–3.19), p=0.002]. Patients who were muscle and fat stable survived significantly longer than those losing >2% fat [HR:2.15 (95%CI:1.16–4.01), p=0.016].

Conclusion: Loss of fat mass (specifically subcutaneous fat) during chemotherapy is prognostic of reduced survival, while a gain of fat mass was associated with better survival. Further work is required to elucidate the impact of concurrent changes in muscle and adipose tissue masses and the potential role of nutrition support in these changes.
Detecting the presence of fungal signals in the asthmatic airway

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Background

Host-microorganism interactions and subsequent prevalence and control of asthma are of increasing interest. We sought to determine if fungi, in particular Aspergillus fumigatus are detectable in the lower airways of a cohort of well-defined asthmatics and if traditional markers of Aspergillus sensitisation bore any relationship to the presence of Aspergillus in the lung.

Methods

69 patients were prospectively recruited and stratified by asthma severity (GINA) and level of control (ACQ-7). Blood serum was assessed for total IgE and Aspergillus fumigatus specific IgE. Bronchoscopy with bronchoalveolar lavage (BAL) was performed. Aspergillus Galactomannan antigen and cytokine detection were performed on serum, plasma and BAL. DNA extraction from BAL and qPCR were carried out for total fungi and A. fumigatus.

Results

IgE was elevated in 55% of patients while 9% showed specific IgE reactivity to Aspergillus fumigatus; across the varying grades of asthma severity. In BAL, fungi were visible by microscopy in 70% of patients and present by qPCR in 86% of patients, while Aspergillus fumigatus was detectable by qPCR in 46%. Serum and BAL cytokines correlated with BAL fungal presence.

Conclusion

Fungi are detectable in the asthmatic airway by microscopy and molecular methods. Systemically patients displayed varying degrees of antibody reactivity to Aspergillus. Both microscopy and molecular methods complement fungi identification and are more sensitive than Aspergillus IgE and Galactomannan. Fungal presence significantly correlated with plasma and BAL cytokines indicating an active immune reaction. Rapid identification of Fungi and cytokines in BAL may aid as a diagnostic.
Using Virtual Reality to Complement the Traditional Transition Model

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Transition is defined as the preparation and movement of a patient from a paediatric specialty unit to an adult specialty unit. Research investigating the patient and family experience during this process has found that moving from a familiar environment with a paediatric focus to an unfamiliar different environment with an adult focus can be the cause of feelings of stress and anxiety. Furthermore patients have advised that meeting the adult health care team and becoming familiar with the environment would ease these negative feelings. With the increase in the number of patients transitioning, Virtual Reality (VR) could provide a means to complement a traditional “transition clinic” model. In this context, VR offers the ability for patients and their families to become familiar with their new unit and health care team via an unthreatening interactive tool before engaging with the clinical multidisciplinary team in person. This research seeks to investigate the use of VR for such a purpose within the context of Cystic Fibrosis patients.

To achieve this, a 3D model of the Adult CF Day Unit in the Cork University Hospital was developed with interest points that provide the patient with information about the area. A welcome video, introducing each member of the multidisciplinary team and what to expect at their first visit, is also provided. This system was developed using the Unreal Engine 4 v4.20 and is deployed to a HTC Vive Head Mounted Display. This VR system is in its final stages of development and pilot testing is anticipated to begin shortly.

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Recent work suggests that disrupted neuronal calcium homeostasis may be an early instigator of Alzheimer’s disease (AD)¹². The aim of the present study was to determine if previous work in our lab, which has demonstrated calciumopathic disruption in primary hippocampal neurons from a transgenic mouse model of AD (3xTgAD mouse), relative to wildtype (non-Tg) controls could be replicated using the more physiologically accurate, *ex vivo* acute hippocampal brain slices.

Acute hippocampal brain slices (250mM) were prepared from age-matched (18.7±10.3 days, n=61) 3xTgAD and non-Tg mice, and loaded with the calcium-sensitive dye fluo-2AM (8μM) in a microfluidic oxygenator⁴. Intracellular calcium (Ca²⁺i) responses dentate gyrus (DG) neurons were monitored and recorded using WinFluor software. Data were analysed by Student’s t-test and are expressed as mean±S.E.M.

Under control conditions (*i.e.* K⁺=2.5mM), DHPG(50μM)-evoked Ca²⁺i signals were significantly (*P*<0.05) larger in 3xTgAD neurons relative to control (123±29%, *n*=20-53). However, in the presence of elevated (7.5mM) K⁺ aCSF, a significant difference in potassium-evoked response alteration was observed (*P*<0.001). Further, we also found that there was no significant difference between mouse genotypes in DHPG-response nicotinamide sensitivity (non-Tg by 11±5.2%; *n*=30 cells, *P*<0.05; 3xTgAD by 23±6.2%; *n*=22 cells, *P*<0.01).

In conclusion, we have shown that a significant calciumopathy is present in 3xTgAD brain slices from an early age. This supports the suggestion that AD pathogenesis may occur well before hallmark neurohistopathological alterations. Additionally, we have also demonstrated that calcium imaging using acute slices is a versatile, less time consuming and, arguably, more physiological methodology than primary neuronal culture.
Reverse epitope mapping of a polyclonal IgG antibody isolated from an infectious HCV serum sample.
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Introduction: The genetic diversity of the hepatitis C virus (HCV), combined with selective pressure from host responses, creates an environment that produces numerous viral variants – known as a ‘quasispecies’. The quasispecies population stimulates the production of antibodies, including neutralising antibodies (NAbs). Using the process of reverse epitope mapping, the binding sites of these neutralising antibodies can be identified and characterised.

Methodology: 19 genotype viraemic 3a HCV sera were received from the National Virus Registry Laboratory (NVRL) (CDG and CB). The IgG was purified and quantified. A HCV pseudoparticle system was used to assess neutralisation potential for each antibody preparation. A scoping assay was performed to assess the neutralisation properties of the purified IgG antibodies against the infectious H77 pseudoparticle. Two unrelated antibody preparations were selected for further examination. IC50 of these antibodies were determined. The antibody with the strongest neutralisation characteristics was selected for reverse epitope mapping against the H77 E2 glycoprotein sequence.

Results: Findings of reverse epitope mapping will be presented.

Discussion: IgG antibodies purified from an unselected set of unrelated HCV sera demonstrated neutralising properties against an infectious HCV reference pseudoparticle. The epitope map will be discussed in the context of previously identified epitopes on the E2 HCV glycoprotein.
Host and Environmental Factors Influencing the Expression of Bacterial-derived Metabolic Enzymes in Faeces: Potential Implications for Microbiota-mediated Drug Metabolism

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Background/Objectives: The gastrointestinal tract houses a reservoir of bacterial-derived enzymes, including β-glucuronidase and β-glucosidase, that can directly catalyse the metabolism of drugs, for example, β-glucuronidase metabolises Irinotecan, an anticancer drug. However, the variation of this metabolic activity across lifespan and experimental species is poorly understood. Therefore, it is important to investigate the host and environmental factors, which may influence the expression and activity of these enzymes, to explore novel mechanisms driving inter-individual variation in drug metabolism. Our aim was to investigate the effects of age, sex, genetic background, germ-free (GF) status, antibiotic treatment, and species on β-glucuronidase and β-glucosidase activity.

Methods: To quantify the microbial enzymatic activity of the gut microbiome, we prepared an in-vitro metabolism assay, Fecalase; a cell-free extract of faeces.

Results/Conclusion: The absence of enzyme activity in GF animals validated the microbial-derived nature of these enzymes. Our data show that the activity of β-glucuronidase and β-glucosidase depends on sex, age, and species. Additionally, we found that an antibiotic cocktail (vancomycin, ampicillin, and neomycin) administered to mice for 21 days significantly impacted enzymatic activity during treatment, which recovered one week after stopping antibiotic administration. Our data, therefore, suggest that multiple factors can influence the activity of bacterial-derived drug-metabolising enzymes. Moreover, antibiotic treatment can decrease the metabolic activity of the gut microbiota which may have potential implications for drug-drug interactions or cause variations in the efficacy of concomitant medication for several days after finishing an antibiotic course. The implications of these findings for drug metabolism and pharmacokinetics warrant further investigation.
The Impact of the Gut Microbiota on Hepatic Drug-Metabolising Enzymes: Potential Implications for Clinical Practice of Neurogastroenterology

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Background/Purpose:

Although the direct microbial metabolism of xenobiotics is increasingly appreciated as an important factor for drug activity and toxicity, indirect microbial modulation of drug metabolism remains a neglected topic of research. The cytochrome P450 (CYPs) enzyme superfamily are implicated in the metabolism of 70-80% of all drugs in clinical use. Microbial regulation of hepatic CYP expression could be an important and modifiable source of the inter-individual variation in pharmacotherapy. Using germ-free (GF) mice, we sought to investigate whether supplementation with butyrate, a microbial metabolite and histone deacetylase inhibitor, could normalise microbially-regulated hepatic CYP gene expression.

Methods:

Sodium butyrate or sodium-matched saline was administered for 21 days via the drinking water (3g/L) to conventional and GF male C57BL/6 mice (n=15/group). Mice were euthanised by decapitation and total RNA was isolated from harvested liver tissue. Reverse-transcriptase PCR was employed to compare the mRNA expression of 12 drug-metabolising CYP1-3 family isoenzymes.

Results/Conclusions:

The expression of CYP2a4 (20 fold; P<0.01) and CYP 3a11 (33 fold; P<0.001) were significantly decreased in the livers of GF mice relative to conventionally-raised mice. Notably, butyrate supplementation significantly increased CYP2b10 (2.85 fold; P<0.05) in conventional animals but had no significant impact in GF animals. These enzymes are important for the metabolism of psychostimulants, anaesthetics and analgesics, and antipsychotics respectively. These results may thus have important implications for clinical neurogastroenterology and may provide the impetus to consider the gut microbiota as an additional source of variation in patient response to neuroactive and gastrointestinal therapies.
Physiotherapists’ perspectives regarding prehabilitation exercise programmes for older people in the community to prevent functional decline
W Yang, A O'Shea, P Gallagher, S Timmons
Centre for Gerontology & Rehabilitation, UCC, Cork, Ireland

Objectives: This study aims to explore whether physiotherapists find prehabilitation exercise programmes useful in preventing functional decline in community-dwelling older people and establish the specifics of the delivery of such programmes.

Design: A mixed methods research design was used to conduct this study.

Participants: Sixty-four physiotherapists in community settings working with older people.

Methods: Data was collected using an online survey. Qualitative data was analysed using content analysis while quantitative data was analysed using descriptive statistics.

Results: Sixty-one (95.3%) participants indicated that prehabilitation exercise programmes would be useful in preventing functional decline in older people. Most participants suggested that prehabilitation exercise programmes should include strength (98.4%) and balance (98.4%) training and the majority of barriers were under the theme of ‘Resources’. Participants indicated that older people with multiple comorbidities (84.4%) should be included in prehabilitation exercise programmes. Most participants felt that decreased balance (81.3%) would indicate that older people would benefit from such programmes.

Conclusion: Most participants believe that prehabilitation exercise programmes are useful in preventing functional decline in community-dwelling older people. The findings of this study would aid in the planning of such programmes for clinical or research purposes in the future.
Prizes for New Horizons Research Conference 2018

- Best Oral Abstract Winner
- Best Elevator Pitch Winner
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Dear Conference Attendee: ________________________________

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We would appreciate your feedback on this year’s conference. Your opinions are important to us and will help us plan future conferences. Please complete this evaluation and then drop it back to the registration desk before you leave the conference. Alternatively, please email to som.horizons@ucc.ie by Friday 16th December. Thank you.

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We welcome any comments you wish to share about this year’s conference. Please include suggestions you would make regarding future conferences.

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