Conference Abstracts

University of East Anglia

FACULTY OF MEDICINE AND HEALTH SCIENCES

Postgraduate Research Student Conference

15 June 2023

14th Faculty of Medicine and Health Sciences

Postgraduate Research Student Conference

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Conference Abstracts

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Contents

Welcome to the Conference!

We take great pleasure and pride in celebrating the research and presentations of members of our Post-Graduate Research student (PGR) community in the Faculty of Medicine and Health Sciences (FMH).

The research presented in this conference, *in planning, in progress, or completed,* by PGRs in all stages of their research degree, from first to fourth year and more, is a sample of the astonishingly wide range of topics and methodologies pursued in FMH.

This conference demonstrates the resilience and determination of the PGR community, still bearing possibly indelible marks from our journey through the traumatic Covid years, despite the myriad difficulties, to share and discuss their work among peers and colleagues, to keep the research flame burning, and to persist in seeking the training and experience needed for their active participation for good in research and in society.

Arrangement of the abstracts and the presentations

Abstracts in this e-brochure are arranged by the abbreviated **mode and number** of each presentation, which precedes the title of the abstract. This number (eg. 'P-23') corresponds to the information in the conference programme, and indicates a 'running order' within each mode. Please find the programme in the http://bit.ly/PGRConf2023 folder.

The Presentation modes are arranged in this brochure in general programme order:-

T: Ten-minute talk - a traditional 10-minute talk with slides on *an aspect of* your research, followed by up to 5 minutes of question time;

P: Poster: a physical poster on an aspect of your research, possibly with a 1-minute recorded summary, and including live Q & A discussion during one of two scheduled 30-minute slots.

3MT: Three-Minute Thesis^{R}: a 3-minute talk with up to one slide, as if to a member of the public, which explains what your **whole thesis/project** is about (an 'elevator pitch'!). This will be done according to the national 3MT^{R} rules as established by the initiators of this mode, the University of Queensland, Australia;

We hope that you will appreciate the significant work summarised in these abstracts and presentations, and feed back your comments to their authors, in person at the conference during the poster sessions or in the breaks, via email (addresses provided on the abstracts) or via any other contact details provided by the presenter.

Dr. Gill Price

(Conference Organiser,

with the PGR Conference Committee - see the last page)

T-01 Early evidence in using a cognitive battery to detect driving fitness in older age

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Background:

With an ageing population, it is projected that the proportion of older drivers will increase in future years. Although driving is vital for independence and health outcomes in older age, older drivers are more likely to have a road collision, which are also more likely to be fatal. It is considered that cognitive changes are the primary cause for this, yet there is little understanding as to how cognitive functioning interacts with driving behaviour and road safety in older age.

Objectives of study:

The DECISION study aims to explore the relationship between cognitive function and driving behaviour to better understand how cognitive functioning affects driving fitness in older age.

Data collection methods:

804 participants (mean age: 71.03) were recruited in a prospective cohort study. Participants self-reported cognition and driving behaviour prior to completing an online cognitive battery comprising tasks in a variety of cognitive domains implicated in both driving performance and age-related cognitive decline.

Results:

We replicate previous findings that driving frequency and distance reduces in older age and report for the first that increased self-reported driving difficulty and avoiding challenging driving situations is associated with deficits to spatial orientation performance. Allocentric orientation was the only cognitive domain that exhibited a consistent interaction with driving behaviour between under-70 and over-70 age groups, a threshold commonly used for age-based driver screening policies.

Conclusion:

Spatial orientation deficits present as a robust indicator of driving performance in older age and should be considered in future driving fitness assessments in ageing individuals. Online cognitive testing provides a promising tool for monitoring changes to driving behaviour over time, which can identify timepoints for driving evaluations across ageing, cognitive impairment, and early dementia.

T-02 Acute myeloid leukaemia alters lipid metabolism in the liver

Rebecca Maynard, Katherine Hampton, Charlotte Hellmich, Dominic Fowler-Shorten, Martha Ehikioya, Niara Beraza, Kristian Bowles, Stuart Rushworth.

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Background

Acute myeloid leukaemia (AML) is a blood cell cancer with high metabolic turnover. Metabolism is a multitude of pathways where the cell makes energy (1). Our group and others have shown that AML cells rely on fatty acid metabolism for survival, which can also confer resistance to treatments (2, 3, 4). The liver is important for fatty acid metabolism of dietary fats and fatty acids released from fat tissue. It can store or produce energy for other cells to access (5). This project aims to determine whether AML alters fatty acid metabolism in the liver to support disease progression.

Results

Mice were injected with AML cells and weighed daily, during early stages of the disease the body weight remained stable but reduced in later stages. Following sacrifice, fat pads were found to be smaller on mice with AML, supporting the suggestion that AML induces lipid release. Flow cytometry of the bone marrow, blood, liver, and fat pads confirmed AML engraftment. Analysis of isolated liver cells, from AML mice, showed reduced expression of fatty acid metabolism genes, when compared with controls. This was corroborated with in vitro liver cells, cultured in the presence or absence of media conditioned by AML. In vitro liver cells were treated with AML conditioned media and a fluorescent tagged long chain fatty acid. Representative images showed reduced uptake by cells in AML conditioned media. These data suggest AML can redirect fatty acids away from the liver by altering liver fatty acid metabolism.

Conclusions

Here we find that AML alters fatty acid metabolism genes in liver cells. In vivo and in vitro studies suggest AML releases products to alter gene expression and thus fatty acid metabolism in the liver. Increasing our understanding of how AML accesses metabolic substrates for further progression, may aid in development of novel therapeutic targets.

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T-03 Venetoclax indirectly targets normal blood stem cells to cause immunosuppression in Acute myeloid leukaemia

Dominic Fowler-Shorten, Charlotte Hellmich, Rebecca Maynard, Katherine Hampton, Martha Ehikioya, Ravindu De Silva, Edyta Wojtowicz, Kristian Bowles and Stuart Rushworth

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Background

Acute myeloid leukaemia (AML) is a lethal blood malignancy that predominately affects older patients. The drug Venetoclax, in combination with low dose chemotherapy has recently shown effectiveness in newly diagnosed AML patients. Venetoclax selectively targets a survival protein called BCL-2 which is overexpressed in AML. However, this treatment regime is associated with immunosuppression in AML patients due to cytopenia, a reduction in mature blood cells (1,2). The underlying cause of immunosuppression in the context of Venetoclax-treated AML remains unknown.

Hypothesis

Here, we hypothesise that Venetoclax depletes normal haematopoietic stem and progenitor cells (HSPCs) in AML to cause immunosuppression.

Methods

To perform this study, AML cells were cultured with HSPCs and BCL-2 gene expression was assessed in HSPCs by real-time PCR. AML cells were next injected into mice followed by treatment with Venetoclax. Bloods and bone marrow were isolated to assess immune cell counts by flow cytometry. HSPCs were also sorted from the bone marrow to assess their BCL-2 gene expression. Mechanisms for increased BCL-2 transcription in HSPCs were later explored using the in vitro system and targeted pathway inhibitors.

Results

We show that BCL-2 gene expression is increased in HSPCs cultured with AML cells compared to HSPC-only controls. Similarly, in vivo analysis of BCL-2 in HSPCs from AML engrafted mice showed increased BCL-2 expression. Next, we confirmed that Venetoclax causes cytopenia in AML engrafted mice allowing us to explore the mechanism. Finally, we found that interleukin-3 induces up-regulation of BCL-2 transcription in HSPCs.

Conclusions

Here, we demonstrate in vitro and in vivo that BCL-2 is overexpressed in HSPCs during AML progression and that Venetoclax depletes HSPCs to cause cytopenia. Finally, we identify interleukin-3 as a potential target which needs to be explored further to determine if we can use inhibitors for interleukin-3 to reverse cytopenia in Venetoclax-treated AML.

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T-04 Triage Nurses Decision-Making Processes: A Qualitative Systematic Review

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Background

Nurses make complex triage decisions within emergency departments, which significantly affect patient outcomes. Understanding how nurses make these decisions and why they deviate from triage algorithms facilitates interventions that work with their decision-making processes, increasing acceptability and effectiveness.

Aims

This qualitative systematic review aimed to understand the decision-making processes emergency nurses use to make acuity decisions during triage assessment at initial patient presentation.

Methodology

A systematic search was conducted of Medline, CINAHL and academic search complete. Papers were double screened with reviewers blinded to each other's decisions. Critical Appraisal Skills Programme qualitative checklists were used to appraise the methodological quality of included studies. Themes were created using thematic synthesis. GRADE-CERQual was used to evaluate certainty of evidence in the findings.

Results

28 studies were included in the review. Data analysis uncovered three superordinate themes of holistic reasoning, situational awareness, and informed decision-making. Seven subordinate themes were also identified. The findings show nurses value holistic assessments over algorithms and rely on knowledge and experience. They also assess the wider situation in the emergency department. Nine findings were rated high certainty and one moderate with GRADE-CERQual.

Conclusions

This review presents new perspectives on nurses' decision-making processes about patient's acuity. Nurses holistically gather information about patients before translating that information into acuity scores. These actions are informed by their knowledge and experience; however, the wider situation also impacts their decisions. In turn, the nurses use interpretations of patients' acuity to control the wider situation.

T-05 Investigating Novel RNAs in Childhood Primary Bone Cancer

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Background:

Primary bone cancers (PBCs) are a heterogeneous group of cancers originating in bone. PBCs primarily arise in children and adolescents. The five-year survival rate for localised disease is ~50%[1,2]. Standard of care has not changed and therefore survival rates have not improved since the 1960s[1,3]. Better understanding of PBC biology leading to more effective treatments is urgent. Metastasis is the leading cause of cancer-related death, but metastatic disease samples are difficult to obtain because surgery is scantly used at late stage disease. We recently developed protocols to isolate circulating tumour cells (CTCs) from PBC patient blood to investigate the “seeds” of metastasis without obtaining surgical samples.

Aims:

We recently identified novel RNA transcripts in CTCs that were not observed in normal or tumour tissue[4]. This data suggests that (i) novel RNAs are specific to metastasis and/or (ii) pro-metastatic cancer cells are capable of producing their own disease-promoting gene networks. This project aims to validate and characterise the mechanism of action of these novel RNAs.

Methods:

7.5mL whole blood samples were obtained from ten patients with osteosarcoma or Ewing sarcoma. The ClearCell FX (Biolidics) was used to isolate CTCs. Single CTCs were manually picked using brightfield microscopy and pipetting. The SMART-Seq® mRNA Single Cell LP kit was used to generate libraries for single cell RNA-seq (scRNA-seq).

Results:

scRNA-seq revealed significant differential expression in 347 genes between CTCs and control cell lines. An uncharacterised transcript that we currently term lnc441 was overexpressed in CTCs compared to controls. Early bioinformatics suggest that this transcript is a long non-coding RNA.

Impact:

Characterising lnc441 will reveal previously unknown pathways driving PBC metastasis and potentially reveal new knowledge on cancer spread mechanisms. Our study may identify a new therapeutic target for reducing or halting PBC spread.

References:

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T-06 Navigating through a changing sea: The emotional journey of current family carers of people living with MND

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Background: Family carers of someone living with Motor Neurone Disease (MND) experience emotional consequences due to the constant changes and losses they face. Carers' feelings and emotional wellbeing might impact their ability to perform everyday activities and their caring role, yet little is known about how carers manage their emotions during the trajectory of MND.

Methods: In-depth interviews were conducted with fourteen current family carers of people with MND living in the UK. Interviews were audio or video recorded and professionally transcribed verbatim. Data collected were analysed inductively with reflexive thematic analysis, within an interpretive descriptive framework.

Results: The analysis produced three themes. *Being drifted out to sea* reflected the emotional impact the diagnosis had on carers, such as emotions of shock, devastation, and hopelessness, and how they transited this new reality. *Learning to navigate in a stormy sea* encompassed how carers experienced and felt about everyday changes and how they adapted and faced these changes to integrate MND into their lives and be able to continue with everyday activities while supporting the person with MND. *Controlling the rudder in a choppy sea* captured how carers identified and used individual approaches to cope emotionally with the continuous changes and maintain their emotional wellbeing through the progression of MND.

Conclusion: These findings suggest that carers experience different emotions during the trajectory of MND. With diagnosis, carers experience a substantial emotional destabilisation, which gradually eases as carers begin to cope emotionally by adapting and accepting the changes and losses happening. As the disease progresses, carers identify approaches that best work for them to manage their emotions (e.g., not thinking about the future, living day by day). These understandings of how carers re- construct their emotional life around MND could help inform future practice and research to better support carers of this population.

T-07 Examining ways to improve sleep quality and support healthy ageing in older adults with sleep disturbances through targeting the gut microbiome with saffron supplementation

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Age-related neurodegenerative diseases are a growing societal burden with numerous repercussions. Lifestyle and the environmental factors play a key role in their development, with sleep quality contributing a major role. Given that 1/3 of the UK population is sleep deprived, strategies to improve sleep quality in older adults is paramount.

Saffron (*Crocus sativus*) has been reported to improve sleep and to affect the gut microbiota (Lian et al., 2022; Pontifex et al., 2022). However, the effect of saffron on sleep quality through the modulation of the microbiome is currently lacking. To address this knowledge gap, we designed a double-blind randomised placebo controlled (RCT) study (n=52) in older adults (65+ years old) with sleep disturbance. Participants received either a placebo or a saffron extract (30 mg per day) for 4 weeks combined with enhanced sleep education (ESE) with sleep tips to implement daily. Sleep quality was assessed both subjectively through validated questionnaires ESS (Epworth Sleepiness Scale), PSQI (Pittsburgh Sleep Quality Index), KSS (Karolinska Sleepiness Scale), ISI (Insomnia Severity Index) and objectively through a portable device (Dreem 3) that enables the recording of brain activity during the different sleep phases (EEG recordings). Faecal samples were collected pre-and post-intervention to track changes in microbiota composition.

Saffron intake improved ESS ($p<0.05$), a test used to assess daytime sleepiness, and PSQI ($p<0.01$) scores, a test used to evaluate sleep quality, with better sleep efficiency observed in females ($p= 0.0208$). Changes in sleep quality were paralleled with an increase in the genus *Faecalibacterium*, a bacteria previously reported to improve circadian disruptions.

These results are promising since polypharmacy is a significant problem in elderly patients.

This study provides further evidence for the effectiveness of bioactive compounds improving sleep quality and gut health in older adults.

This Study was funded by UKRI-Zinc Healthy Ageing Catalyst award (ES/W006367/1).

T-08 Protocol for a randomised, double-blind, crossover, placebo-controlled pilot study of the effect of VItamin C supplementation on Skeletal muscle in older women (VICS).

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Background: Ageing is associated with mitochondrial dysfunction, characterised by reduced ATP production and excess production of reactive oxygen species (ROS). Excess ROS promote proteolysis in skeletal muscle (SM) and may contribute to the development of sarcopenia.1 Animal studies have shown that improved antioxidant defences can reduce age-related mitochondrial dysfunction2 and preserve SM function.3 Vitamin C, a dietary antioxidant, has been associated with SM mass and function in epidemiological studies.4,5 However, its effect on SM mitochondrial function in humans has not been explored.

Objectives: To determine whether six weeks of oral vitamin C supplementation affects mitochondrial oxidative capacity (primary outcome), SM membrane turnover, muscle strength, physical function, vitamin C status, and inflammatory markers (secondary outcomes) compared with a matching placebo.

Methods: This 16-week pilot study will recruit 16 non-smoking women ≥65 years old to randomly receive 500mg/day vitamin C or matching placebo for six weeks, with a four-week washout period between interventions. Participants will have low fruit and vegetable consumption, sedentary lifestyles, no use of antioxidant supplementation or anti-inflammatory medications and no chronic diseases. Tests at baseline, and days 42 and 112 will include functional measures (SM mitochondrial oxidative capacity and membrane turnover - which is thought to be related to ROS production[6] - from ^{31}Phosphorous magnetic resonance spectroscopy, grip and leg-extension strength measured using hand-held dynamometers, and short physical performance battery score) and blood biomarkers (plasma vitamin C and serum C-reactive protein, tumour necrosis factor-alpha, and interleukin-6). Differences in outcomes between intervention groups will be compared using a paired *t*-test or Wilcoxon matched pairs test.

Results: Results will be published in a peer-reviewed scientific journal.

Conclusion: This study will inform future larger intervention trials, providing information on the feasibility of the study design - for measuring and identifying changes in outcome measures - and the size of any observed changes.

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T-09 Correlation between change in upper limb motor impairment and activity in response to exercise-based therapy after stroke: A systematic review with meta-analysis

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Introduction

Knowing whether exercise-based therapy improves motor impairment is important to drive neuromuscular restitution after stroke. This review aimed to identify whether: exercise-based therapy produces greater benefit for upper limb (UL) motor impairment or activity; and, change in impairment and activity is correlated.

Method

Electronic databases were searched from 2011 with key terms: stroke, UL and exercise. Eligibility criteria were: individually-randomised controlled trial; participants with UL motor impairment post-stroke; compared UL exercise-based therapy with no therapy, placebo/sham, or routine rehabilitation; UL motor impairment and activity were measured, and did not have a high risk-of-bias. Two Reviewers worked independently to identify eligible trials, assess risk-of-bias and extract data. Outcome measures were ranked in priority order to ensure participants were included only once in meta-analyses. Top priority measures were Fugl-Meyer Assessment (FMA) and Action Research Arm Test (ARAT).

Using STATA, Cohen's d effect sizes were calculated for the meta-analysis of change in outcomes and correlation between the effect sizes was assessed through meta-regression.

Results

After deduplication there were 1359 records of which 29 studies were included.

Meta-analysis results are presented as Cohen's d [95%CI]. Overall, exercise-based therapy improved motor impairment 0.84 [0.40,1.28], and activity 0.66 [0.27,1.05]. Improvements were 0.95 [0.10,1.80] for FMA and 0.74 [-0.27,1.74] for ARAT. The significant positive correlation between change in impairment and activity overall was (r=0.95; p<0.001) and for just FMA and ARAT (r=0.98; p<0.001).

Conclusions

Exercised-based therapy improves UL motor impairment and activity. There is a strong relationship between changes in motor impairment and activity.

T-10 Former contact sport athlete brain health is better than normal before 50 but worse after 65.

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Studies that examined medical records and retrospective data have found that male former professional contact sport players are at an increased risk of developing dementia (1, 2, 3). Prospective, longitudinal evidence from studies of both sexes and of non-professional athletes is now needed to understand the link between contact sport and dementia risk. The SCORES Project (Screening Cognitive Outcomes after Repetitive head impact Exposure in Sport) is a 10-year longitudinal study investigating the brain health of former athletes as they age, monitoring early signs of dementia. The objective of the present study is to identify early trends in performance between contact-sport exposure groups.

Male former contact sport athletes (n=87) aged above 40 without diagnosed dementia completed the first assessments. Participants repeated an online battery of cognitive, mental health and behavioural assessments at six-month intervals. Age-matched participants exposed to professional contact sport were compared to a large normative sample.

Early group means demonstrate better performance in younger age groups (40-50) exposed to contact sport in tasks of attention, executive function, reaction time, and spatial navigation. However, older age groups (over 65) exposed to contact sport demonstrated worse performance in tasks of attention, executive function, reaction time, and spatial navigation. Trends were also observed in other cognitive, mental health and behavior measures, and variables including level of sport, dementia risk or preventative factors, and factors that might influence performance were considered and adjusted for in analysis.

Preliminary evidence highlights the well-evidenced positive influence that participation in sport has on brain health in earlier age groups. However, our results demonstrate a decline in brain health in older participants exposed to contact sport when compared with a normative sample. Future work will study female athletes, incorporate biomarkers into the study design, and continue to monitor change over time.

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P-01 Evolving Views: A Constructivist Grounded Theory Exploration of Nursing Students' Concepts of Health and Illness.

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Background: Health and illness are fundamental nursing concepts, so unsurprisingly they are core elements of a pre-registration nursing curriculum. There is however limited empirical research exploring the views and perceptions of health and illness held by nursing students and how these may evolve during their undergraduate education.

Aim: To explore the evolving views and perceptions of health and illness of students undertaking a UK full-time pre-registration BSc nursing programme.

Methodology and Methods: A Constructivist Grounded Theory methodological approach was taken. Sampling was initially purposive, progressing to theoretical as the research proceeded. The sample population comprised a total of 21 students registered on a full-time undergraduate pre-registration nursing programme at either of two English universities (one urban, one semi-rural), between September 2016 and August 2021. The sample included students in each of the three years of study and represented all four fields of nursing (adult, mental health, child and learning disability). Qualitative data were collected through nine in-person focus groups and eight individual online interviews. Data were analysed inductively, developing initial and then focused coding, while using the constant comparative method.

Findings: Four data categories emerged - Evolving Views, Developing a Nursing Lexicon, Influencing Care and Caring for Self. Conceptual interpretation of the data identified that evolution of views of health and illness were characterised by developing meaning from experience by reflection.

Conclusion: The relationship between understanding views of health and illness and person-centred care identified by this developing theory provides an original contribution to the practice of nurse education.

Recommendations: It is recommended that within the BSc nursing curriculum students' evolving views of health and illness are a focus for regular guided reflection and discussion. This guided reflection and discussion should occur both during and after periods of placement learning and be co-facilitated by clinical and academic staff.

P-02 Why use ethnography to study older adults' use of digital technologies in deprived coastal communities?

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Older adults from disadvantaged communities are likely to experience deeper health and social inequalities and they may struggle to be digitally engaged. Research exploring barriers and facilitators to older adults' technology use has identified ways to promote digital engagement, but research often presents binary, static conceptions of technology 'users' and 'non-users'. Critical gerontologists are reconceptualising technology use as an active 'process of *doing'*,[1] a practice that people engage with, in the context of everyday life and over time. As such, technology practices are open to change, guided by the meanings that communities attribute to technologies.[2]

I will discuss how my research approach, ethnography, will enable me to conceptualise how older adults actively engage with and use technologies for health and social care activities in deprived coastal communities. Ethnography is a qualitative approach that explores social phenomena in action contexts, so as to yield appropriate data and findings. This involves observing, participating in, and writing about the lives of those within a setting over an extended period.

I will argue that ethnography is well-suited to identifying ways in which older adults activiely interact or choose not to interact with digital technologies. Firstly, it can enable me to responsively immerse myself in everyday lives. This entails observing technology practices in the moments they are enacted, and everyday naturalistic conditions for emergent technology practices. Secondly, this approach requires me to be open to encountering the wide spectrum of technology practices that may emerge and how older adults may shift between these practices. Ethnography is therefore a method highly pertinent to build understanding of how older adults 'do' living in deprived coastal communities when their lives are often less publicly portrayed and documented. Their digital practices may therefore be less likely to be addressed.

References

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P-03 The effect of Menopause on the development of Alzheimer's Disease

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Alzheimer's Disease (AD), responsible for 62% of all dementia cases, is a progressive neurodegenerative condition that leads to cognitive dysfunction [1]. Unlike other forms of dementia, women appear to be at a particularly increased risk of developing AD. Despite this, our understanding of this female AD vulnerability remains limited, which relates to the fact it has been largely overlooked [2]. Menopause has been identified as a potential contributing factor in this female predisposition, with earlier menopause onset associated with greater AD risk [3]. However, the underlying mechanisms responsible for this increased risk are yet to be fully elucidated.

To date models of AD have been predominantly created through the insertion of familial AD genes (FAD). Although such models have been important in developing our understanding of AD pathology, FAD accounts for only a small proportion of AD cases. Deletion of the WD domain, of the autophagy machinery Atg16L (Critical for LC3-associated phagocytosis function, but dispensable for canonical autophagy), leads to spontaneous age-associated AD complete with amyloid-beta deposition, microglia activation, and tau hyperphosphorylation [4].

Using this ATG16L1-δWD model of spontaneous AD, we will determine the impact of menopause on disease progression and pathology in a Late-onset AD-relevant model. 50 female mice will be used, and 25 mice will have menopause induced, via intraperitoneal injections of VCD (4-vinylcyclohexane diepoxide) 25 controls and sham injections as a control measure. At 12 months the mice will undergo endpoint behavioural testing which will involve the Open field Y maze, Object recognition and Barnes maze. After completion of behavioural tests, molecular techniques (directed by behavioural analysis) such as qPCR, western blot, ELISA, immunohistochemistry and omics approaches will be employed to determine the impact of menopause on AD pathology and the mechanisms responsible for this.

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P-04 Predicting prostate cancer aggressiveness with multi-omic patient data and machine learning

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Background: Globally, prostate cancer (PCa) is the second most common cancer in men (1). PCa progression varies patient to patient: some aggressive cancers progress rapidly to kill the patient, whilst others can remain harmless for many years. Unfortunately, providing an accurate prognosis at time of diagnosis is currently difficult which can result in overtreatment and life changing side-effects such as incontinence and impotence. Correctly distinguishing aggressive PCa from indolent disease can avoid unnecessary radical therapy doing more harm than good (2). There is evidence that a core set of biomarkers may be responsible for controlling PCa progression (3) indicating the possibility that an accurate predictor of aggressive PCa could be found.

Objectives: An international collaboration, the Pan-Prostate Cancer Group, has produced a dataset of over 2000 PCa patients from all over the world. Patient information in the dataset relates to changes in cancer genome, methylome, and gene expression as well as clinical data. Using these 'omic biological and clinical data from PCa patients, this project will aim to produce a predictor to distinguish clinically relevant aggressive disease from harmless tumours.

Methods: Statistical analysis and feature selection algorithms will be used to interrogate these multi-omic biomarkers to determine useful characteristics for predicting PCa aggressiveness. Supervised machine learning will be used to associate patterns in these selected biological data with clinical outcomes of aggressive PCa to produce a robust predictor of disease progression.

Potential Impact: The findings could lead to more appropriate treatments being offered to patients, leading to less overtreatment and better care. Any findings regarding alterations in the different layers of biological information could also enhance our current understanding of PCa aetiology, potentially leading to the development of novel therapies.

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P-05 Cryptosporidium parvum dysbiosis of the faecal microbiome of bovine livestock: A computational metagenomic approach

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This study investigated the impact of Cryptosporidium infection on the gut microbiome of cattle. Cryptosporidiosis is a parasitic disease that can lead to significant economic losses amounting to billions of dollars worldwide. Using a bioinformatic pipeline based on shotgun metagenomic sequencing, we found that infection with Cryptosporidium spp. is associated with dysbiosis, a pronounced reduction in bacterial diversity in the gut microbiome of infected hosts. We also observe a positive correlation between the relative abundance of Cryptosporidium and potential pathogens of the genus fusobacterium in the microbiota. The study highlights the importance of understanding the relationship between Cryptosporidium infection and gut microbiome alterations and how the gut microbiome differs between infected and uninfected hosts.

P-06 The effect of the MMP-14 gene variant in Dupuytren's disease

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Background

Dupuytren's disease (DD) is a common condition of the hand where fibrosis of underlying palm tissue causes progressive bending of the fingers, limiting hand use. Previous studies have shown that a metalloproteinase (MMP-14) is associated with increased DD severity and recurrence after surgery.[1-2] The *mmp14* genetic variant rs1042704 was reported to be associated with DD. [3] Our hypothesis is that MMP-14 has a complex role in DD development.

Objectives

This project aims to: 1) Understand the function of the MMP-14 enzyme in DD tissue; 2) Define the best way of blocking the MMP-14 enzyme activity. 3) Define the effects on the tissue after the function of MMP-14 is blocked.

Methods

Tissue will be collected from patients undergoing routine surgery for DD. Genomic DNA will be extracted and genotyped for SNPs associated with DD. An ex-vivo model using human Dupuytren's tissue will be used.[4-5] DD tissue will be maintained in culture and different treatments such as MMP14 blocking antibodies will be tested. The impact of blocking MMP14 activity will be measured using histology, qPCR, gelatine zymography and immunofluorescence microscopy.

Analysis

Data will be analysed using linear regression and statistical analysis using SPSS Version 28.0.1.0 (142).

Results

To date, 106 DD samples have been collected. The variant is present in 46.2%, with 38.7% having one copy of the gene (heterozygous) and 7.5% having two copies of the gene (homozygous).

Conclusion / Recommendations and Impact:

This early data suggests a high frequency of this variant within the local Dupuytren's population. Further analysis will determine the frequency of the SNP in the background local population, correlate the presence of the SNP with clinical disease scores and effect of this variant on disease activity. This will enable the development of therapies to prevent disease progression and, potentially, prevent the need for surgery.

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P-07 LRP1-Mediated Endocytosis of TIMP-3 in Sorsby Fundus Dystrophy.

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Background:

Sorsby fundus dystrophy (SFD) is a rare, inherited form of macular degeneration, caused by mutations in the gene encoding for tissue inhibitor of metalloproteinases 3 (TIMP-3). SFD shares many pathological and clinical characteristics with the more common age-related macular degeneration (AMD), making it an attractive model. Previous studies have indicated that a disruption in trafficking of TIMP-3 occurs in both AMD and SFD. Extracellular TIMP-3 levels are regulated after protein synthesis, by the balance between binding to extracellular proteoglycans and endocytosis by low-density lipoprotein receptor-related protein 1 (LRP1). We aimed to investigate the extracellular trafficking of TIMP-3 in retinal cells, and its potential disruption in AMD and SFD.

Methods:

Wild-type (WT) and SFD mutant TIMP-3 were purified by FLAG affinity chromatography from conditioned medium of HEK-293 cells recombinantly expressing WT, or SFD mutant (i.e. H181R, Y191C or S204C) TIMP-3. Retinal pigment epithelial cells (RPE) were incubated with WT or SFD mutant TIMP-3 and their disappearance from the medium was monitored by western blotting. In some cases, receptor-associated protein (RAP, an LRP antagonist) was added to determine if LRPs are responsible for endocytosis. A one-phase exponential decay model was fitted to calculate a half-lives.

Results:

WT TIMP-3 was taken up readily by RPE cells with a half life of ~2.5 hours. H181R TIMP-3 was endocytosed with a similar half-life to that of WT TIMP-3, however Y191C and S204C TIMP-3 had significantly delayed endocytosis and half-lives could not be calculated. Addition of RAP blocked endocytosis of WT and Y191C TIMP-3.

Conclusions:

TIMP-3 was endocytosed by RPE cells and this process was blocked by RAP, indicating it is an LRP-dependent process. Uptake of Y191C and S204C TIMP-3 was markedly delayed, potentially explaining why these proteins accumulate in the retina and damage vision.

P-08 Multiple Myeloma-Derived IL-6 Reduces Fatty Acid Metabolism in the liver by downregulating CD36 and CPT1A in Hepatocytes

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BACKGROUND

Normally, the liver processes free fatty acids (FFA) and stores small amounts as triglycerides[1]. In multiple myeloma (MM), cancer cells accumulate in the bone marrow and produce paraproteins. MM cells use fatty acid (FA) oxidation to obtain energy in the form of adenosine triphosphate, for proliferation and survival.

OBJECTIVES

To investigate FFA metabolism in response to MM progression and determine the role of the liver in redirecting FFA to the bone marrow.

METHODS

We injected 5TGM1$^{(GFP)}$ cells into KaLwRij mice to model MM. We took blood samples to measure levels of serum paraprotein (to confirm engraftment), IL-6 and FFA. Bone marrow was analysed for engraftment using anti-CD138 antibodies and GFP via flow cytometry. Real-time PCR was performed on liver samples to determine expression of genes associated with FA metabolism.

For in-vitro modelling, primary mouse hepatocytes were co-cultured with conditioned media from 5TGM1 cells or IL-6 cytokine. RNA was extracted and real-time PCR was performed. Seahorse was performed on primary hepatocytes to determine reliance on FFA metabolism.

RESULTS

Levels of FFA in serum of 5TGM1$^{(GFP)}$-engrafted mice was higher than in control. Expression of CD36 and CPT1A in liver samples of 5TGM1$^{(GFP)}$-engrafted mice was reduced compared to controls, and in hepatocytes cultured in 5TGM1 conditioned media.

We and others have previously shown that IL-6 is upregulated in MM and others have shown that IL-6 can regulate liver FA metabolism[2,3]. Serum IL-6 was increased in 5TGM1$^{(GFP)}$-engrafted mice. Seahorse analysis showed that primary hepatocytes had decreased reliance on FA oxidation when treated with IL-6.

CONCLUSION

MM changes FA metabolism in the liver by upregulating IL-6. Expression of FA genes shows that CD36 and CPT1A are downregulated in hepatocytes in response to IL-6. This suggests that MM can redirect FFA away from the liver by downregulating CD36, which mediates FFA uptake in the liver.

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P-11 Ethical conundrums confronting a postgraduate researcher conducting an ethnography.

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Background

As part of my PhD project, I designed and developed the D-DRINC Study, an ethnographic study to identify how people living with dementia drink fluids in care homes (IRAS ID: 317892). I conducted unstructured observations of the routines, practices, actions and interactions of care staff (any role) and residents living with dementia, as well as observing the care home environment. I spent continuous periods within the home, from November 2022-April 2023.

Objective: To share and discuss some ethical challenges and conundrums that I confronted while seeking ethical approval for, and conducting, an ethnographic study in one care home.

Ethical challenges: During the NHS ethical review process, I encountered serious misunderstandings from the committee, when I sought approval to undertake the D-DRINC Study. For example, the ethics committee suggested I employ an experimental design for the ethnography. When conducting ethnographic observations in the care home I was required to spontaneously respond to situational ethical and moral dilemmas. I will compare my expectations of care-work and my experience of working in care settings, with the unexpected psychological burden I experienced in my moral and ethical decision making, during this ethnography.

Conclusion/Impact

The knowledge generated from the D-DRINC study was rich in detail, contextualised and valuable for me, and other dementia researchers, to understand the nuances and intricacies of how residents living with dementia drink fluids in a care home setting. Such knowledge is vital to enable researchers to develop and design contextualised and more appropriate, interventions to increase opportunities for people living with dementia to drink fluids, within the complex system of a care home. Throughout the ethnography, ethical and moral dilemmas were frequently challenging, but reflecting critically and rigorously on the ethical conundrums that I confronted can provide useful insights for other ethnographic and care home researchers.

P-12 Reaching consensus to suggest guidelines for the non-pharmacological management of post-stroke emotionalism using the Delphi Method and mini-focus groups

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Background and Objectives: There is a high prevalence rate of post-stroke emotionalism (PSE) following a stroke. However, little is known regarding the interventions which are used to support those with PSE. The purpose of this study was to identify the opinions of healthcare staff and researchers globally regarding the helpfulness and accessibility of PSE interventions and the context of what factors can impact this.

Purpose: To identify the opinions of healthcare staff and researchers globally regarding the helpfulness and accessibility of non-pharmacological PSE interventions.

Method: 38 participants completed the first round of the Delphi method, 19 the second round. Eight participants then completed three mini-focus groups. Data were summarised in line with Delphi methods with content of the mini-focus group data.

Results: “Ask the patient to take a deep breath”, “Provide education for patient”, “Acknowledge the PSE and then continue current activity”, and “Teach distraction techniques” were rated as the most helpful and accessible interventions, and with the highest level of consensus reached. Content analysis of the mini-focus groups identified factors acting as barriers to PSE interventions. Furthermore, they suggested approaches to maximise the helpfulness and accessibility of PSE interventions in healthcare services.

Conclusion: Clinical services should consider the most appropriate ways of identifying and responding to PSE depending on service context. This could include developing a PSE assessment protocol, developing a range of non-pharmacological interventions and consideration of case complexity/time since stroke and the appropriate staffing/skill mix to deliver these.

Keywords: post-stroke emotionalism, stroke, non-pharmacological interventions, mood changes, Delphi-method, mini-focus groups

P-13 Effectiveness, Experience and Usability of Low-technology Augmentative and Alternative Communication by Nonverbal Adults and their Communication Partners in the Intensive Care Unit: A Mixed-Methods Systematic Review

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Background: Patients in the intensive care unit (ICU) are commonly on mechanical ventilation, either through endotracheal intubation or tracheostomy, which usually leaves them nonverbal. Low-technology augmentative and alternative communication (AAC) strategies are simple and effective ways to enhance communication between patients and their communication partners, but not often used.

Purpose: To systematically review current evidence regarding the effectiveness, experience of use, and usability of low-technology AAC with nonverbal patients and their communication partners in the ICU.

Methods: This review included quantitative, qualitative, and mixed-methods studies of adult ICU patients aged 18 or older who were nonverbal due to mechanical ventilation. Studies using low-technology AAC, such as communication boards and pen and paper, were included. Six databases were searched, and the review was conducted according to PRISMA guidelines. A convergent segregated approach was used for data synthesis.

Results: Thirty-one studies were included, of which 24 were quantitative, 4 were qualitative and 3 used mixed methods. Low-technology AAC improved patient satisfaction, facilitated communication, and met their physical and psychological needs. The preferred method was a communication board with mixed content (e.g. pictures, words and letters). However, it was used less frequently than unaided strategies (e.g. lip reading and eye blinking), with barriers related to patients' medical status, limited tool availability, and staff attitudes. Communication boards should be easy to use, adapted to patient needs, and supplemented with pen and paper. Patients undergoing operations should be introduced to the board beforehand to increase their comfort when using it post-operatively.

Conclusion: The limited existing evidence suggests that low-technology AAC strategies satisfy patients' needs. Better usability could be achieved if the tools are properly implemented and challenges addressed. Further research is needed to establish a more thorough understanding of the design and presentation fundamentals of a communication board that would be easy to use yet sophisticated enough to cover the patients' needs in ICU.

P-14 Interactions between APOE Genotype, the Gut Microbiome and Polyphenol Metabolism

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(*Apolipoprotein* E) APOE genotype is the most significant genetic risk-factor for the development of Alzheimer's disease, with 40-60% of Alzheimer's patients carrying at least one *APOE4* allele. In addition to its effects on ageing and the brain, recent evidence suggests that *APOE* genotype may also affect the gut microbiome. Dietary polyphenols – bioactive molecules found in plants have been reported to slow cognitive decline and to affect gut microbiota speciation and metabolism. However, differences in the metabolism of these bioactive compounds according to *APOE* genotypes have not been previously explored. We ran an animal study addressing this knowledge gap using *APOE3* and *APOE4* targeted replacement (TR) mice. Animals were fed on a low-fat diet (10 kcal% from fat), a high-fat diet (45 kcal% from fat) or a high-fat diet supplemented with flavan-3-ols rich cocoa extract (100 mg/Kg body weight) for 16 weeks. This model has been widely used as a physiologically relevant model for cognitive decline in humans, with consistently higher levels in the *APOE4*-TR vs *APOE3*-TR mice, particularly if fed a high-fat diet. Significant shifts in microbiome beta diversity were observed in *APOE3-TR* mice only under a high-fat diet, with these mice acquiring an *APOE4*-TR-like microbiome. Addition of flavan-3-ol-rich cocoa reversed this shift by increasing *Prevotella*, *Aldercreutzia,* and *Faecalibacterium* genera (Log LDA score >2; FDR p adjusted 0.1) in *APOE3*-TR mice. Surprisingly, flavan-3-ol-rich cocoa did not affect the *APOE4-TR* mice's microbiome. Such results were paralleled by an increased urinary excretion of flavan-3-ols colonic derived metabolites 5-(3',4'-dihydroxyohenyl)-γ-valerolactone ($p<0.05$), 5-(hydroxyphenyl)valeric acid-4-sulfate ($p<0.01$) and 4-hydroxy-5-(hydroxyohenyl)valeric acid sulfate ($p<0.01$) in *APOE4*-TR mice. These preliminary findings were reflected in a human cohort study (COMBAT Study; NCT03679533) following a 12-week consumption of flavan-3-ols-rich cranberries. The relationship between polyphenols intake and *APOE* genotype is intriguing, and further work is required to better understand the mechanisms underlying such disparity.

P-15 Specific Bacteria in Urine Can Indicate Higher Risk for Aggressive Prostate Cancer

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Background

Prostate cancer is one of the most common cancers in the world. Infectious causes for cancer are well documented. A group of five bacteria genera called the Anaerobic Bacteria Biomarker Set (ABBS) [(1)], may help to identify the risk of developing aggressive prostate cancer.

Objectives of Study

To detect bacteria in urine using 16S bacterial sequencing data, and to compare bacteria profiles across samples from participants with different grades of prostate cancer.

Methods

Urine samples from a total of n=46 participants were subjected to 16S rRNA Illumina sequencing and the results were analysed through the DADA2 pipeline to give an output of number of reads for each amplicon sequence variant (ASV).

Analysis

The analysis on the family level taxonomic results was completed using the Phyloseq package in R. A heatmap of abundances was produced. *K*-Means clustering was done with Manhattan distances on a Principal Co-Ordinate Analysis Plot to reveal clusters of participant samples based on bacterial families.

Results

The participant urine samples clustered into three groups in terms of their bacterial communities. One group demonstrated a higher proportion of participants that developed metastases, n=5 out of 6 samples from patients with prostate cancer metastasis were in one cluster while there was only 1 sample in the other two clusters..

Conclusions/Recommendations

The results show that participants with metastatic prostate cancer tend to group in one cluster when they are clustered on bacteria taxa at the family level. The data analysed indicates that specific bacteria that contribute to the urine microbiome may indicate a higher chance of aggressive prostate cancer.

Impact

The outcome of this research may help detect patients at risk of aggressive prostate cancer early and lead to potential treatment options in the future.

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P-16 A functional genomics approach to understanding the role of LmaMORN5 in pathogenicity

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Leishmania major is a protozoan parasite with an infectious metacyclic form transmitted by phlebotomine sandflies that causes cutaneous leishmaniasis in the vertebrate host when bitten. Promastogotes which multiply in the sandly midgut can also be cultured in media and produce metacyclics at high density. Macrophages are initially infected by metacyclics which then become replicating intracellular amastigotes propagating the disease through cycles of proliferation, egress and macrophage infection. Previous work has identified a MORN-domain protein LmaMORN5 of *Leishmania major* as a virulence factor associated with reduced infection of macrophages. These studies evaluated whether the evolution of metacyclic forms, something which could affect was macrophage infection levels, was impacted by the presence or absence of the LmaMORN5 gene. Initial work established the conditions for purification of the metacyclic forms using using a novel method – a spin column of beads conjugated to the lectin peanut agglutinin (PNA) interact with the highly mannosylated serface lipopolyglycan (LPG) of the promastigote but not the metacyclic form allowing the metacyclics but not the procyclics to pass through the column. Metacyclics were then subjected to field emission scanning electron microscopy (FESEM) to evaluate their detailed topological morphology. A CRISPR knockout line of LmaMORN5 was compared with the parental line to evaluate whether growth was affected, whether the level of metacyclics formed was reduced and whether the morphology of the metacyclics was affected. The results of these comparisons are presented.

P-17 Counting Cryptosporidium: A simple and novel drug assay

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Cryptosporidiosis is one of the leading causes of diarrhoeal death in children under 5 globally, and is a severe disease in immunosuppressed individuals, such as those with HIV/ AIDs. Disease is caused by the gastrointestinal parasite *Cryptosporidium* spp. This parasite also causes severe illness in cattle, impacting yields. There are no licensed drugs against Cryptosporidiosis in the UK with Nitazoxanide being the only licensed drug in the US. Additionally, there are only a limited number of treatments for cattle. Currently, parasite cultivation methods are limited to co-culture with cell lines that cannot sustain infection, or infection models such as mice and gnotobiotic piglets. The lack of a cultivation system has compounded into an absence of treatment for those most at risk. Our study takes advantage of the cell line, COLO-680N, which was previously reported to support co-culture of the parasite. This system was adapted in order to develop a novel *in vitro* drug assay for *C. parvum*. COLO-680N cells were infected using excysted sporozoites, parasite growth and development were initially assayed microscopically by counting free swimming merozoite forms, which are released from COLO-680N cells over time. We tested two drugs in our cultivation system: Paromomycin and Nitazoxanide and the licensed natural product Excential Alliin Plus©. We found significant reductions (p=>0.0001) in merozoite output at 120 hours post-infection and an overall suppression in parasite growth over time with all three compounds. An Alamar Blue assay was evaluated as a potential high-throughput screening method, based on evaluating host protection against infection. Alamar Blue is a colorimetric and fluorescent dye which is metabolised by living cells. A decrease in Alamar Blue output from COLO-680N cells was recorded as the parasite burden increased. In the future it is anticipated that the adoption of a luciferase expressing parasite into the high throughput assay system may provide an alternative screening method against transfected strains of *Cryptosporidium* spp.

P-18 Monocyte response after elective percutaneous coronary intervention

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Introduction

Inflammation plays a central role in the pathogenesis of atherosclerosis and in the sequelae of percutaneous coronary intervention (PCI). Previous work demonstrated that intermediate monocytes (CD14++CD16+) are associated with adverse cardiovascular events, yet monocyte subset response following elective PCI has not been described. This study explores the changes in monocyte subset and humoral response after elective PCI.

Methods

In this prospective study we recruited patients undergoing elective PCI for stable angina due to de novo coronary artery disease, either with DES or DCB utilised at the discretion of the operator. We excluded patients with significant renal impairment or any significant inflammatory condition on immunosuppression. All patients provided written, informed consent. Patients had blood tests at baseline (prior to PCI), four hours, two weeks and two months later. Analyses were performed in terms of monocyte subsets (classical CD14++CD16-, intermediate CD14+CD16+ and non-classical CD14+CD16++), gene expression of CD14+ leucocytes and humoral biomarkers.

Results

Some 30 patients were recruited in the study; two patients were lost to follow-up and two patients were excluded as they had raised baseline (pre-PCI) troponin; therefore 26 patients were included in analysis. Intermediate monocytes decreased significantly four hours after PCI, were recovered at two weeks, and increased significantly at two months post elective, uncomplicated PCI. Subgroup analysis showed that the intermediate monocytes remained significantly elevated in the DES group but not in the DCB group.

Conclusion

Intermediate monocytes, a highly proatherogenic monocyte subset, increase significantly two months following elective, uncomplicated PCI. They remain significantly elevated in the DES group but not in the DCB group suggesting that the PCI strategy could be one of the ways to modulate the inflammatory response post PCI and improve patient outcomes.

3MT-01 Understanding Postgraduate Research Students Disclosure of Mental Health Challenges within the UK University Context

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Background:

Postgraduate research student (PGR) mental health is a growing area of interest to Higher Education Institutions (HEIs) and researchers, and has important implications for PGR wellbeing, success, and attrition. To understand how universities and supervisors can enable PGRs to disclose their mental health status and seek support when needed, we need to understand what HEIs are doing currently, and experiences of PGRs and supervisors.

Aim:

The aim of this PhD was to explore perceptions and experiences of disclosing a mental health challenge within the university context, particularly for PGRs.

Methods:

This PhD consisted of four stages. Stage one was a systematic review evidence map of student and PGR disclosure experiences. Stage two was a quantitative survey (N = 228) exploring disclosure distress, mental health literacy and help seeking behaviours. Stages three and four involved in-depth qualitative interviews with PGRs (N = 20), and PGR supervisors (N = 15) respectively.

Results:

Few studies were identified on the PGR experience of disclosing mental health challenges, and the differences between PGRs and taught students is often unacknowledged in policy and practice. The experience of doing a PhD can have substantial impact on the mental health of PGRs (both positive and negative) and PGRs are reluctant to talk about mental health due to the importance of the supervisory relationship, and impact on supervisory perceptions. Supervisors felt ill-equipped to encourage and support disclosures, whilst institutions expected them to support the mental health and pastoral needs of their PGRs. HEIs are not adequately recognising, rewarding, or work-loading the complex and valuable role that supervisors play in PGR success.

Impact:

Recommendations for HEIs, doctoral colleges, supervisors and PGRs will be presented in relation to policy, process, and individual action, using a health systems framework approach.

3MT-02 Toward enhancing communication process between nonverbal adults and healthcare professionals in critical care settings in Saudi Arabia

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Background: Patients in intensive care unit (ICU) are commonly attached to a ventilator, resulting in their inability to speak. Nonverbal communication can be facilitated using augmentative and alternative communication (AAC) strategies. In multicultural healthcare systems, such as in Saudi Arabia, communication remains problematic. Here, the absence of evidence based AAC strategies and the presence of many non-Saudi healthcare professionals (HCPs), whose cultures and languages differ from those of the Saudi community, create particular challenges in providing, receiving, and explaining information to patients, potentially compromising quality of care.

Purpose: This PhD project aims to improve communication between patients and HCPs in the context of ICU in Saudi Arabia by exploring their communication experiences and evaluating the acceptability of using a prototype low-technology AAC strategy based on Saudi multicultural healthcare perspectives.

Methods: This mixed-methods project has three phases. First, the effectiveness, experience and usability of low-technology AAC within ICU was explored from an international healthcare perspective through a mixed methods systematic review. Second, a qualitative interpretive study was conducted to explore patients' and HCPs' lived experiences of the communication process in different ICUs in Saudi Arabia. Third, the resulting data will be used to design a prototype low-technology AAC and evaluate its feasibility among HCPs and nonverbal patients in ICU.

Expected results and impact: This project is expected to contribute new knowledge about communication with nonverbal patients and to help develop an evidence-based tool that could enhance communication between patients and HCPs in the context of ICU in Saudi Arabia.

3MT-03 The impact of an unsaturated fat-rich Mediterranean diet versus a saturated fat-rich Western diet on mood, anxiety and cognitive performance: MediMood randomised controlled trial protocol

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Introduction

The long-term impact of a Mediterranean-style diet (MD) rich in mono- and poly-unsaturated fatty acids (MUFA and PUFA) on cognitive and overall mental health has been repeatedly described (1,2). However, the research into the acute or short-term impact of a MD on brain health is in its infancy.

Methods

MediMood is an efficacy crossover randomised controlled trial (RCT), informed by the research gaps identified by our systematic review (3). Individuals (n=25) over 18 years with mild to moderate level anxiety and/or depression will be recruited. Participants will complete 5-day MD and 5-day Western Diet (WD) interventions with a 4-week wash-out period, with foods, meal plans and instructions provided. The primary outcomes are mood and anxiety. Secondary outcomes include cognitive functions including attention, brain perfusion using MRI, select cardiometabolic and inflammatory biomarkers, ketones, brain-derived neurotrophic factor, several hormones (i.e. catecholamines, serotonin), gut microbiome speciation, sleep quality and behaviour change. The assessment time points during each arm are baseline, postprandial, 24-h and day 6.

Diets are designed using the MD Adherence Screener (MEDAS) and isocaloric, with a 14 score for the MD and zero MEDAS score for the WD. The total energy and lipid profiles of both interventions are presented in Table 1.

Discussion

MediMood will be the first well-controlled RCT examining the acute and short-term (up to 5 days) effects of a MD and a WD, (with special attention to the fatty acid profile) on mental wellbeing and cognition in a targeted risk group. It will identify the potential of a MD to improve daily symptoms and quality of life in those with existing mood and anxiety disorders.

Funding

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Conflict of interest

None

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3MT-04 Characterising sedentary and screen-based behaviour in adults

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Background

Many adults now spend a considerable amount of time in sedentary behaviours (SBs), such as TV viewing, reading, and using motorised transport[1]. SB has been identified as a public health concern due to its association with multiple health conditions[2]. This thesis aims to advance understanding of contemporary patterns in sedentary and screen-based behaviours among adults to inform population surveillance and the design of behaviour change interventions.

Methods

Diverse and innovative methods were used to examine trends over time, patterns, measurement, and correlates of SB. Industry data were used to describe duration and changes over time in a range of SBs including TV viewing and mobile phone use. Data from the UK Time Use Survey were used to examine variation in screen and SBs across the day, and activities that were undertaken concurrently. A review of SB assessment in national surveillance was undertaken to describe questionnaire characteristics and the types of behaviours that are measured. Finally, data from four waves of the multi-country Eurobarometer survey were used to explore factors that may be associated with increased sitting time in different sub-groups.

Results

Time spent watching online TV and using a mobile phone increased between 2012 and 2019, whilst traditional TV viewing decreased[3]. Engagement in screen and sedentary-based behaviours varies across the day, often occurring alongside a range of other activities such as social activities or household tasks. Despite the complex and evolving nature of SB, most questionnaires used for surveillance focus on overall sitting time with limited focus on specific behaviours[4]. Both country-level and individual-level factors appear to be associated with sitting time, but associations are generally small.

Conclusions

The nature and duration of adults screen and SB patterns has changed in recent years, highlighting new targets for behaviour change interventions and the need for surveillance tools to be updated.

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3MT-05 How can therapists recognise subtle abuse of women in intimate heterosexual relationships? Preliminary findings of a doctoral study.

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Background:

There is a lack of literature defining subtle intimate partner abuse (IPA). In addition, there is no literature on how psychological therapists might recognise clients who are unknowingly experiencing subtle IPA. Existing literature indicates women attending psychological therapy can be misunderstood by therapists, who cannot help them to identify the abusive relationship. This can lead to the continuation of the abuse and its detrimental mental and physical health consequences.

Methods:

A qualitative research study using semi-structured interviews was conducted with 15 participants purposively sampled from two groups; 1) women of high educational and socio-economic status who reported experiencing subtle IPA from intimate heterosexual ex-partners (n=11), and 2) psychological therapists who had worked with similar women who had experienced subtle IPA (n=4). Interviews were analysed using reflexive thematic analysis.

Findings:

There were two key findings from recruitment; 1) over half of group 1 volunteers were therapists who had experienced subtle IPA, and 2) it was difficult to identify participants who met criteria for recruitment to group 2, perhaps further indicating the need for this research on therapist recognition. Initial findings from interview data indicate a subtle and insidious form of abuse perpetrated by their partners on women participants and an ongoing cycle of emotional and psychological processes within the women described by both victims and therapists.

Conclusions and recommendations:

Subtle IPA and its effects were described by both women victims and therapists. In order to educate therapists and minimise the effects of therapist misunderstanding, final analysis will include recommendations for therapists with definitions and examples. Given the paucity in literature to support therapists in this sphere, it is recommended that findings from this study be disseminated as therapist teaching materials.

3MT-06 Rescuer Or Enemy; The role of metformin in the antibiotic crisis

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Background

Metformin is a highly used antidiabetic drug prescribed to more than 120 million patients globally each year. However, it has shown some antibacterial activity against different bacterial genera. And it is known that the overuse of antibacterial agents can contribute to the emergence of antibiotic resistance.

Objectives:

This study aimed to investigate the effect of the continuous exposure of different bacterial species to metformin on the emergence of less susceptible mutants to metformin and different antibiotics.

Methods:

Six parallel replicates of *Pseudomonas aeruginosa* ATCC 27853 and *Staphylococcus aureus* NCTC 6571 were exposed to metformin (1.25 mg/mL) for 18 passages. After exposure, the inhibitory activity of metformin was investigated on the evolved strains and controls using the broth microdilution method, and by determining growth curves in the presence of different concentrations of metformin (10, 5, 2.5, 1,25 and 0 mg/mL). Biofilm formation and protease production in different concentrations of metformin were also determined. All strains were whole genome sequenced using Illumina technology for detecting different mutations.

Results:

There was no change in terms of the MICs of metformin. However, there was a significant decrease in the ability of metformin to inhibit the growth of two *S. aureus* mutants compared to its inhibitory activity on the ancestor. Also, the biofilm and protease inhibition by metformin was reduced in 4 mutants of *P. aeruginosa* at the concentration of 10 mg/mL. In addition, there were some mutations in different genetic points in both strains after the sequencing data analysis.

Conclusion:

The continuous exposure of bacteria to metformin caused some changes in some phenotypic properties of evolved strains in addition to some gene mutations. Further investigation will determine if this also leads to cross-resistance to other antibiotics or altered bacterial virulence and the genetic basis for the adaptation.

Keywords:

Metformin; Antibacterial; Antibiotic resistance

3MT-07 The Genetics of Cholesteatoma: The Story So Far

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Background

Cholesteatoma is a non-cancerous, locally invasive skin cyst in the middle ear causing progressive hearing loss, facial nerve damage and possible intracranial complications. Up to 1 per 10,000 people are affected per year and the only treatment is surgical excision[1].

Recent gene expression studies have contributed to understanding of disease pathology, but how and why this cyst arises in the middle ear remains poorly understood. Although cholesteatoma is considered a spontaneous disease, family history in ~10% of cases[2] supports a heritable component. However, there have been few studies investigating its genetics.

The Genetics of Cholesteatoma project

Observations of family clustering in East Anglia[3] led to the establishment of the Genetics of Cholesteatoma (GoC) project aiming to assess the heritability of cholesteatoma and identify genetic risk variants. A preliminary study on an East Anglian family with cholesteatoma identified *BTNL9* and *EGFL8* as variants of interest[4].

A larger whole exome study of 21 individuals from 10 affected families was recently published by the GoC team[5]. In this study, we identified 398 rare, loss of function variants which co-segregated with cholesteatoma. Six genes (*DENND2C*, *DNAH7*, *NBEAL1*, *NEB*, *PRRC2C* and *SHC2*) were affected across multiple families. Several pathways including GTPase activity, calcium binding and extracellular matrix degradation, were enriched for deleterious variants indicating heterogeneous pathways to disease.

Follow-on Genome-Wide Association Study

My PhD project is a direct follow-on to this study and uses approximately 1,000 cases and 5,000 matched controls from the UK BioBank to perform the first large, controlled genome-wide association study of cholesteatoma. Any underlying genetics are expected to be complex, so downstream analyses such as gene-set analysis will be required to make the most of the GWAS results. New insight into the mechanisms of disease could pave the way for non-surgical treatments or identification of at-risk individuals.

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3MT-08 Exploring the Role of Competitiveness and Perfectionism on Mental Health in Trainee Clinical Psychologists

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Background: Competitiveness plays a large role in gaining experience and applying, to Clinical Psychology training. Existing evidence suggests that competition between students contributes to stress and well-being, for example, in disciplines such as medicine (Byrnes et al., 2020; Radcliffe & Lester, 2003). Comparable research is lacking in samples of trainee clinical psychologists ("trainees") who pose similarities with medical students.

Objective: This study is the first to examine competitiveness in trainees and sought to understand: (a) can competitiveness predict psychological distress and quality of life in trainees and (b) is this mediated by perfectionism.

Method: Trainees (N= 242) recruited from clinical psychology courses across the UK accessed an online survey to complete self-report scales measuring: individual competitiveness, perfectionism, anxiety, depression and quality of life. Data were analysed using mediator analyses and hierarchical regression.

Results: The findings suggest that competitiveness does not predict wellbeing assessed through anxiety, depression or quality of life in trainees. However, perfectionism showed a significant role in contributing to wellbeing. Trainees' discrepancy between their perceived performance and expectations was the only consistent independent predictor to all outcome variables.

Conclusion: This study suggests competitiveness does not contribute to mental health outcomes in trainee clinical psychologists. However, competitiveness was defined and measured as a trait of the individual therefore the contribution of environmental factors was not examined. The study does highlight the importance of recognising how disparity in trainees' self-evaluation may be detrimental to their mental health.

Recommendations: Clinical psychology courses should recognise the need to support trainees' wellbeing and seek to reduce self-evaluative discrepancy in trainees where possible. Higher education providers could target wellbeing support to students who experience higher levels of self-evaluative discrepancy. Future research could extend to examine the role of environmental competitiveness on mental health within professional training courses.

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3MT-09 Short chain fatty acids (SCFAs): Important mediators for the Gut-Brain communication?

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There is clear evidence that select food bioactives and healthy dietary patterns promote cognition, and that the gut-brain communication and gut microbiota plays an important role in this crosstalk (Chakrabarti et al., 2022; *Cell Mol Life Sci*). Gut microbiota participate mainly through their metabolites, with SCFAs emerging as key cognition mediators (Connell et al., 2019; *Mol Neurodegener)*.

We hypothesised that modulation of the gut microbiota by purified dietary fibres (microbial substrates) may affect serum concentrations of SCFAs and their transporters in the brain as well as blood brain barrier (BBB) integrity.

C57 BL/6J male mice aged 12 weeks were fed either a chow diet (rich in fibres), a refined purified diet (low in fibres) or a refined purified diet supplemented with purified fibres (inulin, psyllium, and pectin; 75 g/kg); either in isolation or in combination as described by (Pontifex et al., 2021; *Nutrients*). Liquid Chromatography Tandem Mass Spectrometry (LCMS/MS) based method was developed to quantify all straight and branched SCFAs. No significant difference in serum concentrations of SCFAs was evident, despite significant changes in faeces ($p \leq 0.05$), following dietary fibre interventions. However, a trend was observed for straight SCFAs with lower acetic (C2), propionic (C3), and butyric (C4) acids in psyllium-fed groups; and lower valeric (C5) and caproic (C6) acids in inulin-fed groups. Real time RT-qPCR analysis revealed significant downregulation of genes involved in SCFA transport (e.g., *Mct1*, *Mct4* and *Smct1; $p \leq 0.05$*) and BBB integrity (e.g., *Ocln*, *Cldn1* and *Zo1; $p \leq 0.05$)* in the brain cortical tissue. Pairwise comparison showed a negative association between these SCFA transporters and BBB integrity markers, with the effects being significant (p=0.031) for both inulin and psyllium combination groups. These initial findings support further investigation into the role of SCFAs as mediators of BBB function.

This work is funded by the Commonwealth Scholarships Commission in the UK.

Guest Doctoral Graduate panel: 'Where to from here?'

Discussion Chaired by Amy Zile, HSC

with closing comments by Drs Rebecca Wyand and Rosemary Bass

What are some of the paths I can take after my doctoral degree – what are good options for stepping stones, or major destinations? If I am not sure where I want to end up career-wise, how can I start off on the post-doctoral job market with options so that I can decide later? If I know where I want to end up, how many job-steps should I expect to get there?

If you are thinking similar -- or very different -- questions about your career path after your doctoral training, hear the stories of our Guest Panel of people who gained their PhD **at UEA, in FMH**, and have taken several steps along that journey in different directions. We are delighted to have these invited alumni joining us at the conference.

This is a panel discussion, and after their introductory stories, and hearing their responses to some questions posed by the PGR conference committee and RSF, you will have a rare opportunity to ask the panelists your own questions about post-doctoral jobs and careers. Through the session Chair, please ask all of the panelists together, or any one of them, for their views from further-along the path you are treading now!

Panelist information:	**Daniel Yara**	**Vaisakh Puthusseryppady** (joining online from USA)	**Sarah Hanson**
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Current role: employer	Serology Senior Scientist: Scientific Research and Innovation Diagnostics Division MHRA UK	Postdoctoral Research Scholar: Spatial Neuroscience Lab University of California-Irvine USA	Assoc. Professor in Community Health: HSC UEA
PhD details:			
School of reg. and year of graduation*	Norwich Medical School 2021	Norwich Medical School 2021	Norwich Medical School 2016
Subject area of PhD	Medical microbiology	Cognitive Neuroscience (Applied Dementia Research)	Public Health - walking groups and inequalities

Short post-doctoral career path statement from each Guest panelist:

See next page

Short post-doctoral career path statement from each Guest panelist:

Daniel Yara:

Upon completing my PhD, I attained two part-time roles: 1) at the NNUH to test samples for SARS-CoV-2, and 2) at the Quadram Institute as a lab technician. This allowed me to experience science both in a healthcare setting and an academic setting. Following this, I attained a post-doc position at the Quadram Institute, giving me the opportunity to carry out novel research, manage individuals and present work to stakeholders. I then made the decision to relocate after receiving a job offer by the Medicines and Healthcare products Regulatory Agency (MHRA), with the role as a research scientist to help develop in-vitro assays to test for vaccine batch potency and formulation. Following this, I achieved my current position as a senior scientist at the MHRA in the serology and emerging diseases division, where I now examine the serological responses to novel vaccines and determine if resulting responses are effective in protecting against evolving pathogens.

Vaisakh Puthusseryppady:

My PhD research, conducted under the supervision of Prof. Michael Hornberger (Norwich Medical School, UEA), investigated spatial disorientation in Alzheimer's disease. I was awarded my PhD in May 2021. From May- August 2021, I worked part-time as a research associate in Prof. Eneida Mioshi's team (School of Health Sciences, UEA), where I conducted research on functional disabilities seen in people with dementia. In September 2021, I joined as a postdoctoral research scholar in Prof. Elizabeth Chrastil's Spatial Neuroscience Lab at the University of California Irvine (USA). Here, my research investigates how healthy and pathological aging impacts one's spatial navigation abilities.

Sarah Hanson:

My profile and the sort of research that I am doing since my PhD can be found here https://research-portal.uea.ac.uk/en/persons/sarah-hanson . Broadly my work is community based, health promotion work. My real interest is under-researched communities and the social determinants of health that affect our health and wellbeing over the life-course. I feel very fortunate and privileged to be doing the sort of research that I do, especially the partnership working with community groups and bridging the gap between them and academia. This includes work in Great Yarmouth with a women's group and Norwich Food Network and Norwich Foodbank.
My teaching activities include supporting PhD, ProfDoc and EdD and Master's students and leading a Master's module on qualitative methods. I volunteer with Norfolk Citizen's Advice to inform my practice. I run the Early Career Researchers Club in HSC which brings a diverse group of people together in an informative and supportive way to support their early years in academia and research.

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An enormous 'Thank you and Well Done!' to all conference contributors:

First and foremost to the intrepid and hard working PGR presenters – the show is yours!

to their supervisors and co-authors;

to the invited Guest Panel speakers, Doctoral graduates of FMH;

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and to many others who have given us their support and help.

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