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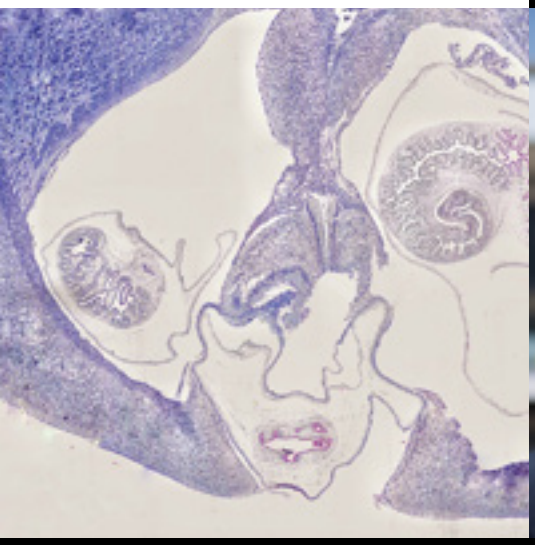
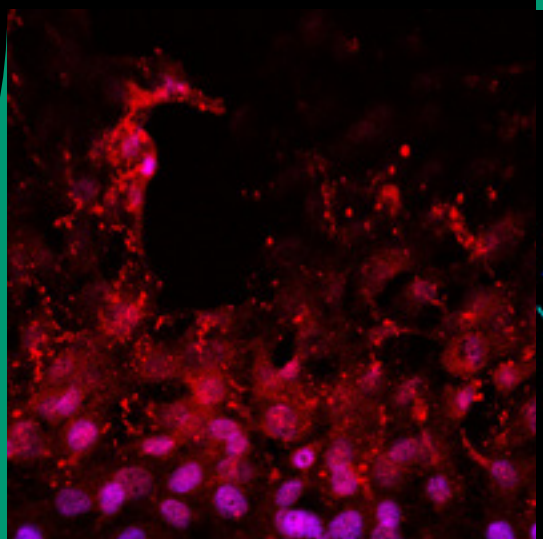
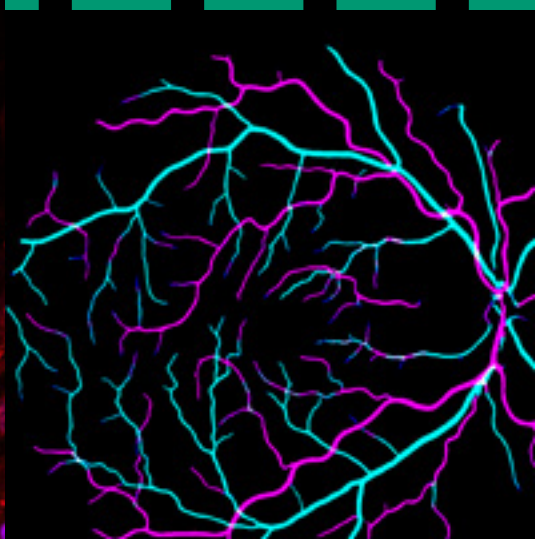



# Research Day 2024

## Wednesday 11 December 2024





Research Day 2024
Photos: Left to right, top to bottom

Research Image of the Year:
**Commended**
A rat brain experimentally infected with neurocysticercosis
**Luz Toribio**

**Professor Chris Whitty**
Chief Medical Officer for England
Presenter of the Research Day Thomas Young Lecture 2024

Research Image of the Year:
**Winner**
Visual representation of our Migrant Health Community Research Network
**Professor Sally Hargreaves**

Research Image of the Year:
**Shortlisted**
Human bone cells after injury
**Andisheh Niakan**

Research Image of the year:
**Shortlisted**
AI-generated image of retinal blood vessels
**Professor Chris Owen**

# Welcome to St George's School of Medical and Health Sciences Research Day 2024

**Professor Jonathan Friedland**

Welcome to the 2024 St George's School of Medical and Health Sciences Research Day, a major highlight of our calendar.

The event is a celebration of research excellence at (legacy) St George's and provides an opportunity to showcase new arrivals, outstanding research award winners and the notable Thomas Young Lecture. It is a long-standing testimony to the research intensity, with this year's event marking the 19th year since its inception.

The success of this event would not be possible without the dedication of our organising team, our sponsors, and the research community. I encourage you to take full advantage of this day by actively participating, exchange ideas, and foster internal networks and collaborations.

Thank you to all of you who submitted a poster this year. We have had a great response, highlighting the diversity and high calibre of the research taking place across the University, which I'm immensely proud of. The St George's Outstanding Research Awards are always highly competitive, and this year was no exception, and we look forward to the presentations from the winners in the first afternoon session following the actual awards ceremony.

Finally, I am delighted and honoured that the Thomas Young lecture will be given by Professor Chris Whitty, Chief Medical Officer and Expert adviser. His talk entitled "The role of the state in in preventing disease" will be enlightening and worth attending.

Thank you for being a part of Research Day 2024. Here's to a memorable and impactful event!

**Vice-President designate (Research and Innovation) and**
**Professor of Infectious Diseases**

Exhibitors Research Day 2024

This event has been supported by the following exhibitors:

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# St George's School of Health and Medical Sciences Research Day 2024

## Wednesday 11 December 2024

10:15-10:20 ***Welcome***

10:20-11:20 ***New Arrivals***

**Dr Roddy Walsh**, 'Identifying novel genetic factors underlying Brugada syndrome in diverse populations'

**Dr Sierra Clark**, 'Unhealthy homes: The burden of disease from damp and mouldy homes in England'

**Dr Nuria Sanchez Clemente**, 'From big data to clinical practice: Towards a better future for paediatric migrant health'

**Dr Olga Kopach** 'Nanoengineered Drug Encapsulation: A Novel Approach in Neurotherapeutics with Minimal Side Effects'

11:30-14.30 ***Poster Presentations***

12:00 ***Lunch***

15:00-15:15 ***Prizegiving***

15:15-16:15 ***St. George's Outstanding Research Awards***
***Presentation by winners in each category***
Outstanding Research Publication (2023-24): Professor Amina Jindani and Professor Shamez Ladhani

Outstanding Postdoctoral Research Scientist or Award: Dr Farah Seedat

Outstanding Research Achievement by a University Lecturer: Dr Louise Hill

Outstanding Research Achievement by a University Senior Lecturer: Dr Rachel Wake

Excellence in Public/Civic Engagement in Research: Rachel Bowsher

16:15-16:30 ***Break***

17:00-18:00 ***The Thomas Young Lecture: Professor Chris Whitty***
'The role of the state in in preventing disease'

18:00-20:00 ***Reception***

# Thomas Young Lecture 2024

# Professor Chris Whitty

Professor Chris Whitty is the Chief Medical Officer (CMO) for England, the UK government's Chief Medical Adviser, and head of the public health profession.

He is a practising NHS Consultant Physician at University College London Hospitals and the Hospital for Tropical Diseases, and undertook clinical training at St George's as well as Africa, Asia and elsewhere in the UK. Before his role as CMO he was Chief Scientific Adviser (CSA) at the Department of Health and Social Care, head (CEO) of NIHR, CSA at the Department for International Development and interim Government Chief Scientific Adviser.

He was Professor of Public and International Health at the London School of Hygiene and Tropical Medicine (LSHTM), undertaking research in Africa and Asia where he continues as an honorary professor.

# New Arrivals

## Dr Roddy Walsh

'Identifying novel genetic factors underlying Brugada syndrome in diverse populations'

Dr Roddy Walsh is a lecturer in the Cardiovascular and Genomics Research Institute and joined City St George's in October of this year. Dr Walsh researches the genetic aetiology of heritable cardiac diseases, specifically focusing on cardiomyopathies and arrhythmia syndromes, conditions that affect at least 1 in 200 people and can cause sudden cardiac death and heart failure in the young. His research focuses on developing methods for establishing gene and variant pathogenicity and exploring the increasingly complex genetic architecture of these cardiac conditions - including the contribution of non-rare genetic risk variants, the spectrum of dominance and recessiveness for cardiac disease genes and the role of rare non-coding variants identified by genome sequencing.

Dr Walsh collaborates with research groups worldwide, with a focus on genomics research in understudied populations (Egypt, Thailand, etc). He completed his PhD at Imperial College London studying the genetics of hypertrophic cardiomyopathy and was subsequently based at Amsterdam UMC in the Netherlands.

## Dr Sierra Clark

'Unhealthy homes: The burden of disease from damp and mouldy homes in England'

Dr Sierra Clark is a Lecturer in Population Health at City St George's, having previously worked in government as a scientist at the UK Health Security Agency in the Noise and Air Quality teams as well as at Health Canada. She holds a BA (hons) in Geography and a MSc in Epidemiology from McGill University in Montreal and completed her PhD at Imperial College London. Her research interests are in environmental epidemiology, with a focus on the health impacts of exposure to noise pollution and poor air quality in indoor and outdoor settings in the UK and globally. Sierra is also interested in innovative approaches to measuring and modelling the spatial distribution of environmental exposures and quantifying the environmental burdens of disease on a population scale. She serves on the committee for the UK Indoor Environmental Group (UKIEG) and contributes to the European Chapter of the International Society for Environmental Epidemiology.

## Dr Nuria Sanchez Clemente

'From big data to clinical practice: Towards a better future for paediatric migrant health'

Dr Nuria Sanchez Clemente is a Senior Lecturer in the Infection and Immunity Research Institute and Paediatric Infectious Diseases Consultant at City St George's and Evelina Children's Hospital. Her research aims to reduce the burden of infectious diseases in the most overlooked paediatric populations. She joined City St George's as an NIHR Clinical Lecturer in 2022, having previously lived in Brazil for several years, where she completed her PhD on congenital Zika Virus infection at the University of Sao Paulo/LSHTM.

Her current work seeks to use large routine health datasets, longitudinal studies and community engagement and co-design to improve the health of migrant children in the UK.

## Dr Olga Kopach

'Nanoengineered Drug Encapsulation: A Novel Approach in Neurotherapeutics with Minimal Side Effects'

Dr Olga Kopach is a Lecturer in the Neurosciences and Cell Biology Research Institute. After obtaining her PhD in Physiology, Olga started her postdoctoral research in the field of pain, working on the central mechanisms of persistent pain. She investigated the role of glutamate receptors in spinal cord nociceptive plasticity, exploring both pharmacological and genetic strategies to cure chronic pain. As a Research Fellow and later Senior Research Fellow at the UCL Queen Square Institute of Neurology, Olga studied synaptic plasticity in the brain, contributing to discovering several fundamental mechanisms of learning and memory through neuron-glial interaction. Her current research is focused on investigating the mechanisms of nerve cell dysfunction in ischaemia, dementia, and other neurodegenerative disorders, implementing electrophysiology and fluorescent imaging techniques *in vitro*, *in situ*, and *in vivo*. Olga's interests also include innovative drug delivery technologies to elaborate new methods for advancing targeted treatments in neurology.

# St. George's Outstanding Research Awards

## Joint winners of Outstanding Research Publication (2023 to 2024)

## Professor Amina Jindani

'The RIFASHORT Trial'

Amina Jindani has been involved with clinical trials of tuberculosis since the 1960s when she coordinated the first East African/British Medical Research Council trial of short-course chemotherapy in Africa.

A Bachelor's degree from the University of London in 1962 was accompanied by special awards in Paediatrics and Pharmacology and membership of the Royal College of Physicians of the United Kingdom.

Her post-doctoral thesis was based on the early bactericidal activity of tuberculosis drugs on the rate of reduction of the bacterial load in the sputum. This method is now applied in the evaluation of new drugs for tuberculosis.

In June 2003, she was elected as a Fellow of the Royal College of Physicians of London. Currently, she is Emeritus Professor at St George's, University of London where she established the International Consortium for Trials of Chemotherapeutic Agents in Tuberculosis, known as INTERTB. The principal objective of the Consortium is to evaluate increasing doses of rifampicin in reducing treatment duration for tuberculosis.

## Professor Shamez Ladhani

'Smart Vaccination: optimising immunisation schedules to balance personal and population protection'

Prof Shamez Ladhani PhD MRCPCH(UK) MSc(distinction) MBBS(hons) BSc(hons) is a paediatric infectious diseases consultant at St George's Hospital, professor of paediatric infectious diseases and vaccinology at St George's University of London and consultant epidemiologist at UK Health Security Agency (UKHSA), where he is the clinical lead for a number of national vaccine preventable infections, including Haemophilus influenzae, Streptococcus pneumoniae and Neisseria meningitidis, which are all major causes of childhood bacterial meningitis. He completed his medical training at Guy's and St Thomas's Hospitals, London, and then worked in a children's hospital in rural Kenya. Upon returning to London, he obtained his PhD in genetic epidemiology and vaccine failure in children and completed his specialist paediatric infectious diseases training at St George's and Great Ormond Street Hospitals, London. During the COVID-19 pandemic, he was the clinical lead for SARS-CoV-2 in Children at UKHSA. His work has focused on national surveillance of SARS-CoV-2, PIMS-TS and long COVID, immune responses to SARS-CoV-2 in children compared to adults as well as infection, transmission and outbreaks in educational settings and COVID-19 vaccines for children. He has published extensively in the field of paediatric infectious diseases and vaccine-preventable infections.

## Dr Farah Seedat

## Winner of the award for Outstanding Research Achievement by a Postdoctoral Research Scientist

'Innovating Community Engagement and Involvement: Building Collaborative Bridges at Home and Abroad'

Dr Farah Seedat is a Senior Research Fellow in Global Health within the Migrant Health Research Group, specialising in infectious disease epidemiology, migration health, and health screening. Her work has informed health policies for the UK Department of Health and Social Care, the WHO, and the UN Migration Agency. She currently leads the Scientific Working Group for the Middle East and North Africa Migrant Health Project, focussing on community-informed, data-driven digital interventions to address migrant health. Dr Seedat is currently exploring approaches to embedding community engagement and involvement at the core of global health research, which she will discuss in her presentation today.

## Dr Louise Hill

### Winner of the award for Outstanding Research Achievement by a University Lecturer

'The NeoSep1 trial: PRACTICAL considerations'

Dr Louise F Hill is a Clinical Lecturer in Paediatric Infectious Diseases. Louise's research interests are focused on neonatal sepsis and strategic antibiotic trials. She co-ordinated the EC FP7 funded NeoVanc trial which compared a neonatal optimised vancomycin regimen to a standard regimen and led on the microbiological sub-analyses. Her PhD focused on the optimisation of vancomycin in treating neonatal Gram-positive sepsis and she was an invited member of the UKHSA *Staphylococcus capitis* Incident Management Team as a result of this work. She is the co-Chief Investigator for the NeoVanc Long-term Follow-up study which will assess hearing outcomes in NeoVanc participants. Louise is involved in several global neonatal sepsis prevention and treatment randomised controlled trials, including NeoVTAMR and NeoSep1. NeoSep1, sponsored by the Global Antibiotic Research and Development Partnership, aims to recruit 3000 neonates globally. Louise has led on the extensive feasibility process of potential sites across five WHO regions and has undertaken work to modify neonatal adverse event grading tools to the LMIC setting, adapting them to facilitate grading regardless of the availability of resources, expertise or equipment. Louise was recently invited to speak at a WHO Paediatric Drug Optimization for antibiotics meeting presenting on the challenges and opportunities in conducting neonatal antibiotic trials. In addition to her research, Louise is co-Lead for the Clinical Trials module as part of the MSc in Applied Biomedical Science.

## Dr Rae Wake

### Winner of the award for Outstanding Research Achievement by a University Senior Lecturer

Rae Wake is a Senior Lecturer and Consultant in Infectious Diseases and Microbiology. Following her PhD studying HIV-related cryptococcosis, she has continued to accrue evidence to optimise cryptococcal screening and management of patients with advanced HIV disease (AHD) and has developed her research interest in another WHO critical priority fungal pathogen, antifungal resistant *Candida* spp, with a focus on clinical solutions in resource-limited settings. Rae is now leading ambitious projects to tackle these global threats to health, together with Prof Nelesh Govender at the University of the Witwatersrand. ADVANCE GERMS-SA (funded by the NIHR and Bill & Melinda Gates Foundation) takes a three-tiered approach to generate national population-level to granular facility-level data to investigate the aetiology of severe infections, including AMR burden, among hospitalised patients with AHD. COMBAT *Candida* (funded by the Wellcome Trust) is a programme of work including a randomised trial of combination antifungal treatment

for *Candida* bloodstream infections, complemented by ICU cohort studies garnering evidence around *Candida* epidemiology, transmission dynamics, and resistance mechanisms induced by antifungal exposure in patients, and using a murine model of *Candida auris.* This work will take place in South Africa, which currently shoulders a colossal burden of both AHD and antifungal resistant *Candida* infections and will generate evidence that is relevant and readily applicable to tackling these problems globally.

## Rachel Bowsher

## Winner of the Excellence in Public/Civic Engagement in Research Award

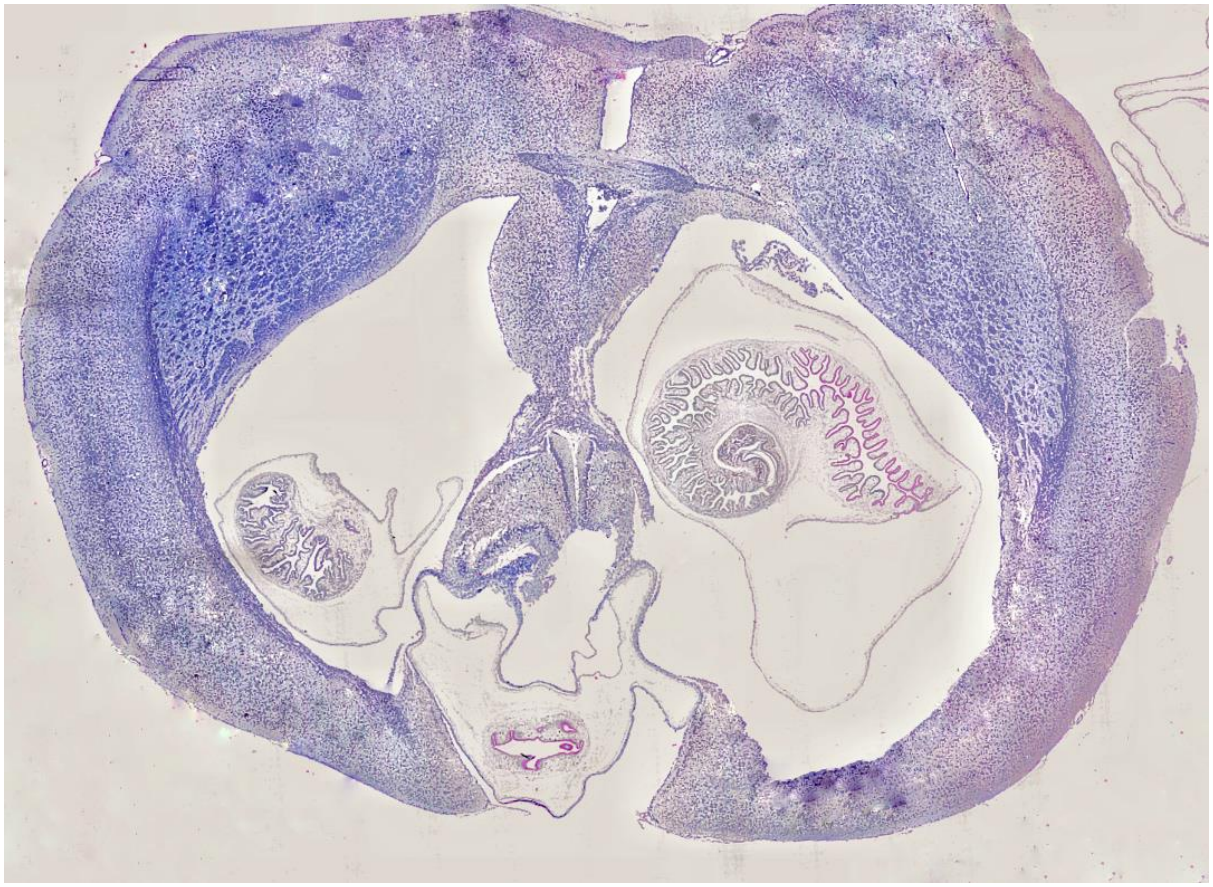
'From lab to community: Public engagement experiences throughout my PhD'

A final year PhD student here at City St George's in collaboration with the UK Health Security Agency. The PhD focuses on investigating the impact of electronic cigarettes and cigarette smoke, on an individual's susceptibility to SARS-CoV-2, but this talk will focus on the public engagement undertaken alongside this laboratory work.

## Research Image of the Year 2024: The Migrant Health Group


The image was co-produced during a series of academic-community workshops both online and in person over the last 12 months funded by a Research England Participatory Research Grant, the NIHR, and UKHSA to form a sustainable migrant health research-focused partnership alongside discussing a range of key health topics. London-based Bosnian artist Ada Jusic attended all workshops and through a series of collaborative activities the network developed the name for the group (MHCRN), our core values and aims, and what we stand for, which Ada developed into this image. Several rounds of feedback both in person and online allowed for the whole group to input into this final image.

## Commended: Luz Toribio



My image depicts a section of a rat brain experimentally infected with neurocysticercosis, stained using H&E. The contrast between the brain tissue and the parasitic cysts structures highlights the pathological changes induced by the infection, characterised by the recruitment of inflammatory cells in the surroundings of the cysts this striking visual not only illustrates the disease's impact but also, the arrangement of the brain tissue and parasitic cysts creates a curious resemblance to a cartoon face.

# Poster Abstracts 2024

**1. Dr Gina Abdelaal**

Understanding the regulation of p16 in replicative senescence

*Abdelaal G, Bishop C, Chikh A, Bennett D*

Background: Cellular senescence is a programmed arrest of cell proliferation, permanent in the absence of genetic change, following specific triggers and accompanied by specific molecular markers, including DNA damage foci and cell-cycle inhibitors (p16, p21 and/or p53). In replicative senescence (after many cell divisions), telomere shortening causes the cell cycle arrest through the DNA damage response (DDR). In melanocytes and several other cell models, p16 is the key mediator of senescence, while p53 predominates in other cells. A plethora of literature shows that the DDR activates and stabilizes p53 through phosphorylation. Human p16 can also be phosphorylated, yet only 4 papers exist on p16 phosphorylation to date. p16 is also a major tumour suppressor and a prognostic marker for melanoma patients, yet there is an inconsistency in findings potentially due to differential phosphorylation patterns picked up by commercial p16 antibodies. Additionally, the link between telomere shortening, DDR signalling and the acquisition of p16 expression has yet to be unravelled.

Aims: To investigate any link between DDR signalling and p16 expression through DDR protein kinases CHEK1/2. To develop methodologies for the detection of p16 phosphorylation.

Results: Inhibition of CHEK1/2 by AZD7762 reduced p16 levels in HeLa (cervical cancer cells), Hmel-p16-2 (primary melanocytes) and Hermes 3C (immortalised melanocytes). CHEK1 siRNA knockdown in HeLa cells gave a significant reduction in p16, validating the chemical inhibition data and suggesting a link between DDR signalling and p16 stability.

Antibodies raised against phosphoserine (pSer)152 p16 from two companies were assessed for their phospho-specificity through phosphatase treatments and peptide dot blots. Unfortunately, both antibodies failed the test, showing similar reactivity to phospho- and non-phospho-p16, similar to a total p16 antibody, indicating a lack of specificity. As an alternative approach, we used proximity ligation assays. These gave a positive signal with total p16 and pan-phosphoserine antibodies in HeLa cells, indicating close proximity and suggesting the presence of phospho-p16.

Conclusions: Our data establish a potential link between DDR and p16 stability. The next step will be to investigate the connection between DDR and p16 phosphorylation with Phos-tagTM gel electrophoresis.

**2. Dr Flavie Ader**

SCN4A loss of function zebra fish model: insights into congenital myopathy

*Ader F, Pitman A, Matthews E, Osborn D*

SCN4A is a gene encoding for the muscular sodium channel. Bi-allelic loss of function (LOF) of SCN4A was identified as a cause of congenital myopathy. To date, no in vivo model recapitulates congenital

myopathy due to SCN4A-LOF, and thus few hypotheses exist on the patho-mechanisms leading to this disease.

We have turned to the zebrafish to provide an in vivo model to assess SCN4A-LOF association with congenital myopathy.

The CRISPR mediated knockdown approach shown a cutting efficiency >79% confirmed by next generation sequencing and 10-20% of remaining expression of scn4ab transcript (qPCR and RNASeq data at 3dpf). Early stages (3-5 dpf) data shown that death rate was similar between scn4ab-KD (0%, n=138) compared to controls (3% n=196), but rate of heart oedema was significantly higher in scn4ab-KD (21%, n=138) compared to controls (11%, n=196, p=0.008) at 3 days post fertilization (dpf). No obvious morphological or muscle structure changes (n=15 per condition) were observed. Cartilage staining revealed a significant shorter palate length in scn4ab-KD (1005+/-99um, n=5) comparing to control (1193+/- 88.3um, p=0.01, n=5) at 5dpf.

Regarding the functional phenotyping, the scn4ab KD fishes presented a significant reduction of the distance moved (8437+/-5324mm) comparing to the control (13993 mm+/-4842mm, p=0.01, n=24) at 28dpf. Scn4ab-KD heart beat always seated above controls.

The molecular phenotyping (RNAseq at 3 dpf) evidenced several significantly downregulated genes including unc45b, a myosin chaperone (confirmed by qPCR). Myosin protein level progressively decreased from 13% to 39% in the scn4ab-KD comparing to controls (Western blot at 5dpf, 2, 3 weeks).

Scn4ab-KD model presents a progressive muscular defect, associated with adverse cardiac performances. In parallel, we observed a decrease of myosin level, which could be linked with unc45b down-regulation. Interestingly, unc45b-LOF is associated with congenital myopathy and cardiac dysfunction. Our model is the first presenting a functional muscular defect and could provide useful new insights into the pathomechanisms of congenital myopathy.

**3. Ms Marina Adjei**

Elucidating the role of new genes in Fovea Hypoplasia using the zebra fish model

*Adjei M, Nicholls J, Monfries C, Pittman A, Cavodeassi F*

The fovea is a structural specialisation of the retina essential for high-acuity vision in humans (1). Malformation of the fovea pit leads to low acuity vision, a congenital disease known as fovea hypoplasia (FH). FH is associated with other ocular malformations such as nystagmus, achromatopsia, albinism, or aniridia (2). In a multi-study of 907 cases, only four genes associated with FH were found: SLC38A8, AHR, PAX 6, and FRMD7. These genes account for 32.5% of FH cases with 67.5% unknown causal genes (3). Our group has generated a model for FH in the zebrafish. This animal model is devoid of the high acuity area, a structure equivalent to the fovea in humans (4). A transcriptomic comparison of the eyes of these animals with wildtype eyes has identified altered expression of a subset of photoreceptor-specific genes (unpublished); phosphodiesterase 6ha (pde6ha) has been linked to human diseases such as retinal cone cell dystrophy (5) and achromatopsia (6); pde6ha codes for phosphodiesterase that hydrolyses cGMP to GMP in the phototransduction cascade (6), however, little is known about its effect on fovea pit formation and subsequently FH. Other genes of interest are recoverin 3 (rcvrn 3), retinitis pigmentosa 2 (rp2), opsin 1 medium-wave-sensitive (opn1mw2), retinal G protein-coupled receptor b (rgrb), serpin peptidase

inhibitor, clade E member 3 (serpine 3) and G protein-coupled receptor kinase 7a (grk7a). Human orthologue of rp2 is associated with retinitis pigmentosa 2 (7) whereas rgrb is associated with retinitis pigmentosa 44 (8). These 7 photoreceptor cell-specific genes will be the focus of my research on FH. Our aim is to determine the function of these genes during the maturation of the zebrafish high acuity area, and their potential role as FH causative genes.

References:

1. PMID: 21529956

2. PMID: 30637189

3. PMID: 35157951

4. PMID: 36520654

5. https://www.alliancegenome.org/disease/DOID:0081025

6. PMID: 25739440

7. https://omim.org/entry/312600

8. https://zfin.org/ZDB-GENE-050522-447#summary

**4. Miss Yemi Ajelara**

Development and utility of genetically encoded fluorescent biosensors for imaging brain cellular processes in health and disease

*Ajelara Y, Ullah S, Thomas O – supervised by Török K*

We are characterising and using laboratory-developed biosensors to image cell signalling, neurotransmission and metabolism in model HEK293T cells, astrocytes and glioma (C6) cells. This approach allows for capturing real-time, high-resolution spatial data in living cells with the goal of improving our understanding of health and disease mechanisms.

Neurotransmission: Glutamate, the primary excitatory neurotransmitter in the mammalian central nervous system (CNS), requires tight regulation to maintain neural function and prevent neurotoxicity. Traditional techniques to study glutamate have limitations, particularly with real-time monitoring. The emergence of genetically encoded, real-time fluorescent sensors – such as NEMOc for calcium signalling, iGluSnFR for glutamate transporters, and GlnH-600n-N61 for glutamine detection – now enable precise monitoring of neurotransmission and metabolic dynamics in real-time. Specifically, using iGluSnFR, we can visualise the role of impaired glutamate function in neurological disorders and these findings could potentially inform the development of therapeutic strategies.

Signalling: Intracellular calcium fluctuations are essential for many bodily processes and can be monitored using biosensors. Enhanced NEMOc variants have been fine-tuned to match the kinetics of cellular calcium transients, offering a more accurate tool for detecting or measuring calcium signalling in biological systems than current biosensors. These biosensor variants could play a significant role in advancing our understanding of calcium signalling in the nervous system and aid in assessing the side effects of several drugs.

Metabolism: Glutamine is one of the most prevalent amino acids in the body, it supports cellular function and is heavily utilised for biosynthesis and energy. Glutamine uptake in both healthy and cancerous cells is mediated by the ASCT2(Alanine-Serine-Cysteine Transporter 2) family, a sodium-dependent neutral amino acid exchanger, making it a valuable target in cancer research. To track glutamine activity, we will be using a genetically encoded fluorescent sensor called GlnH-600n-N61. By conducting this research, we hope to use glutamine uptake as a potential biomarker for assessing cancer cell growth rates and treatment efficacy.

This research leverages advanced biosensors to study the mechanisms of underlying neurotransmission, signalling and metabolic processes in health and disease. Findings from our work could inform therapeutic strategies targeting glutamate and glutamine transport in cancer and neurological disorders.

**5. Dr Phoebe Allebone-Salt**

Epidemiology and resistance emergence in colonising Candida in the ICU

*Allebone-Salt P, Logan C, Mazzella A, Davidson H, Caswall B, Kong KF, Griffin AE, Symes L, Lonsdale D, Hemsley C, Wyncoll C, Abdolrasouli A, Schelenz S, Saha R, Wong J, Howard A, Harrison T, Bicanic T.*

Objectives: Antifungal drugs are used extensively in intensive care, often empirically. Antifungal exposure impacts rates of colonisation, species distribution and drug resistance, however the exact nature of this relationship is unknown. Candida infections are an increasingly important global health problem with resistant species causing ICU outbreaks; it is imperative to understand the role that antifungal use has on colonising flora.

Methods: The prospective observational cohort study CandiRes (ISRCTN14165977) enrolled 307 ICU patients at risk of invasive candidiasis at 4 UK hospitals between January 2022 and March 2023. Demographics, risk factors and antifungal exposure data were collected. Gastrointestinal Candida colonisation was assessed by mouth and perianal swabs twice-weekly throughout ICU admission and invasive isolates stored. Isolates were speciated, MIC determined and population analysis profiling used to identify heteroresistant subpopulations. We describe the impact of antifungal exposure on species epidemiology and resistance emergence (in terms of MIC and heteroresistance).

Results: At enrolment, 72.3% of participants were colonised with Candida spp: C.albicans (162/310, 52%), C.glabrata (56/310, 18%), C.dubliniensis (29/310, 9%) and C.parapsilosis (25/310, 8%). 96/307 (31%) participants received echinocandins; 52/307 (17%) received azoles (median 7d duration). C.albicans prevalence was maintained in those exposed to azoles, despite >95% of isolates being susceptible to fluconazole (841/859). In isolates exposed to azoles, fluconazole MIC increased >4-fold in 8/59 isolate series (14%) vs 5/105 (5%) unexposed to antifungals (p=0.068). The prevalence of non-albicans species increased with echinocandin exposure, despite >98% of all isolates being susceptible to anidulafungin (849/859). In isolates exposed to echinocandins, anidulafungin MIC increased >4-fold in 8/115 series (7%), vs 2/105 (2%) not exposed to antifungals. 9/24 Candida isolate series exposed to >7d echinocandins and/or with a >4-fold MIC increase (between first and last) demonstrated anidulafungin heteroresistant populations at baseline. Increasing size of heteroresistant populations preceded MIC increase in 3/9 series (1 becoming resistant, 1 intermediate). 3/9 azole-exposed series had heteroresistant populations at baseline; 2/3 developed resistance.

Conclusions: Widespread empiric antifungal exposure influences colonising Candida species distribution and drives emergence of resistant subpopulations and resistance, in particular to azoles. These findings have important implications for antifungal stewardship in the ICU.

**5. Dr Phoebe Allebone-Salt**

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Methods: The prospective observational cohort study CandiRes (ISRCTN14165977) enrolled 307 ICU patients at risk of invasive candidiasis at 4 UK hospitals between January 2022 and March 2023. Demographics, risk factors and antifungal exposure data were collected. Gastrointestinal Candida colonisation was assessed by mouth and perianal swabs twice-weekly throughout ICU admission and invasive isolates stored. Isolates were speciated, MIC determined and population analysis profiling used to identify heteroresistant subpopulations. We describe the impact of antifungal exposure on species epidemiology and resistance emergence (in terms of MIC and heteroresistance).

Results: At enrolment, 72.3% of participants were colonised with Candida spp: C.albicans (162/310, 52%), C.glabrata (56/310, 18%), C.dubliniensis (29/310, 9%) and C.parapsilosis (25/310, 8%). 96/307 (31%) participants received echinocandins; 52/307 (17%) received azoles (median 7d duration). C.albicans prevalence was maintained in those exposed to azoles, despite >95% of isolates being susceptible to fluconazole (841/859). In isolates exposed to azoles, fluconazole MIC increased >4-fold in 8/59 isolate series (14%) vs 5/105 (5%) unexposed to antifungals (p=0.068). The prevalence of non-albicans species increased with echinocandin exposure, despite >98% of all isolates being susceptible to anidulafungin (849/859). In isolates exposed to echinocandins, anidulafungin MIC increased >4-fold in 8/115 series (7%), vs 2/105 (2%) not exposed to antifungals. 9/24 Candida isolate series exposed to >7d echinocandins and/or with a >4-fold MIC increase (between first and last) demonstrated anidulafungin heteroresistant populations at baseline. Increasing size of heteroresistant populations preceded MIC increase in 3/9 series (1 becoming resistant, 1 intermediate). 3/9 azole-exposed series had heteroresistant populations at baseline; 2/3 developed resistance.

Conclusions: Widespread empiric antifungal exposure influences colonising Candida species distribution and drives emergence of resistant subpopulations and resistance, in particular to azoles. These findings have important implications for antifungal stewardship in the ICU.

**6. Dr Ali Alzarka**

Cardiac screening with ECG in the young: significance of T wave inversion, T wave depth and T wave/QRS ratio

*Alzarka A, Abioye D, Maclachlan H, Bhatia R, Papadakis M, Sharma S, Finocchiaro G*

Background: In young apparently healthy individuals, repolarization changes at the ECG may suggest an underlying cardiomyopathy.

Purpose: This study aims to investigate the clinical significance of T waves depth and T/QRS ratio in young individuals who underwent cardiac screening and exhibited T wave inversion (TWI) at the ECG.

Methods: We analysed a database of individuals aged 14 to 35 years who underwent cardiac screening, which included a health questionnaire and 12-lead ECG with a charitable organisation, between 2008 and 2013. All individuals included had recently responded to a follow-up online health questionnaire or had documented outcomes on a national digital database. The amplitudes of QRS (peak to peak) and T waves (mV) were measured in the leads where TWI was present; the average T/QRS ratio and average TWI depth were calculated.

Results: Our cohort comprised 5360 subjects (mean age of 21 ± 6 years, 61% males). Of the 358 (7%) who were referred for further investigations based on their screening findings, 255 (5%) had an abnormal ECG. TWI was documented in 120 (2%) individuals [anterior TWI in 78, inferior TWI in 16, lateral TWI in 6, and overlaps in 20 cases]. After further investigations, 16/120 (13%) individuals were diagnosed with cardiomyopathy [9 hypertrophic cardiomyopathy (HCM), 5 arrhythmogenic cardiomyopathy (ACM), 1 dilated cardiomyopathy (DCM), and 1 left ventricular non-compaction cardiomyopathy (LVNC)]. Of the remaining 104/120 individuals, 18 were diagnosed with other cardiac conditions and 86 were not found to have a cardiac disease. During a mean follow-up of 8.1 ± 1.2 years, no deaths were documented among the 16 individuals diagnosed with a cardiomyopathy, but 3 of them experienced a sudden cardiac arrest (all of them had ACM). In individuals diagnosed with a cardiomyopathy both average T/QRS ratio and average TWI depth were higher compared to the rest (0.128 vs 0.117; p = 0.54 and 0.281 vs 0.162 mV; p = 0.03, respectively). Average T/QRS ratio and average TWI depth were higher in individuals diagnosed with HCM compared with the ones diagnosed with other cardiomyopathies (0.133 vs 0.115; p = 0.68 and 0.336 vs 0.164 mV; p = 0.05, respectively).

Conclusion: T wave inversion is a relatively common ECG finding in young apparently healthy individuals and this feature leads to a diagnosis of cardiomyopathy in 13% of cases. Among subjects exhibiting TWI, T/QRS ratio and T wave depth appear higher in the ones who are eventually diagnosed with cardiomyopathies.

**7. Dr Selma Audi**

Total Triage through a Hermeneutic window: perspectives from a large south London general practice

*Audi S, Balzano M, Shah R*

Background: The Total Triage (TT) system was introduced at Bridge Lane Group Practice to improve patient access, enhance workflow efficiency, and alleviate administrative staff stress. While this

system has been promoted to streamline primary care, it may lack the deeper interpersonal connection seen in traditional consultations.

The hermeneutic window applies interpretative methodologies to patient care. This approach emphasises engaged listening, considering the broader life context of the patient, exploring clinician intuition, and fostering communication through reflective practice. In contrast to the algorithmic approach, hermeneutics supports a more personalised interaction between clinician and patient, co-creating meaning throughout the consultation.

Aim: To evaluate the impact of TT on patients, triaging GPs, and administrative teams, focusing on communication quality, feeling of connectedness, job satisfaction, and perceived patient care.

Design and Setting: Mixed-methods observational study in a large urban general practice in South London.

Method: Surveys were administered one-month post-implementation of TT. Likert scale responses were analysed quantitatively, while open-ended responses underwent thematic analysis.

Results: Patients reported timely care and communication, though challenges with accessibility for patients uncomfortable with IT were highlighted. GPs expressed concerns about the superficial nature of interactions but acknowledged increased efficiency. Administrative teams reported reduced stress and easier appointment management but also noted the need for better personalisation of patient interactions.

Conclusion: Total Triage appears to reduce stress and increase efficiency but requires further adaptation to ensure personalisation and better access for vulnerable groups. Ongoing feedback from all stakeholders is crucial to refining the system.

**8. Dr Selma Audi**

The Hermeneutic Window and Machine-Based Interactions: how do we prevent depersonalisation?

*Audi S, Shah R*

Background: Digital technologies are transforming healthcare delivery by enhancing accessibility and providing innovative ways to manage increasing patient demand. With the rise of Artificial Intelligence (AI) and Machine Learning (ML), a tsunami of further digitisation is on the horizon. However, concerns remain regarding the lack of personalisation, context, and empathy in machine-based interactions.

Hermeneutics, the interpretation of human experience, may offer a valuable lens through which to evaluate how well digital health tools maintain personalisation in patient-clinician interactions.

Aims: To develop a targeted questionnaire with specific domains informed by hermeneutics that can be applied to assess novel digital health tools.

Method: Prior to implementing a new digital system in a London general practice, we conducted a literature review and gathered feedback from clinicians and patients to identify key concerns surrounding the technology. These concerns were then grouped, and, using the hermeneutic window, a set of questions was developed to assess personalisation, empathy, and understanding in machine-mediated healthcare.

The final questionnaire was administered to both clinicians and patients. Following this, group feedback sessions were held with both cohorts to evaluate whether the questionnaire effectively addressed the concerns regarding depersonalisation, empathy, and understanding.

Results: Feedback from patient participation groups indicated that questions effectively captured core concerns regarding the loss of personalisation, with participants highlighting the need for a 'human at the core' of digital health use. However, specific instances of mutual mis-understanding were uncovered, with suggestions for editing the questionnaire. Recommendations for adapting the questionnaire to other healthcare settings are provided.

**9. Dr Alexis Bailey**

Epigenetic control of stress and environmental enrichment interplay on anxiety and prefrontal cortex BDNF expression

*Silva N; Costa G; Gomes de Almeida M, Marianno P, Belo da Silva A, Petenati Da Rovare V, Beu Rae M; Aparecida dos Santos Eichler R, Chivers P, Camarini R*

While the detrimental effect of chronic stress in the development of stress-related psychopathologies is well recognized, the complex interplay between environmental enrichment (EE) and chronic stress and the mechanisms underlying them is unclear. Chronic stress causes impairment of brain-derived neurotrophic factor (BDNF) signaling in the prefrontal cortex (PFC) and epigenetic modifications which are all implicated in the development of depression/anxiety. In contrast, EE is known to enhance BDNF levels, induce beneficial epigenetic modifications, and is considered protective against stress-related psychopathologies. Here, we first investigated the impact of chronic unpredictable mild stress (CMS) on anxiety-like behaviour, expression and protein levels of Bdnf and the epigenetic profile of Bdnf in the PFC of mice reared in EE conditions. We also investigated whether the effect of CMS on EE-reared mice is mediated by a mechanism involving DNA methylation. CMS precipitated anxiety-like behaviour in EE mice but not in standard housed ones. This effect was reversed by the methylation inhibitor 5-aza-2'-deoxycytidine, revealing an epigenetic mechanism. CMS caused a reduction in exon I, II and IX Bdnf gene expression in EE mice but no effect on BDNF protein levels. Neither CMS, EE nor their combination affected DNA methylation profile of Bdnf exon IX. These findings shed light on the emotional behavioural consequences and the molecular mechanism underlining the complex interplay between CMS and EE, which may have implications for the management of certain stress-related psychopathologies.

**10. Mr Oscar Bandmann**

Eligibility for R444.1 germline genetic testing in breast cancer patients: A single centre retrospective evaluation

*Bandmann O, Singh A, Kelleher M, Snape K*

Purpose: Olaparib is a NICE approved PARP inhibitor that has been shown to demonstrate benefit in the adjuvant treatment of high-risk HER-2 negative early breast cancer in BRCA1/2 variant carriers (1). The National Genomic Test Directory was updated to include a new germline genetic testing panel termed R444.1 for patients who are potentially eligible for Olaparib (2). There is no published data on estimated proportions of breast cancer patients who would be eligible for this panel. We

therefore undertook a retrospective service evaluation of a cohort of breast cancer patients to identify the proportion of who would meet R444.1 eligibility.

Methods: Data was collected on all patients who had invasive breast cancer treated at St George's University Hospital diagnosed between 01/04/2022-01/04/2023. Parameters essential for R444.1 eligibility evaluation were recorded, including tumour size, tumour grade, ER score, PR score, HER-2 score, HER-2 FISH/DDISH status (if performed), lymph node status, number of lymph nodes affected, if adjuvant chemotherapy received, if patient had neoadjuvant therapy: residual disease breast status, residual disease lymph node status and CPS + EG score =>3.

Results: 207 patients were diagnosed with invasive breast cancer within the evaluation period. 204 (99%) were female and three were male (1%). 12 (5.8%) of this cohort met R444.1 criteria. Three were eligible under criteria 1, one under criteria 2, two under criteria 3, and four under criteria 4. 6 (50%) of those who meet eligibility for R444.1 were also eligible for the R208 panel and underwent testing. One of the patients tested for the R208 panel was found to carry a pathogenic variant in BRCA2.

Conclusion: This single institution service evaluation demonstrates that 5.8% of a cohort of early breast cancer patients are eligible for R444.1 germline genetic testing panel with 50% patients also being eligible for R208.

**11. Dr Arka Banerjee**

Nailbed biopsies in subungual melanoma – how can we improve diagnosis?

*Banerjee A, Madaan A, Vinnicombe Z, Odili J*

Subungual melanomas are a sub-type of acral lentiginous melanoma that arise in the nailbed. Unlike other melanomas, subungual melanomas are not related to sun exposure. Subungual melanomas have a prevalence of 3% in populations with lightly pigmented skin. However, subungual melanomas represent a total 30% of melanomas in populations with darkly pigmented skin. Indeed, subungual melanomas are the most common variant of melanoma in people of Afro-Caribbean (75% of melanomas in Afro-Caribbean populations), Asian (25% of Chinese and 10% of Japanese) and Hispanic ethnicity. Subungual melanomas most commonly present as a dark, black vertical band that involves a single nail, usually wider than 3mm with proximal widening, irregular side borders and possibly nail plate dystrophy (65% of cases). The hallux and thumb are the most common digits affected by subungual melanoma – representing 75-90% of cases.

Cutaneous melanoma treatment and prognosis has improved vastly over the years. This can be attributed largely to improved early detection. Unfortunately, this has not extended to subungual melanoma. Resultingly, subungual melanomas (and other acral lentiginous melanomas) display a poorer prognosis than cutaneous melanoma, with a 5-year survival rate of 16-87%. The result of this is felt disproportionately in Black, Asian and minority ethnic communities.

Subungual melanomas are definitively diagnosed by nailbed biopsy. The question arises – who to biopsy? There are no current guidelines on this. Resultingly, many centres report very low positive predictive values (PPVs) in nailbed biopsy for diagnosing subungual melanoma. Unnecessary nailbed biopsies cause significant pain, morbidity as well as poor cosmetic outcomes for patients.

In this study, we consider a cohort of 158 patients who have nailbed biopsies between April 2010 – June 2023. We first calculate the PPV and negative predictive value (NPV) of nailbed biopsies for

subungual melanomas. We then apply a modified criteria to detect subungual melanomas (Levit et al, 2000) to our cohort to determine if there is a change in the PPV and NPV and make recommendations regarding best practice for diagnosis of subungual melanomas.

**12. Dr Arka Banerjee**

Surgical Discharge Summaries: Comparing the Performance of a London Tertiary Centre Colorectal Surgery Team to National Standards

*Banerjee A, Mitchell R, Hagger R*

Background: Discharge summaries are critical to continuity of care, particularly surgical patients discharged with drains, large wounds, and complex analgesia requirements. The Professional Records Standard Body and Royal College of Physicians have published national guidelines on hospital discharge summaries. The aim of this audit was to assess the adherence of discharge summaries by the colorectal surgery team in a London tertiary centre to these guidelines.

Methods: Criteria were created to assess the adherence of discharge summaries to national guidelines:

1. Reason for admission
2. Events/procedures during admission
3. Investigation results (if any)
4. Medication changes (if any)
5. Post-op plan
6. Safety netting advice
7. Follow-up plan & requested actions

100 consecutive discharge summaries, from March 2024 to April 2024, were scored on these criteria (Cycle 1).

Results: The median and modal scores were both 5.00/7.00. The mean score was 4.15/7.00. 4 patients did not have discharge summaries recorded on the system. The events/procedures during admission had the highest adherence (89%), while safety netting advice had the lowest adherence (14%). The most comprehensive discharge summaries included important negatives.

Key Messages: A succinct discharge summary proforma populated from admission to discharge with relevant information daily can improve discharge summary quality and adherence to national guidelines.

References: https://theprsb.org/wp-content/uploads/2019/02/eDischarge-Summary-Maintenance-Release-Implementation-Guidance-Report-v2.1-23.1.19.pdf, accessed 14 May 2024

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**13. Dr Arka Banerjee**

Audit of Inpatient Venous Thromboembolism Prophylaxis in the Plastic Surgery Department at a UK Tertiary Referral Centre

*Banerjee A, Vissers G*

Background: Venous thromboembolism (VTE) prophylaxis is vital for preventing thromboembolic episodes in patients. Surgical patients are at greater risk due to a pro-thrombotic internal milieu and limited mobility post-operatively. The aim of this audit was to assess the adherence of the Plastic Surgery Department in a London tertiary centre to hospital guidelines for VTE prophylaxis and VTE prophylaxis plan documentation, and to implement changes to improve adherence and documentation.

Methods: VTE Risk Assessment and VTE Prophylaxis Prescription was assessed for Plastic Surgery inpatients from 17 June 2023 – 30 June 2023 (Cycle 1: 53 inpatients) and 19 August 2024 – 1 September 2024 (Cycle 2: 53 inpatients). Time till completion of VTE Risk Assessment and time till completion of VTE Prophylaxis Prescription was calculated and compared to the standards. Percentage of patients with guideline-compliant VTE Risk Assessment, VTE Prophylaxis Prescription, and overall guideline compliance, was also calculated.

Results: The second cycle showed reduction in times to completion of risk assessment and VTE prophylaxis prescription, and demonstrated increased completion rates of VTE Risk Assessment, VTE Prophylaxis Prescription, increased VTE plan documentation rates and increased overall guideline compliance.

Key Messages: Completion of VTE Risk Assessments and documenting a VTE plan allows safe compliance with guidelines in a surgical setting

Reference: S. Mounter, P. Kanagasabapathy, (2022). St George’s Hospital Venous Thromboembolism Policy [available on Trust Intranet]

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**14. Mr Simon Beach**

Antimicrobial susceptibility and Characterisation of AMR genes from GBS isolates from Kampala Uganda

*Beach S, Farley C, Shelley D, Portal E, Spiller O, Davies H, Wamawobe A, Nsimire J, Kyohere M, Le Doare K*

Introduction: Group B Streptococcus (GBS) is a leading cause of neonatal sepsis and infant mortality globally. This study aimed to characterise the antimicrobial susceptibility and carriage of Antimicrobial Resistance (AMR) genes in a range of GBS isolates from pregnant women and infants from Kampala Uganda.

Methods: 1068 GBS Isolates from rectal & vaginal swabs from colonised pregnant women, rectal & nasopharyngeal swabs from colonised infants and blood cultures from infant sepsis cases were identified via MALDI-TOF. Minimum inhibitory concentrations (MICs) were determined for tetracycline, chloramphenicol, levofloxacin, benzylpenicillin, gentamicin, erythromycin, and clindamycin, using agar dilution and susceptibility determined concordant with EUCAST guidelines. PCR screening was also performed, using primers targeting 6 AMR associated genes.

Results: Twenty-nine Isolates (2.7%) from 21 patients showed high gentamicin resistance (MICs >128 mg/L) and resistance to erythromycin and tetracycline, however, they were sensitive to chloramphenicol, benzylpenicillin, and clindamycin. They all carried the AAC(6')-APH(2') and ermA genes. Forty-five isolates (4.2%) from 34 patients were resistant to chloramphenicol (MICs = 16-32 mg/L), erythromycin and tetracycline but were sensitive to clindamycin, benzylpenicillin and gentamicin. All carried the catQ, ermA and mefA genes. Ninety-four isolates (8.8%) from 73 patients were resistant to clindamycin (91/94; MICs >4 mg/L & 3/94; MICs = 1-2 mg/L). All but 3 harboured ermA or ermB, showing erythromycin resistance. These 3/94 strains were susceptible to erythromycin with lincosamide specific resistance genes. In total 335/1068 (31.3%) strains from 248/693 (35.8%) patients were resistant to erythromycin (MIC > 0.5mg/L). All isolates were susceptible to benzylpenicillin.

Conclusion: Resistance to WHO “Access” category antibiotics was low but still significant. Erythromycin resistance was high and often found in conjunction with resistance to other antimicrobials. The prevalence of multi-drug resistant strains carrying multiple AMR associated genes emphasises the importance of routine GBS surveillance and susceptibility testing.

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**15. Giselle Best**

Novel virulence factors of avian paramyxoviruses

*Best G, Goodbourn S, Ross C, Banyard A*

Avian paramyxoviruses (APMVs) are negative-sense RNA viruses of birds. In poultry, virulent APMV serotype 1 (APMV-1) causes Newcastle disease (ND), an acute and highly contagious disease which frequently causes epizootics worldwide. When in commercial poultry, the associated increases in morbidity and mortality can result in detrimental socio-economic consequences.

To qualify as an ND virus, APMV-1 must have either an ICPI score of >0.7, or a motif in the F2/F1 cleavage site of the fusion (F) surface glycoprotein consisting of multiple basic amino acids and a phenylalanine at position 117. As the presence of this multi-basic site determines the mechanism of viral entry used, it is widely regarded as the primary virulence factor.

Pigeon paramyxovirus-1 (PPMV-1) is an antigenic host variant of APMV-1 endemic in Columbiformes in the UK. Recent PPMV-1 isolate analysis has highlighted a reduction in pathogenicity in contemporary strains in comparison to 1980s/90s strains; yet, crucially, both groups were found to consistently encode this multi-basic motif. Consequently, we hypothesised that virulence is no longer governed by viral entry, and that other regions of the viral genome have evolved to fill the gaps.

We identified two strains of PPMV-1 which demonstrated this shift: virulent PPMV-1/Fantail/United_Kingdom/1996|VI.1 (“AV250-96”) and ‘avirulent’ PPMV-1/Pigeon/United_Kingdom/2015|VI.2.1.1.2.2 (“AV593-15”), Previous studies have implicated the ribonucleoprotein complex as a virulence factor, as the interplay of components NP, P and L facilitates viral replication. We therefore generated expression vectors for NP, P and L from both strains to investigate transcription functions via minigenome assays. Here, we observed high relative transcription levels for AV250-96, whereas AV593-15 appeared non-functional. We additionally ruled out a potential relationship between virulence and interferon (IFN) antagonism efficacy by demonstrating that V proteins of both isolates blocked chicken IFN2 expression to the same degree.

From these preliminary findings, we propose a novel function as virulence factors of the NP, P and L transcription components. We aim to explore this hypothesis further through reverse genetics systems alongside experiments in ovo and in vitro.

**16. Mr Martin Bird**

Variants in LPA are associated with mutation-negative Familial Hypercholesterolaemia: whole genome sequencing analysis in the 100,000 Genomes Project.

*Bird M, Rimbert A, Pittman A, Humphries S and Futema M*

Background: Familial Hypercholesterolaemia (FH) is an inherited disease of high LDL-cholesterol (LDL-C) caused by defects in LDLR, APOB, APOE and PCSK9 genes. A pathogenic variant cannot be found in ~60% of clinical FH patients. Using whole genome sequencing (WGS) we examined genetic determinants of FH.

Methods: WGS data generated by the 100,000 Genomes Project (100KGP) included 536 FH patients diagnosed using the FH Simon Broome criteria. Rare variants in known FH genes were analysed. Genome-wide association study (GWAS) between 443 FH variant-negative unrelated FH cases and

77,275 control participants of the 100KGP was run using high coverage WGS data. Polygenic risk scores for LDL-C (LDL PRS) and lipoprotein(a) (LPA PRS) were computed.

Results: An FH-causing variant was found in 17.4% of FH cases. GWAS identified the LPA gene locus being significantly associated ($p<1x10-8$). FH variant-negative participants had higher LDL and LPA PRSs in comparison to the controls ($p<1.0\times10-16$ and $p<4.09\times10-6$, respectively). Similar associations were found in the monogenic FH with both LDL and LPA PRSs being higher than in controls ($p<4.03\times10-4$ and $p<3.01x10-3$, respectively). High LDL PRS was observed in 36.4% of FH variant-negative cases, whereas high LPA PRS in 18.5%, with 7.0% having both high LDL and LPA PRSs.

Conclusions: This genome-wide analysis of monogenic and polygenic FH causes confirms a complex and heterogenous architecture of hypercholesterolaemia, with LPA playing a significant role. Both Lp(a) and LDL-C should be measured for precision FH diagnosis. Specific therapies to lower Lp(a) should be targeted to those who will benefit most.

Keywords: Familial hypercholesterolaemia, whole genome sequencing, Lp(a), LPA, genome wide association study

**17. Mr Martin Bird**

Novel start codon variant in the 5'UTR of LDLR associated with Familial Hypercholesterolaemia

*Bird M, Jyun-Peng Tung C, Pittman A, Nohturfft A, Futema M*

Familial Hypercholesterolaemia (FH) is a genetic disorder, due to pathogenic variants in LDLR, APOB, and PCSK9 genes, characterized by elevated low-density lipoprotein cholesterol (LDL-C) concentration and a significantly increased risk of premature coronary heart disease. Using the 100,000 Genomes Project FH cohort's whole genome sequencing data and an in silico UTRannotator, we identified a novel variant c.-35C>G in the 5' untranslated region (5'UTR) of LDLR, predicted to introduce an upstream open reading frame (uORF). Through a literature search, we also found the c.-22delC LDLR variant predicted to create uORF. Using luciferase and HiBiT (High Bit peptide) assays, we demonstrate that the c.-35C>G and c.-22delC variants reduce LDLR promoter activity and utilize the upstream AUG (uAUG) start site introduced by the variant for translation initiation of the gene. These findings confirm a novel FH-causing LDLR variant, leading to a premature start of translation and a truncation after 36 codons, underscoring the need for expanded genetic screening beyond coding regions. Future studies should focus on further characterizing 5'UTR variants to better understand their role in FH.

Keywords: Familial hypercholesterolaemia, whole genome sequencing, 5'UTR

**18. Dr Gabrielle Blumer**

*Blumer G*

Background and Objectives: Children and young people with acquired brain injury (ABI) are vulnerable to experiencing difficulties with their mood, cognition and behaviour. Specialist individual assessment and intervention is offered to young people with ABI who have the highest level of clinical need but many children with lower levels of emotional and behavioural difficulties may not receive support. The paediatric neuropsychology service at St George's Hospital is re-structuring the service offering towards a tiered framework for interventions, based on clinical need. In 2024, pilot groups have been facilitated to attempt to meet the needs of the 'targeted intervention' tier population, who do not require intensive support but would benefit from a lower-level intervention.

Method: Children and young people with ABI were invited to attend one-day groups at St George's hospital. The children's group (aged approximately 6-11) followed the narrative Beads of Life methodology and the young person's group (aged approximately 12-16) followed the narrative Tree of Life methodology. Alongside each group, a parallel parent support and psychoeducation group was run simultaneously. The effectiveness of the child group was measured using a standardised outcome measure as well as qualitative feedback from semi-structured interviewing. Parents were also asked to provide feedback on their experience.

Results and Implications: Outcomes and feedback from children, young people and parents have been used to guide the service development. Feedback was positive and groups have been repeated incorporating changes as appropriate. The second group was co-facilitated by an attendee of a previous group.

**19. Mr Greg Booth**

Development of a Physical Activity Maintenance intervention for people with PERsistent musculoskeletal pain (PAMPER): study protocol

*Booth G, Bearne L, D'Lima D, Hudda M, Ussher M*

Background: Persistent musculoskeletal pain is a disabling condition. Many people with the condition attend pain management programmes (PMPs) for self-management support. Physical activity (PA) is promoted on PMPs as it improves pain, function and quality of life. However, PA is often not maintained after PMPs. This project will develop an intervention to support PA maintenance after PMPs for people with persistent musculoskeletal pain. Phases 1 and 2 will explore the factors influencing PA maintenance in people with persistent musculoskeletal pain and identify potential intervention components. Phase 3 will co-design the intervention.

Methods: Setting: UK NHS.

Phase 1: Qualitative study. Participants (n=35): people with persistent musculoskeletal pain 6-18 months post-PMP, their PA supporters, and PMP healthcare professionals. Semi-structured interviews will explore factors influencing PA maintenance after PMPs and identify potential intervention components. Data will be analysed inductively using thematic analysis and deductively using the Behaviour Change Wheel (BCW) and Template for Intervention Description and Replication (TIDieR) checklist.

Phase 2: Prospective longitudinal study. Participants: people with persistent musculoskeletal pain (n=100-120). Assessments will be at PMP completion and six-months post. Measures: factors influencing PA maintenance identified in phase 1 and objective PA (accelerometry). The questionnaire will ask about intervention components. Regression analyses will assess the associations of each factor with PA maintenance. Qualitative data will be analysed using the TIDieR checklist and BCW.

Phase 3: Intervention co-design. Participants: people with persistent musculoskeletal pain 6-18 months post-PMP, their PA supporters, and healthcare professionals. Participants will attend workshops to co-design and refine the intervention. data analysis will be informed by the BCW and TIDieR checklist.

Conclusions: This project will result in a new PA maintenance intervention for people with persistent musculoskeletal pain that have completed PMPs, addressing the personal and healthcare burden. The intervention will be ready for full development and testing in a trial.

**20. Dr Liza Bowen**

Global blood pressure screening during and after pregnancy: May Measurement Month 2019

*Bowen L, Stevens R, Schutte AE, Beaney T, Poulter N, McManus RJ, Chappell LC*

Background: Hypertensive disorders of pregnancy are associated with high maternal and fetal morbidity and mortality. There are limited global data on characteristics of women during and after pregnancy hypertension.

Methods: May Measurement Month is a global campaign to raise awareness of the importance of blood pressure. Adults (=18 years) recruited through opportunistic sampling during May 2019 had blood pressure measured and comorbidities and lifestyle data collected. This secondary analysis included 16,519 pregnant women and 529,172 non-pregnant women (16,457 with previous raised blood pressure in pregnancy), from 64 countries.

Results: Almost half of the pregnant women (43.3%) reported not having had their blood pressure measured in the past year, and 14.3% (95% CI 12.1, 16.6) had hypertension (blood pressure =140/90 mmHg or taking antihypertensive medication). Diabetes was self-reported in 7.6% (5.9, 9.3) of pregnant women with hypertension and 2.8% (1.9, 3.6) of pregnant women without hypertension.

In non-pregnant women with and without a history of pregnancy hypertension, age-standardised proportions with current hypertension were 53.2% (50.8, 55.7) vs 33.3% (29.3, 37.3); with diabetes were 14.4% (11.8, 17.0) vs 8.5% (6.3, 10.9); and with BMI=30kg/m2 were 28.4% (23.5, 33.3) vs 16.6% (13.0, 20.2).

Conclusions: Hypertension in pregnancy was common in this global sample but many cases had not previously been identified. There was clustering of cardiovascular risk factors in both pregnant women with current hypertension and previous raised blood pressure in pregnancy. This work highlights the importance of screening pregnant women for hypertension, which remains a challenge in large parts of the world.

**21. Ms Caitlin Bowles**

Investigating the effects of NALCN inhibition on cancer cell invasion and metastasis

*Bowles C*

Metastasis is the process by which cancer cells spread through the body and form secondary tumours in new areas of the body. It is the cause of death in over 90% of cancer patients, but the mechanisms are poorly understood. Inhibiting metastasis has the potential to drastically improve care and prognosis for cancer patients, but current treatments have limited efficacy.

The sodium leak channel non-selective protein (NALCN) is an ion channel that maintains membrane potential through sodium background leak conductance. The first study investigating the role of NALCN in tumours found that deletion of NALCN dramatically increased both metastasis and the number of circulating tumour cells. However, another study reported that NALCN signalling enhances metastasis through signalling through the proto-oncogene Src. No mechanism of action for NALCN in metastasis has yet been identified. To design a therapeutic intervention to halt metastasis by altering NALCN signalling, it is essential to understand the role it plays.

Firstly, I aim to understand how the expression of NALCN changes during disease progression, assessing expression of markers in healthy cells, benign tumours, and malignant metastatic tumours using western blotting and proteomic profiler arrays.

The second aim of the project is to study how NALCN dynamics are altered when the channel is blocked in our cancer cell lines to identify any changes in metastasis when NALCN signalling is absent. Patch clamp electrophysiology and immunocytochemistry will be used to assess the effectiveness of the inhibitors.

Thirdly, we will aim to establish the relationship of NALCN with Src kinases, and how this relationship effects the metastatic properties of cells. Inhibitors of NALCN and Src kinases will be administered to cells, and the effects on invasion and metastasis will be studied using migration and wound healing assays in comparison with untreated controls.

Studying the expression of NALCN through disease progression will provide insight into whether the tumour cells are using NALCN signalling to promote disease. I will then block NALCN signalling to assess whether this affects the metastatic properties of cancer cells. Identifying a role for NALCN in metastasis could provide a therapeutic target to prevent metastasis in patients.

**22. Ms Rachel Bowsher**

Comparison of Mortality in People with Type 2 Diabetes between different Ethnic Groups: Systematic review and Meta-analysis of Longitudinal Studies

*Bowsher R, Bailey A, Marczylo T, Wright MD, Gooch, Marczylo E.*

Current associations between smoking and COVID-19 are conflicted with limited research on the impact of vaping. With 5.6 million adults in the UK now vaping (as of August 2024), understanding toxicological impacts and any associations with respiratory viruses is essential to improve public health guidance.

HBEC3-KT cells were grown at the air-liquid interface for 14d to allow for differentiation into a pseudostratified epithelium and the barrier integrity and gene expression for markers of interest

was assessed. Using this validated model, cells were exposed to e-cigarette or tobacco cigarette condensate for 2h and 24h later, infected with SARS-CoV-2 (Victoria strain) for 2h. 24h post-infection, cells were harvested to analyse gene expression changes in key genes and pathways of interest.

Mostly non-significant changes were observed in viral entry genes following e-cigarette exposure and SARS-CoV-2 infection, compared to the infection alone. Whereas immune markers were significantly downregulated in e-cigarette exposed and SARS-CoV-2 infected cells, compared to the control. As the endpoint for gene expression was 24h post-infection, this suggests e-cigarette exposure causes a dampened immune response and therefore that vapers may have a reduced ability to respond to infection.

Exposure to tobacco cigarette alone causes significant downregulation in viral entry genes such as ACE2 and TMPRSS2. However, when the exposure is combined with infection, these gene expression alterations were not significantly different to the infection alone, suggesting no altered susceptibility. This demonstrates the importance of utilising a cell model that does not infer susceptibility without the presence of infection. Similarly, immune markers were non-significantly altered compared to the control suggesting smokers do not experience increased disease severity.

In summary, e-cigarette and tobacco cigarette exposure likely does not increase an individual's susceptibility to SARS-CoV-2. Despite this, e-cigarette users may experience a dampened immune response to be able to fight infections and could have a longer period of symptomatic disease. This demonstrates the need for further research into e-cigarettes and their interactions with the immune system as it may also be relevant for other respiratory viruses. This project will help to provide scientific evidence for public health advice and inform e-cigarette public health policies.

**23. Dr Lottie Brown**

The Diagnosis of Mucormycosis by PCR: a Systematic Review and Meta-analysis

*Brown L, Tschiderer L, Barnes RA, Cruciani M, Donnelly JP, Hagen F, Willeit P, White PL, Prof Lackner M*

Background: This systematic review and meta-analysis examine the performance of polymerase chain reaction (PCR) assays for diagnosing mucormycosis.

Methods: A standardised search was conducted from conception to November 10th 2023 using PubMed, Embase, Global Health and Cochrane library. Using a bivariate meta-analysis, the diagnostic performance of PCR was examined against the European Organisation for Research and Treatment of Cancer–Mycoses Study Group Education and Research Consortium 2020 (EORTC-MSGERC) definition of proven and probable invasive mould disease, as applied to mucormycosis.

Findings: Of 4697 articles, a total of 26 met inclusion criteria, including 5389 PCR reactions on 4736 non-duplicate specimens from 700 patients who met the EORTC-MSGERC definitions of proven/probable mucormycosis and 3983 patients who did not meet the criteria. According to specimen type, sensitivity of PCR varied ($p<0.001$) whereas specificity was similar ($p=0.205$). Bronchoalveolar lavage fluid offered highest sensitivity of 97.2% (95% CI 82.3–99.6%), specificity of 96.0% (95% CI 89.8–98.5%), LR+ of 24.3 and LR- of 0.03. Tissue provided sensitivity of 88.9% (95% CI 81.4–93.6%), specificity of 87.1% (95% CI 68.2 – 95.5%), LR+ of 6.9 and LR- of 0.13. Blood provided sensitivity of 80.6% (95% CI 71.5–87.3%), specificity of 95.5% (95% CI 88.1–98.4%), LR+ of 18.0 and

LR- of 0.20. Formalin-fixed paraffin-embedded (FFPE) specimens provided the lowest sensitivity of 70.5% (95% CI 60.9–78.5%), specificity of 98.7% (CI 95% 94.1–99.7%), LR+ of 54.3 and LR- of 0.30. The covariates best explaining heterogeneity of the overall analysis were specimen type, study design (cohort versus case-control) and patient population (COVID-19 versus other), while disease prevalence and PCR (conventional versus quantitative) had less impact on heterogeneity.

Interpretation: This meta-analysis confirms the high performance of PCR for diagnosing mucormycosis and supports the instatement of PCR detection of free-DNA in blood, BALF and tissue into EORTC-MSGERC definitions and diagnostic guidelines for mucormycosis.

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Interpretation: This meta-analysis confirms the high performance of PCR for diagnosing mucormycosis and supports the instatement of PCR detection of free-DNA in blood, BALF and tissue into EORTC-MSGERC definitions and diagnostic guidelines for mucormycosis.

**24. Ms Megan Brown**

Development of a Breast Milk Assay to Evaluate IgG and IgA Antibodies in SARS-CoV-2 Vaccinated Women

*Brown MA, Galiza E, Clark D, Daniel O, Hall T, Le Doare K, Heath P, and Preg Cov study team*

The COVID-19 pandemic has highlighted the need for effective immune protection strategies for infants, especially in the context of maternal vaccination. Immunological components transferred to the infant via breastmilk are thought to be a crucial mechanism of passive immunity in the infants first few months of life.

Multiplex assays for SARS-CoV-2 specific antibodies (Nuclear, Receptor Binding Domain, Spike 1 and Spike 2) in breastmilk allows insights into potential immune benefits for breastfed infants. This assay has been used to assess 84 participants colostrum and breast milk samples (taken at delivery and between 12-14 days post-delivery respectively) from women taking part in the Preg-Cov study (A Phase II, randomised, single-blind, platform trial to assess safety, reactogenicity and immunogenicity of COVID-19 vaccines in pregnant women in the United Kingdom).

The Bio-Rad Pro human SARS-CoV-2 serology kit methods were adapted to analyse breastmilk and subsequent quantification of the IgG and IgA levels in each sample. Preliminary results indicate that both IgG and IgA specific to SARS-CoV-2 antibodies are detectable in breast milk post-vaccination, with IgA levels generally higher than IgG but showing significant variability in antibody levels between participants. IgG was detected at lower but more consistent concentrations across samples. These findings suggest that vaccination induces an antibody response in breast milk, with IgA potentially contributing to mucosal immunity and IgG to systemic immunity in infants and lays the foundation for further work to testing the impact of antenatal vaccination timing.

**25. Ms Aurora Campagna**

Generating novel 3D cell models to study the role of γδ T cells in the infiltration and killing of Prostate Cancer

*Campagna A, Cieza-Borrella C, Valderrama F, Bodman-Smith M.*

Prostate Cancer (PrCa) is the most common cancer in men worldwide.

Current challenges refer to the difficulty distinguishing aggressive PrCa from indolent disease and the low availability of treatment options; this is partly due to the lack of accurate cellular models representing the disease to develop more conclusive prognostic models and effective therapeutic strategies.

Spheroids are three-dimensional cell culture models which use human tissue and allow cells to organise into structures that resemble the in vivo architecture of the organ of origin. This model can incorporate other cell populations which makes it a promising tool for studying cellular changes associated with PrCa development and the interactions between cancer cells and the tumour microenvironment components.

Our group has developed PrCa spheroids that closely resemble physiological and structural characteristics of the disease stage from which they originated. We are interrogating our model to obtain a molecular signature informative of the malignancy status of PrCa spheroids to employ as a diagnostic tool and help in patient stratification for treatment.

We are also using our model to investigate new treatment options for PrCa, focusing on immunotherapy. Gamma-delta ɣδ T cells are one of the most recent candidates for cancer immunotherapy because of their capability to kill cancerous cells.

By using fluorescent confocal microscopy, we have observed migration of ɣδ T cells towards PrCA spheroids; we have then identified a chemokine signature involved in triggering this behaviour by using an immunoblotting approach and validated their role by chemokine receptors blocking on ɣδ T cells.

Using immunostaining and a confocal microscopy approach, we have also shown ɣδ T cell infiltration and destruction of PrCa spheroids upon drug pre-treatment. We then used these findings to interrogate the role of stress markers involved in the pathway of ɣδ T cell-mediated recognition and killing of PrCa spheroids.

Finally, we have investigated the mechanisms of ɣδ T cells infiltration into the tumour mass by investigating weaker points of adhesion between tumour cells, using a molecular signature based on cell-cell contact markers optimised in our laboratory, aiming to shed light to the complex interaction between solid cancer and the immune system.

**26. Dr Iain Carey**

Effects of long-term HbA1c variability on serious infection risks in patients with type 2 diabetes and the influence of age, sex and ethnicity: a cohort study of primary care data

*Carey I, Critchley JA, Chaudhry U, Cook D, DeWilde S, Limb, Bowen L, Woolford S, Whincup P, Sattar N, Panahloo A, Harris T*

Aims: Long-term HbA1c (glycated haemoglobin) variability is associated with micro- and macrovascular complications in Type 2 diabetes (T2D), but it is not well established if it also increases the risk of infections. We explored prospective associations between HbA1c variability and serious infections, and how these vary by HbA1c level, age, sex and ethnicity.

Methods: 411,963 T2D patients in England, aged 18-90, alive on 01/01/2015 in the Clinical Practice Research Datalink with =4 HbA1c measurements during 2011-14. An HbA1c Variability Score (HVS) was estimated (% of successive measurements whose difference exceeds a pre-defined threshold), and patients were categorised (0-<20, 20-<50, 50-<80, 80-100). Poisson regression estimated incidence rate ratios (IRRs) for infections requiring hospitalisation during 2015-19 by HVS and average HbA1c level, adjusting for confounders, and stratified by age, sex, ethnicity and average level. To assess the potential overall impact of variability versus average level, attributable risk fractions (AF) were calculated using reference categories for variability (HVS<20) and average level (42-48mmol/mol).

Results: While increasing HbA1c level and variability were both independently associated with infections, an increased infection risk (IRR>1.2) was seen with even modest variability (HVS=20, 73% of T2D patients), whereas for average level it was observed only at higher values (=64mmol/mol, 27% patients). The positive association between variability and infection was more apparent among patients with the lowest average HbA1c levels (<48 mmol/mol) and observed at all average levels except the very highest (=86 mmol/mol). Estimated AFs were markedly greater for variability than average level (17.1% vs. 4.1%). Associations with variability were greater among older patients, and those with lower HbA1c levels, but not observed among Black ethnicities.

Conclusions: HbA1c variability between T2D patients' primary care visits appears to be associated with more serious infections than average level overall. Well-designed trials can establish whether there are long-term benefits of directly treating variability in HbA1c on infections, quality of life and other diabetes complications.

**27. Dr Veronica Carroll**

Hypoxia and TGF-ß co-operate to induce pulmonary vascular remodelling

*Miah A, Rossinyol Boladeres M, Rodríguez E, Kreutzer J, Carroll V*

Hypoxia is a primary driver of vessel remodelling in the pulmonary vasculature in lung diseases which can lead to pulmonary hypertension (PH) and, ultimately, right ventricular heart failure. Phenotypic changes that occur in hypoxia to pulmonary vascular cells are mediated by the transcription factors, hypoxia-inducible factors, HIF-1 and HIF-2. HIFs regulate genes involved in endothelial to mesenchymal transition, smooth muscle cell plasticity and fibrosis, but the complexity of the regulation of vascular remodelling in PH, such as cooperation with other critical factors, is still poorly understood.

Here, we investigated the role of hypoxia on transforming growth factor (TGF)-ß signalling in pulmonary artery smooth muscle cells using an ex-vivo cell model that recapitulates lung oxygen levels using an Oxygenie portable hypoxic platform which is compatible with time lapse microscopy. Using this system, we studied the effects of TGF-ß on vascular smooth muscle cell growth, proliferation and migration at 21% and 5% oxygen tensions. We could show that TGF-ß inhibits cell proliferation in normoxia, but this inhibitory effect was prevented under hypoxic conditions. Our data show that hypoxia switches the function of TGF-ß to promote vascular smooth muscle cell proliferation which suggests that hypoxia can drive vascular remodelling by reprogramming the effects of TGF-ß in vivo.

This work furthers our understanding of abnormal vessel remodelling in PH and suggests that targeting HIFs may be an effective therapeutic strategy for PH.

**28. Jessica Carter**

The Role of Primary Care in Hepatitis B Elimination in the UK Migrant Context, a Mixed-Methods Study

*Carter J, Kabagambe K, Ko J, Flanagan S, Ghosh I, Jack K, Elsharkawy A, Harris P, Moore D, Brown M, Matthews P, Hargreaves S*

Background: 300 million individuals live with chronic hepatitis B (CHB), with consequences including cirrhosis and cancer. In the UK migrants are disproportionately affected. Many are unaware of their diagnosis and face barriers accessing services. The WHO has called for elimination by 2030. Primary care (PC) is ideally placed but poorly engaged and utilised in CHB care. This study aims to explore UK PC contribution and approaches to strengthen CHB care from migrant and PC perspectives.

Methods: An online survey (21 questions on CHB knowledge/practice/barriers/care delivery) was advertised to PC practitioners. In-depth views were explored through (i) PC focus groups, (ii) semi-structured interviews with migrants with CHB lived experience. Results were analysed to give descriptive statistics and qualitative data using reflexive thematic analysis.

Findings: 218 survey questionnaires, five PC focus-groups (n=16), and sixteen migrant participant interviews were completed. 63.5% of PC practitioners reported regularly seeing patients from high-prevalence countries but only 14.2% had screening policies and 80.3% were unaware of WHO targets. Barriers to CHB screening and management included knowledge, unstandardised pathways, workload, and stigma. 75.8% were under-confident interpreting results. Facilitators included simplified algorithms, specialist support, translated materials and peer-support. Almost 60% stated they would be comfortable with a CHB shared-care model with specialist oversight and funding. Contact-tracing, vaccination, and re-engaging those lost-to-care were identified improvement areas. Focus-groups reflected survey data, preliminary themes included potential of integrated care and empowerment of PC. Migrant participant interview data highlighted the impact of missed opportunities for CHB care on patient experience, importance of "making that first contact count" and sharing power and knowledge through a culturally competent patient-centred approach.

Interpretation: Integrated CHB care is in line with patient and provider preference and could support elimination progress. PC needs to be equipped with simplified pathways, sustainable integrated-care models, specialist support, funding, and culturally competent resources.

**29. Mr Ben Caswall**

Identification of antifungal heteroresistant subpopulations in echinocandin treatment- refractory Candida auris bloodstream isolates

*Caswall B, Bicanic T*

Candida auris is a major cause of fungal invasive bloodstream infections globally and has been categorised as a critical priority pathogen by the World Health Organization due to its propensity for multi-drug resistance. Up to 90% of C. auris isolates are resistant to fluconazole, and in a few cases C. auris showing pan-resistance to all licensed antifungal drugs have been isolated. Currently the recommended treatment for C. auris bloodstream infections is echinocandin therapy, of which about 2% of C. auris isolates are resistant to. However, treatment can still fail despite isolates not being classified as resistant by minimum inhibitory concentration (MIC) testing. In two such cases where patients had a Candida auris bloodstream infection failing to be cleared by anidulafungin (echinocandin) therapy, we have identified anidulafungin heteroresistance, whereby subpopulations within a clonal isolate exist, which display decreased susceptibility to the anidulafungin. The presence of these subpopulations provides a potential link between heteroresistance and failure of anidulafungin therapy, which is the current first line recommended treatment for invasive C. auris infections. Additionally, we have identified, for the first time in a Candida auris isolate, two separate subpopulations, which display different growth phenotypes in the presence and absence of drug compared to the main population of cells. Future work will assess the ability of combinations of antifungal drugs to eliminate these heteroresistant subpopulations.

**30. Dr Umar Chaudhry**

Comparing all-cause mortality risk in people with type 2 diabetes between different ethnic goups: a systematic review and meta-analysis

*Chaudhry U, Fortescue R, Bowen L, Woolford S, Knights F, Cook D, Harris T, Critchley JA*

Background: Type 2 diabetes (T2D) is more common in certain ethnic groups and a leading cause of mortality worldwide. Complications from T2D in people of South Asian and Black ethnicity also vary, when compared to people of White ethnicity. More recent analyses comparing mortality differences between ethnic groups require scrutiny. This systematic review compares mortality risk between people with T2D from different ethnic groups and includes more recent, larger studies.

Methods: We conducted this systematic review following RISMA guidelines (PROSPERO CRD42022372542). We searched nine databases for community-based prospective studies among adults with T2D from at least two different ethnicities. Studies published between January 2000-May 2024, contained ≥100 participants in each ethnic group were included. Two independent reviewers undertook title/ abstract and full-text screening, data extraction, quality assessment using the Newcastle-Ottawa Scale and data analysis; group consensus or a third reviewed helped to resolve conflicts. The primary outcome compared all-cause mortality rates between ethnic groups (hazard ratio (HR) with 95% confidence intervals).

Results: Following an updated search, 33,922 records were screened, of which 13 studies met inclusion criteria and 7 were meta-analysed. The 13 studies incorporated 593,058 T2D participants and 12/13 were of good quality using the NOS. All-cause mortality risk was lower amongst people with T2D from South Asian [HR 0.68 (95%CI 0.65-0.72); 4 studies], Black [0.82 (0.77-0.87); 5 studies] and Chinese [0.57 (0.46-0.70); 2 studies] ethnicity compared to people of White ethnicity. Narrative synthesis corroborated these findings and also highlighted that people of indigenous Māori ethnicity had greater mortality risk compared to people of European ethnicity.

Conclusions:People with T2D of South Asian, Black and Chinese ethnicity have a lower all-cause mortality risk than White ethnicity; Māori ethnicity having higher mortality risk. Factors explaining mortality differences require further study, including understanding complication risk by ethnicity, to improve diabetes outcomes. Clinical risk factors, predisposing influences or clinical management could explain ethnic differences in T2D mortality risk, and therefore require further scrutiny to improve overall diabetes outcomes.

**31. Dr Anissa Chikh**

The ADAM17 signalling axis in cutaneous squamous cell carcinoma

*Omar R, Laidlaw L, Chikh A*

Squamous cell carcinomas (SCCs) are the most common cancers worldwide and occur in all epithelial tissues including skin, cutaneous squamous cell carcinoma (cSCC) and oesophagus. cSCC is the second most common keratinocyte skin cancer, accounting for 15-20% of all cutaneous malignancies. Excessive exposure to ultraviolet radiation (UVR) is by far, the most common risk factor for cSCC. A disintegrin-metalloproteinase (ADAM17) shedding activity has been implicated in the pathogenesis and progression of cutaneous squamous cell carcinoma (cSCC) as well as the pathogenesis of several inflammatory skin disorders. ADAM17 or TNFa-converting enzyme (TACE) modulates the secretion of various cytokines, growth factors, adhesion molecules and receptors.

ADAM17 is the major protease for processing Notch and therefore plays a role in the activation of Notch pathway. Notch and ADAM17 are both endocytosed with HECT-type E3 ubiquitin ligase (ITCH)- participating in Notch's endocytic pathway regulation. ITCH is known to regulate the degradation of key players involved in processes like apoptosis, cell growth and proliferation. In addition, alterations in ITCH are associated with malignancies.

Our work identified a role of ITCH in ADAM17 regulation in control keratinocytes and cSCC. Proximity ligation assay (PLA) experiments were performed in control keratinocytes and showed intense signals corresponding to the formation of complexes between ADAM17 and ITCH. Thus, immunoblottings of a panel of cSCC cell lines (including premalignant and moderately differentiated stages) and control keratinocytes showed an inverse correlation in the expression of ADAM17 and ITCH. Interestingly, keratinocytes depleted for ITCH by siRNA revealed an accumulation of mature ADAM17 protein however during cSCC progression, ITCH regulates positively ADAM17 expression. In addition, we observed by immunohistochemistry that ITCH expression is accumulated in the nucleus of cSCC tissues compared to healthy skin. Together these findings elucidate a novel ITCH associated pathway that identifies ADAM17 as a potential target to treat premalignant and cSCC metastasis.

**32. Dr Isaac Chung**

Stanniocalcin-1 in Chronic Kidney Disease

*Chung I, Whitley G, Banerjee D*

Introduction: Stanniocalcin-1 (STC 1) is a glycoprotein shown to be protective in animals against vascular injury. However, it's role in chronic kidney disease (CKD) patients, prone to vascular events is unknown. It has previously been shown to be produced by endothelial cells under stress in the context of pregnancy. We hypothesize that STC-1 is produced in kidney disease due to uremic stress.

Methods: Serum samples from a previous perspective study on endothelial dysfunction in patients with CKD and healthy controls were assayed for STC-1 using standard ELISA kits. Endothelial dysfunction was measured by brachial artery flow mediated dilation and brachial artery nitroglycerin mediated dilation as part of the protocol of the previous prospective study. Arterial stiffness was measured by pulse wave velocity and aortic augmentation index.

Results: There were 16 patients with CKD and 8 healthy controls. There was a statistically significant difference in STC-1 concentrations between the CKD and healthy control groups (median 144 [IQR 81 – 323] vs median 52 [IQR 12 – 90], p = 0.01). Patients with CKD had significantly lower kidney function compared to healthy controls (median 33 [IQR 26 – 39] vs median 92 [IQR 78 – 111[, p < 0.01). CKD patients also had higher pulse wave velocity (10 ± 2 vs 7 ± 2, p = 0.02), signaling stiff arteries.

Conclusion: Patients with CKD have a higher level of STC-1 when compared to healthy controls. STC-1 may be a molecule of interest in kidney research. There may be a connection between STC-1 molecule and arterial stiffness.

**33. Dr David Clark**

Rapid Detection of SARS-CoV-2 nucleocapsid using electrochemistry-based graphene biosensing

*Ponce M, Clark DJ, Paul MJ, Eckersley NM, Brown MA, Tyrrell G, Christie P, Pounder M, Staines HM*

Background: The importance of rapid diagnostic testing in clinical and non-clinical settings became evident during the COVID-19 pandemic. PCR-based testing, whilst highly sensitive, took considerable time from sampling to result and requires expensive equipment. Rapid Diagnostic Tests (RDTs/LFAs) were also used on a global scale to assess infection by both healthcare professionals and citizens. However, they lacked sensitivity and digital integration into healthcare systems. Here we describe a portable diagnostic platform that will be easy to use at home, with the added value of increased sensitivity and secure digital connection. At the heart of the platform is graphene biosensing. Graphene sensors bridge the diagnostic gap between PCR and RDTs, due to their high sensitivity and high detection speed. A prototype has been developed to detect SARS-CoV-2 nucleoprotein (NP) by antibody capture. Its speed and sensitivity have been demonstrated for SARS CoV 2 NP and there is potential to apply the platform to a wide range of existing, antibody-based applications.

Methods: Commercially available anti-SARS-CoV-2 antibodies were screened by Enzyme-Linked-Immunosorbent-Assay (ELISA) and Surface Plasmon Resonance (SPR); the highest affinity candidate was used to coat graphene biosensors. Two different techniques for detecting antigen binding were used: Square Wave Voltammetry (SWV) and Electrochemical Impedance Spectroscopy (EIS). Three different conditions (NP alone, viral lysis buffer spiked with NP and nasal swabs spiked with NP in viral lysis buffer) were used to assess the biosensor.

Results: the graphene-based biosensor detected SARS-CoV-2 in all three sample types in a dose-dependent manner with a higher sensitivity than ELISA.

Conclusion: Graphene-based biosensors have the potential for integrating a broad range of diagnostic tests that currently utilise ELISA testing, which is slow and often expensive. The findings in these studies demonstrate the potential utility of this prototype graphene-based biosensor-capture antibody combination with clinical samples. Following further optimisation, the intent is for use at home or in a POC setting. Together with secure data collection and monitoring, this diagnostic platform will provide real-time information on a customisable dashboard, via secure cloud-based software analytics, to enable evidence led health policy decisions and guide interventions.

**34. Mr Zack Croxford**

Engineering and optimizing next-generation bispecific immune checkpoint inhibitors for expression in Nicotiana benthamiana

*Croxford, Z*

Immune checkpoint inhibitors have revolutionized cancer treatment. However despite their clinical success challenges persist. Including low response rates, immune-related adverse events and high cost. High cost in particular resulting in limited access to patients in low-to-middle income countries (LMICs). This project aims to overcome these challenges by adapting the most recent bispecific antibody technologies that overcome these challenges and adapting them for expression and assembly in plants – in this case Nicotiana benthamiana. N. benthamiana offers a cheap, sustainable, scalable production platform that is easily transferable to LMICs and low-resource settings.

In order to generate a bispecific immune checkpoint inhibitor, scFvs comprising of the VL and VH of existing ICIs were constructed and attached to an engineered IgG1-based Fc region. Fc regions contained Knob in Hole mutations in order to promote heterodimerization upon assembly as well as the Fc effector silencing 'AAG' mutations. Each 'half antibody' was cloned into the modular plant expression vector pMIDAS. pMIDAS containing the relevant bispecific components were infiltrated into N. benthamiana plants.

'Half antibody' (monomers) can be successfully expressed in N. benthamiana at a level similar to that of IgG1 ICIs. However, infiltration with a single 2-TU pMIDAS construct did not promote dimerization as expected, with most detectable recombinant protein remained monomeric. Monomeric product also did not demonstrate detectable binding to both checkpoint ligands.

Co-expression of 2 1-TU pMIDAS constructs promotes more efficient assembly, enabling dimerization. With an infiltration ratio of 2:1 being identified as the ratio that promotes the highest levels of expression and dimerization. However, trimerization also occurs at equal levels. This mixture of tri/dimers demonstrate binding to both targets.

These observations suggest that in vivo assembly of bispecific ICIs is not the most efficient route to generating bispecific antibodies. Current work aims to determine whether dimers can bind both ligands simultaneously. Future work will explore the potential of in vitro assembly of monomers, a process widely used in the manufacturing of mammalian cell-derived bispecific antibodies.

**35. Ms Ramla Cusman**

The tricarboxylic acid cycle regulates fibroblast-driven tissue remodelling via hypoxia-inducible factor 1a during Mycobacterium tuberculosis infection

*Cusman R, Kutschenreuter J, Chong DLW, Friedland JS*

Background: Mycobacterium tuberculosis (Mtb) causes extensive lung tissue remodelling, driven by matrix metalloproteinases (MMPs). Fibroblasts are a major source of MMPs in a monocyte-dependent network during Mtb infection. Metabolic pathways including the tricarboxylic acid (TCA) cycle, which produces many intermediate compounds, may modulate innate immune responses. Itaconate is a key TCA cycle derivative, which regulates the transcription factor, hypoxia-inducible factor 1a (HIF1a), that drives pro-inflammatory responses in tuberculosis (TB). We investigated the role of itaconate in regulating fibroblast-dependent tissue remodelling and inflammation during Mtb infection.

Methods: Primary human lung fibroblasts (PHLF) were treated with 4-octyl itaconate (4OI, a cell permeable derivative of itaconate) for 1 h prior to stimulation with conditioned media from Mtb-infected monocytes (CoMTb). MMP-1 (a collagenase), MMP-3 (an MMP-1 activator) and IL-1b secretion, and gene expression were measured by ELISA and qRT-PCR respectively. Functional MMP activity was quantified using the EnzChek™ Collagenase Assay Kit which fluoresces upon collagen degradation. HIF1a protein expression in PHLF was measured at 4-48 h by western blot.

Results: PHLF pre-treated with 4OI upregulated CoMTb-induced MMP-1 and MMP-3 secretion in a dose-dependent manner at 24, 48 and 72 h. The maximal effect was observed with 100 uM 4OI at 72 h when PHLF MMP-1 secretion increased from 156.9 to 232.6 ng/ml ($p=0.0002$) and MMP-3 concentrations increased from 425.9 to 529.3 ng/ml ($p<0.0001$). IL-1b secretion was also upregulated with 4OI pre-treatment from CoMTb-stimulated PHLF (286.9 vs. 592.8 ng/ml,

p=0.0002). Furthermore, mmp1 gene expression in PHLF stimulated with CoMTb was increased in response to 4OI treatment (p=0.034). Increased collagen degradation was observed from CoMTb-stimulated PHLF pre-treated with 4OI when compared to CoMTb stimulation alone (p=0.0006). Lastly, CoMTb stimulation induced HIF1a protein expression in PHLF from 8 h onwards, which was increased with 4OI pre-treatment.

Conclusion: Itaconate, which modulates the TCA cycle, increases Mtb-dependent MMP-1, MMP-3 and IL-1b secretion and gene expression in human monocyte-fibroblast networks in TB, as well as upregulation of HIF1a expression in fibroblasts. Specific TCA cycle metabolites may represent potential targets for host-directed therapies to limit inflammation and tissue destruction in TB.

**36. Mr Royce Daran Shakespeare**

Retinal vasculometry associations with cognition status in UK Biobank

*Shakespeare R, Rudnicka AR, Welikala R, Barman SA, Khawaja AP, Foster PJ, Owen CG*

Introduction: Retinal vasculometry (RV) provides a neurovascular biomarker which may relate to cognitive status. However, the presence and form of association remains unclear and unexamined at scale.

Methods: Artificial intelligence-enabled RV measures from 66,350 UKBiobank study participants were related to combined cognition scores. Differences in RV were examined per standard deviation (SD) increase in cognitive score, using multilevel linear regression, adjusted for age, sex, measurement centre, ethnicity, and within-person RV clustering.

Results: 110,282 retinal images from 63,165 (95%) participants (mean age 56.6 years, 55.5% female) were analysed. A one SD increase in cognition score was strongly associated with increased arteriolar width, arteriolar tortuosity, increased venular width particularly among those <50 years and venular area among those >50 years; also, inversely associated with venular tortuosity, and arteriolar and venular width-variance.

Discussion: These easily accessible, affordable and non-invasive RV measures should be evaluated further as an early predictor of future neurodegenerative disease.

**37. Harriet Davidson**

WasteCan: Investigating Wastewater in the context of a Candida auris Outbreak

*Davidson HC, Symes L, Griffin A, Monahan I, Laing K, Bicanic T*

Rationale: Candida auris is a multi-drug resistant WHO fungal priority pathogen which has resulted in costly nosocomial outbreaks. It is not currently subject to routine surveillance in the UK. Clinical surveillance is cost- and labour-intensive, with a low detection rate. Wastewater surveillance (WWS) has been used to quantify other pathogens, offering a pooled sample. Recent work in USA and South Africa has demonstrated that culturable C.auris can be recovered from community wastewater treatment plants receiving effluent from healthcare facilities experiencing C.auris outbreaks.

A London hospital undergoing a year-long outbreak of Candida auris affecting 100 patients invited us to sample wastewater in conjunction with a point prevalence survey in patients being undertaken by the local infection control team.

Methods: Samples were taken from sluice rooms (sluice sinks, macerators and hand sinks) in the wards where PPS was being undertaken – 50ml wastewater and direct swab. Samples were processed within 6h with 2 culture methods in parallel – direct culture on Candida Chromagar and enriched selection culture in Salt-Sabouraud-Dulcitol broth. Direct culture were incubated at 35-37°C and SSDB were placed in shaking incubation at 40-42°C. Cultures were read daily and all yeast colonies were speciated using MALDI-ToF.

Results: C.auris was found in 5/9 wards surveyed. In all 5 of these wards, C.auris was found in patients. 2 further wards had C.auris in the patients. 115 candida isolates were isolated from 35 sites, 32 of which were C.auris, from 10 sites. C.auris grew from the swab in 9/10 sites, and pellet in 4/10 sites. Enriched culture isolated C.auris in 10/10 sites, with 6/10 sites identifying C.auris on direct culture. Macerators were most colonised (5/11 sampled), followed by sluice sinks (4/11), then hand sinks (1/13).

Discussion: C.auris can be isolated from near-patient hospital wastewater. Direct methods show the diversity of Candida spp in WW, and enriched culture method increases sensitivity of C.auris detection. Limitations are the inability to distinguish patient from staff carriage, and the possible exclusion of ambulatory patients colonised with C.auris, whose wastewater may not pass through the sluice rooms. Future work includes sequencing to confirm the relationship between clinical and WW isolates.

**38. Mr Benjamin De Leon**

Investigation of the Quenching Effect of Glutamate Metabolites on cp-EGFP-based Biosensors

*De Leon B, Török K*

Background: Glutamate, regulated by Excitatory Amino Acid Transporters (EAATs) in astrocytes, is a critical neurotransmitter in the central nervous system (CNS). EAAT2, in particular, clears excess glutamate, and its dysfunction is linked to neurodegenerative diseases such as epilepsy. Effective tools for visualising glutamate uptake are essential for studying EAAT2 function and potential disruptions. The iGluU biosensor was developed to monitor extracellular glutamate levels, though observations suggest it may be sensitive to cellular conditions, raising questions about potential interactions with intracellular components.

Hypothesis: We hypothesised that iGluU fluorescence could effectively track glutamate uptake through EAAT2 and that interactions with intracellular metabolites might modulate this fluorescence.

Aims: 1. To examine the effect of glutamate on iGluU fluorescence in EAAT2-expressing cells.

2. To investigate whether intracellular metabolites, such as lactate and acetate, influence iGluU fluorescence, hypothesising that these interactions could impact the biosensor's accuracy.

Methods: HEK293T cells were co-transfected with iGluU and EAAT2-mCherry plasmids. Live-cell imaging confirmed the membrane localisation of both proteins. Fluorometry measured changes in iGluU fluorescence in response to various concentrations of glutamate, lactate, and acetate.

Results: The successful expression and membrane localisation of iGluU and EAAT2-mCherry were verified in HEK293T cells. Changes in iGluU fluorescence were observed with glutamate concentrations of 50, 100, and 500 µM, with a 0 µM control confirming these observations. Similar fluorescence changes were induced by lactate and acetate, suggesting potential interactions between metabolites and the biosensor.

Conclusions: Our results show that iGluU fluorescence responds to glutamate uptake in a concentration dependent manner. Thus, even though the iGluU fluorescence changes may be modulated by intracellular metabolites, iGluU could be useful for studying glutamate transport mediated by EAAT2, and would allow comparison of healthy and impaired transporter function and may be useful in the research of neurodegenerative disorders. Further studies may involve pharmacological agents to test this biosensor's applicability in evaluating transporter functions.

**39. Dr Lorenzo-Lupo Dei**

The Impact of Surgical Myectomy on Exercise Capacity Among Patients with Obstructive Hypertrophic Cardiomyopathy Evaluated with Echo-CPET

*Lupo Dei L, Halasz G, Giacalone G, Beltrami M, Sciarra L, Romano S, Finocchiaro G, Re F*

This study examines the impact of surgical myectomy on exercise capacity in patients with obstructive hypertrophic cardiomyopathy (oHCM), a condition characterized by left ventricular outflow tract obstruction (LVOTO) and associated exercise intolerance. Although pharmacological treatments, such as beta-blockers, calcium channel blockers, and disopyramide, provide limited symptom relief, myectomy offers a viable surgical alternative for patients with persistent symptoms. While septal myectomy is well-documented to improve symptom burden and quality of life, its effects on exercise capacity remain controversial.

Nineteen oHCM patients with confirmed sarcomeric mutations underwent combined cardiopulmonary exercise testing (CPET) and stress echocardiography before and, on average, 13.6 months after myectomy at San Camillo Forlanini Hospital. Key outcomes included peak oxygen consumption (pVO2), the VE/VCO2 slope, and quality of life measures, such as the New York Heart Association (NYHA) class and the Minnesota Living with Heart Failure Questionnaire (MLHFQ). Resting and exercise echocardiograms, performed according to a standardized protocol, evaluated LVOTO gradients and cardiac function parameters.

Results revealed significant LVOTO gradient reductions, both at rest (from 52 ± 33.5 to 10.7 ± 12.5 mmHg) and during peak exercise (from 59.6 ± 43 to 14.4 ± 6.2 mmHg, p=0.002), confirming effective LVOTO relief. Improvements were noted in functional capacity, with an increase in pVO2 (from 16 to 18.6 mL/kg/min, p=0.02), though 26% of patients (non-responders) exhibited minimal changes. Quality of life also improved, with better NYHA class and MLHFQ scores (from 30 to 24.2, p=0.04). Importantly, left ventricular systolic function and other structural parameters were preserved post-surgery; however, no significant improvements were observed in diastolic function or atrial size.

These findings support surgical myectomy's role in alleviating LVOTO and enhancing both exercise capacity and quality of life in symptomatic oHCM. Yet, persistent diastolic dysfunction in a subset of patients suggests additional therapeutic needs. Emerging therapies, such as cardiac myosin inhibitors, could serve as valuable adjuncts by directly addressing diastolic dysfunction, improving ventricular relaxation, and potentially enhancing pVO2 across all patients, including non-responders.

Future studies should examine the role of cardiac myosin inhibitors in conjunction with surgical intervention to optimize outcomes and expand functional capacity for oHCM patients.

**40. Dr Joseph Delo**

The role of CD155 in monocyte dysfunction in patients with decompensated cirrhosis

*Delo J, Forton D*

Background and Aims: Monocytes are a key first-line of defence against bacterial infections, and in patients with liver cirrhosis, monocytes exhibit impaired phagocytosis and anti-microbial function. CD155 is an immune checkpoint expressed on monocytes that binds the inhibitory receptors TIGIT and CD96 on T cells and NK cells. Signalling via CD155 can mediate a transition to an M2-like, immunosuppressive phenotype in tumour associated macrophages, and impair macrophage ability to active T cells during antigen presentation. This study aimed to investigate the role of the CD155 and TIGIT/CD96 immune checkpoint axis in monocyte dysfunction in liver cirrhosis.

Methods: The study included patients with stable decompensated cirrhosis (SD, n=11), acute decompensated cirrhosis (AD, n=21), and acute-on-chronic liver failure (ACLF, n=19), recruited within 48 hours of hospital admission, along with healthy controls (HC, n=18). Flow cytometry was used to assess the expression of TIGIT, CD96 and CD155 on immune cell subsets in peripheral blood. Healthy control PBMCs were conditioned in patient plasma for 48 hours and monoclonal antibodies were used for TIGIT, CD96 and CD155 blockade. Monocyte function was evaluated by measuring activation/exhaustion markers (CD86, HLA-DR, MERTK, CD206), phagocytosis (pHrodo E coli BioParticles), and cytokine production (IL-6, IL-10, TNF-alpha and IL-1beta) after LPS stimulation.

Results: CD155 expression was higher on the intermediate (CD14+CD16+) subset of monocytes in AD and ACLF patients, and the expression correlated positively with other measures of liver disease severity (Child Pugh Score and MELD score). Conditioning healthy control PBMCs in ACLF plasma induced upregulation of CD155 expression. CD96 and CD155 blockade reduced expression of exhaustion markers MERTK and CD206 on monocytes, and boosted IL-6 production in response to LPS.

Conclusion: This study identifies a potential mechanism for monocyte dysfunction in cirrhosis. The CD155-TIGIT/CD96 axis could serve as a novel immunomodulatory target to boost anti-bacterial immunity in decompensated cirrhosis and reduce reliance on antibiotics.

**41. Mr Filip Djukic**

Antibiotic resistant bacterial colonisation in 5 neonatal units in the UK as part of the NeoIPC study

*Djukic F, Cook A, Martin J, Berkell M, Reid AE, Tanney K, Booth N, Clarke P, Roehr C, Bielicki J*

Background: Colonisation by antibiotic-resistant bacteria (ARB) is a risk factor for severe hospital-acquired infection/sepsis, especially for infants born <32 weeks' gestation (high-risk). We investigated colonisation pressure at the neonatal unit-level in preparation for a trial.

Methods: Five English units conducted 4 cross-sectional surveys in a one-month period as part of the NeoIPC Feasibility study; at each survey clinical data, skin swabs and stool samples were collected. Samples were analysed by RT-qPCR for the detection of bacterial resistance genes. Stool samples

were analysed for carbapenemases, extended-spectrum-beta-lactamases (ESBLs), and vancomycin-resistant-enterococci (VREs) and skin swabs for methicillin-resistant Staphyloccocus aureus (MRSA); ARB colonisation was defined as detection of at least one target gene in an infant's sample.

Results: 237 infants participated; 96/237 (40%) were high-risk. 209 (88%) infants had received antibiotics at least once and 48 (20%) had ever had surgery. Between 113 and 127 infants were present per survey; 44 (18%) infants were present in all 4 surveys. Of possible samples, 475/482 (99%) skin swabs and 332/482 (69%) stool samples were collected; 7/475 (1%) skin swabs and 26/332 (8%) stool samples were positive. Only 10/26 (28%) of positive samples were from high-risk infants. ESBL genes were the most commonly detected (24/26 samples) resistance genes, while 0/26 stool samples were positive for VREs and only 2/26 were positive for carbapenemases. Of note, 447/475 (94%) skin swabs were MRCoNS positive.

Conclusion: Resistant bacterial colonisation was generally low across English neonatal units with both low-and-high-risk infants being colonised. Unit-level IPC interventions target both direct and indirect effects of colonisation regardless of risk level.

**42. Dr Joshua Erhabor**

A Systematic Review on Outcome Predictors of Traumatic Brain Injuries.

*Erhabor J*

Introduction: Traumatic Brain Injuries (TBI), are attributed to the physiological insult occurring from an external direct mechanical force applied to the cranium. Such force may also impact intracranial structures and lead to temporary or permanent psychosocial and physical impairments.

Approximately 1.4 million people are annually admitted to hospitals for TBIs in the UK, with TBIs being reported as the most common cause of death for patients under 40 years of age.

Since 2005, it is reported that around 3.2 million TBI survivors have been reported to experience long-term disabilities. 5 Examples include both neurological and psychosocial disabilities which have impacted the healthcare system's clinical management financially.

At the moment, there are at least 4 CT classification systems currently used to prognosticate and stratify TBI patient outcomes: Marshall, Rotterdam, Stockholm, and Helsinki.

Methods: This systematic review was conducted via the PRISMA Statement outlined in the 'Cochrane Handbook for Systematic Reviews of Interventions.

The Patient Group included adults diagnosed with Moderate or Severe Traumatic Brain Injuries. The intervention investigated included the Marshall Score Outcome Predictors. The comparators were the 3 other classification systems (Rotterdam, Helsinki, Stockholm). The primary outcome investigated was Neurological Outcomes (GCS + GOSE) while secondary outcomes included Mortality Risk Stratification, In-hospital or up to 90-day mortality.

Three databases (MEDLINE, CINAHL and EMBASE) were utilised to search via NHS Open Athens with citations of the included studies which were also screened. Access via the electronic databases was granted via the author's university subscription.

Results: After completing the search strategy previously mentioned, there was a total of 1,353 unique articles that were retrieved, following the exclusion of duplicate articles. After completing

the title and abstract screening, 56 articles were remaining for scrutinisation via full-text screening and evaluation which resulted in only 5 containing enough raw data for analysis and were eligible for inclusion.

Conclusion: Most of the studies were retrospective and relied heavily on data gathered from electronic medical records, and no current statistical model could be used to analyse and compare known outcomes to a potentially predicted outcome.

**43. Dr Joshua Erhabor**

How does the surrounding presence of non-cancerous cells suppress the proliferation of tumours in pancreatic ductal adenocarcinomas: The role of LKB1 in tumour suppression

*Erhabor J*

Background:

- Pancreatic ductal adenocarcinoma (PDAC) is a pancreatic exocrine cancer with a rising incidence and a poor prognosis, as less than 20% of patients survive 1 year after diagnosis.
- Effective therapies have not yet been developed to match the growing burden of PDAC.
- A KrasG12D; p53R172H; Pdx1-Cre (KPC) mouse model was developed to represent the tumour microenvironment of the human pancreas to determine complex genetic interactions.
- The aim was to identify potential genetic therapeutic targets from the tumour micro-environment in the early stage of PDAC.

Methods:

1. A culture of KPC tumour cells, which were transfected with a green fluorescent protein (GFP) and non-cancerous wild-type mice pancreatic cells were taken.

2. Short Hairpin RNAs (shRNAs) were used to reduce gene expression

3. Fluorescent microscopy was used to capture images of the proliferated tumour cells.

4. A computer software analysed the green pixels on the fluorescent microscopy which was used to calculate the green pixels seen on the image into a percentage of GFP.

Results:

- The cancer was least suppressed when the serine-threonine liver kinase B1 gene (LKB1) was modified with a GFP of 65% compared to the control sample plate which yielded an 8% GFP.
- LKB1 may play a role in the suppression of tumour proliferation in PDAC, making it a potential target for future drug therapy alongside early identification of PDAC.
- LKB1 also had the strongest link to cancers and tumour syndromes such as Peutz-Jeghers.
- LKB1 not only regulates cell growth and polarity but is also a tumour suppressor involved in mTOR and AMPK signalling pathways.
- This pathway may be associated with an increased risk of pancreatic cancer due to novel single nucleotide polymorphisms (SNPs).

Conclusions:

- PDAC is a devastating cancer associated with a poor prognosis and currently lacking effective therapies or reliable early detection.
- Unmodified surrounding non-cancerous cells help suppress tumour proliferation in PDAC genetically.
- LKB1 may be associated with tumour growth and may be worthy of future investigation as a future chemotherapy target in PDAC.

**44. Dr Joshua Erhabor**

Title: Neurosurgical Equipment Donations: A Qualitative Study

*Sichimba D, Bandyopadhyay S, Dalle D, Kotecha J, Egiz A, Bankole NDA, Higginbotham G, Erhabor J, Ulrick S*

Background: Neurosurgical care services remain hardly accessible in low- and middle-income countries (LMICs) despite the vast majority of the global neurosurgical disease burden in these settings. An estimated 13.8 million out of 22.6 million new cases every year require surgery. However, the lack of the most basic neurosurgical equipment makes it hard for LMICs to provide safe, timely, and affordable essential neurosurgical care. Medical equipment donation to LMIC is usually a means to meet this need.

Methods: In this qualitative study, individual semi-structured interviews were conducted until data saturation was achieved. Participants were neurosurgeons from Ireland, the United Kingdom (UK), and low- and middle-income countries (LMICs) in Africa. The interview data was examined through a thematic analysis involving open and axial coding.

Results: There was recognition of a worldwide inequity in neurosurgical equipment access across all participants. Neurosurgical donations were seen as a solution by some while others deemed them to be further exacerbating the mind frame of a dependency relationship unless an exchange process was built into the mechanics. Drains and microscopes were identified as being the priority equipment needed in LMICs. However, these were not the equipment that was identified as being common donations. There was a belief that an organisational framework was needed to coordinate transparent neurosurgical donation procedures. However, creating bilateral partnerships within this organisation structure and training LMIC surgeons in the use of the equipment in their own country were identified as being key facets that needed to be considered too.

Conclusion: There is a need for an international neurosurgical body to create a consensus as to the best method through which neurosurgical donations or exchanges should take place. This should be advertised to centres with the creation of bilateral partnerships and training programmes in LMICs being at the heart of the initiative.

**45. Darlington Faijue**

Delivering Catch-Up Vaccination in Low- and Middle-Income Countries (LMICs) in Adolescents and Adults: A Systematic Review of Interventions, Policies, Practices, Barriers, and Facilitators

*Faijue DD, Bouaddi O, Hargreaves S*

Background: Catch-up vaccination in low- and middle-income countries (LMICs) is essential for broadening immunization coverage, particularly among adolescents, migrants, and other vulnerable groups who have missed routine vaccines. The World Health Organization defines catch-up vaccination as the provision of vaccines to those who missed scheduled doses, aiming to prevent vaccine-preventable diseases and support health equity. While high-income countries have well-documented strategies for catch-up vaccination, research on similar initiatives in LMICs—especially for adult and life-course immunization—remains limited. This review evaluates policies and interventions in LMICs to improve vaccine access for underserved populations.

Methods: This systematic review examines catch-up vaccination interventions for adolescents (12-18 years) and adults (19-65 years) in LMICs. We include studies from diverse settings and assess primary outcomes related to intervention effectiveness and vaccination uptake. Secondary outcomes include the identification of barriers and facilitators to successful catch-up vaccination. An initial search across five databases and grey literature yielded 1,764 studies. Screening for inclusion is currently underway based on predefined eligibility criteria.

Results: Emerging data on catch-up vaccination strategies in LMICs underscore the effectiveness of school-based vaccination programs, which achieve coverage rates exceeding 70%. Grade-based approaches are shown to be more effective than age-based ones. Additional interventions such as automatic appointment scheduling, culturally adapted communication, and community engagement have been effective in increasing vaccine uptake, especially among migrant populations. Other promising strategies include integrating digital reminders and strengthening primary healthcare systems to streamline vaccine delivery and uptake. Tailored outreach programs, community involvement, and gender-sensitive approaches have also proven beneficial in reducing access barriers and improving vaccine acceptance across various communities.

Conclusions: Catch-up vaccination strategies in LMICs should focus on enhancing community engagement, leveraging digital tools, and addressing systemic challenges to increase immunization coverage. By addressing these factors, LMICs can improve public health outcomes and make significant progress toward achieving global immunization targets in the post-COVID-19 landscape. Implementing tailored catch-up interventions for underserved groups can help close the immunization gap, reducing the incidence of vaccine-preventable diseases and advancing health equity.

**46. Wanyun Feng**

The role of snRNA-activating protein complex (SNAPC) in determining sex-specific stress responses in mitochondrial disease

*Wanyun F*

Background: Mitochondria, as the cell's energy hubs, produce energy via the oxidative phosphorylation (OXPHOS) system. Impaired mitochondrial function not only leads to various diseases but also triggers mitochondrial stress, activating retrograde signaling that can drive

morphological remodeling or mitochondrial biogenesis. A key regulatory mechanism recently identified in mitochondrial diseases, such as those involving MRPL44 mutations, is the mitochondrial sex-specific response (mtSSR), which appears to differ by sex. Understanding the molecular basis of mtSSR could help explain sex-based differences in disease presentation and therapy response. Currently, MRPL44-related diseases have been observed only in females, where mitochondria with MRPL44 mutations show an mtSSR♀UP♂DOWN response. SNAPC5 has emerged as a potential regulator of this response.

Aims and Objectives: This study used gene manipulation techniques, including overexpression and CRISPR-Cas9 knockout, in HEK293 cells to investigate whether SNAPC5 regulates mtSSR♀UP♂DOWN and OXPHOS gene expression. Protein expression levels were analyzed through immunoblotting, with RNA sequencing to further validate findings.

Results: Overexpression of SNAPC5 impacted OXPHOS proteins as follows: increases in OXPHOS V (+44%) and III (+29%), and decreases in OXPHOS II (-20%) and IV (-25%). For mtSSR♀UP♂DOWN, U2AF35 and MRPL52 increased by 10% and 40%, respectively, while RPS28 and COX17 decreased by 10% and 30%. However, these changes lacked statistical significance. CRISPR-Cas9 successfully generated knockout cell lines for SNAPC-1, -2, -3, and -5, with final confirmation of clonal lines ongoing.

Conclusion: Initial data suggest SNAPC5 may minimally influence mtSSR♀UP♂DOWN and OXPHOS gene expression, though further validation is necessary. A key outcome of this study is the development of SNAPC gene knockout cell lines, which will enable future research into SNAPC's regulatory role in OXPHOS and mtSSR♀UP♂DOWN expression. This investigation could ultimately enhance our understanding of mitochondrial function regulation and sex-specific responses in mitochondrial diseases.

**47. Professor Mark Fisher**

Experimental localization of metal-binding sites reveals the role of metal ions in type II DNA topoisomerases

*Najmudin S, Wang B, Pan XS, Mykhaylyk V, Orr C, Wagner A, Govada L, Chayen NE, Fisher LM, Sanderson MR*

Metal ions play an important role in supporting the catalytic activity of DNA-regulating enzymes such as topoisomerases. Bacterial type II topoisomerases, gyrases and topoisomerase (topo) IV, are primary drug targets for fluoroquinolones, a class of clinically-relevant antibacterials requiring metal ions for efficient drug binding. Whilst the presence of metal ions in topoisomerases has been elucidated in biochemical studies, accurate location and assignment of metal ions in structural studies have historically posed significant challenges. Recent advances in X-ray crystallography address these limitations by extending the experimental capabilities into the long-wavelength range, exploiting the anomalous contrast from light elements of biological relevance like Ca, K, Cl, S, P, Mg and Na. This breakthrough enables us to confirm experimentally the locations of Mg2+ in the fluoroquinolone-stabilized S. pneumoniae topo IV complex. Moreover, we can unambiguously identify the presence of K+ and Cl- ions in the complex with one pair of K+ ions functioning as an additional inter-subunit bridge. Overall, our data extends the current knowledge in the functional and structural roles of metal ions in type II topoisomerases.

**48. Dr Eva Galiza**

Effect of timing of COVID-19 vaccine dose in pregnancy on maternal anti-spike SARS-CoV-2 IgG antibodies at delivery and placental transfer of maternal derived anti-spike SARS-CoV-2 IgG antibodies – the UK preg-CoV study

*Galiza EP, Marchevsky N, Greening V, Eccleston E, Wan M, Eordogh A, Mujadidi YF, Abdul-Kadir R, Basude S, Cox C, Hanna G, Kelly T, McFarland R, Mukherjee S, Mullins E, Parry-Smith W, Simpson N, Watkins K, Jones C, Le Doare K, Khalil A, Liu X, Heath PT.*

Introduction: The COVID-19 pandemic had a significant impact on pregnant women and infants. The Preg-CoV study examines the safety, immunogenicity, and optimal timing of COVID-19 vaccine doses administered during pregnancy. With pregnant women at increased risk of severe COVID-19 outcomes, this study assesses maternal immune responses and antibody transfer to the fetus, aiming to inform tailored vaccination strategies for maternal and infant protection. The maternal anti-spike SARS-CoV-2 IgG antibodies at delivery, and the placental transfer of maternally derived anti-spike SARS-CoV-2 IgG antibodies following COVID-19 vaccination in pregnancy is reported.

Methods: The Preg-CoV study is a Phase II, multi-centre, hybrid randomised and observational platform study of pregnant women and their infants. From August 2021 to October 2022, participants were enrolled across 13 sites. Maternal and cord blood were taken at delivery (including infant blood taken within 3 days of birth). Anti-spike SARS-CoV-2 IgG levels and geometric mean placental transfer ratio (PTR) for cord blood samples are reported.

Results: 317 (309 evaluable) participants were recruited. Median age at enrolment was 34 years (interquartile range 30.4-36.7), gestational age (GA) 28.6 weeks [23.0-34.4], 54% had co-morbidities, 38% were SARS-CoV-2 seropositive, median birth GA was 39.4 weeks [38.9-40.6] and 35.9% were delivered by caesarean section. A trend of increasing maternal anti-spike SARS-CoV-2 IgG levels at delivery was demonstrated when the last COVID-19 vaccine dose was given during the 3rd trimester (figure 1), although this did not achieve statistical significance. No differences were observed in geometric mean PTR according to GA at receipt of last COVID-19 vaccine dose in pregnancy: 1st trimester GMC 16703 (95% CI: 7602-36702, n=8) and PTR 1.44 (95% CI: 1.02-2.03, n=8); 2nd trimester GMC 20538 (15428-27339, n=47) and PTR 1.53 (1.28-1.83, n=46); 3rd trimester GMC 22332 (10116-49303, n=10) and PTR 1.46 (1.13-1.88, n=10) (figure 2).

Conclusions: There was no evidence of an effect of pregnancy trimester at the time of last maternal COVID-19 vaccination on placental transfer of maternally derived anti-spike SARS-CoV-2 IgG antibodies. Vaccines can be administered at any time in pregnancy to protect infants against COVID-19.

**49. Dr Eva Galiza**

Effect of maternal anti-spike SARS-CoV-2 IgG antibody levels at delivery following COVID-19 vaccine booster dose during pregnancy on risk of postnatal maternal and infant infection – the UK preg-CoV study

*Galiza EP, Marchevsky N, Greening V, Eccleston E, Wan M, Eordogh A, Mujadidi YF, Abdul-Kadir R, Basude S, Cox C, Hanna G, Kelly T, McFarland R, Mukherjee S, Mullins E, Parry-Smith W, Simpson N, Watkins K, Jones C, Le Doare K, Khalil A, Liu X, Heath PT.*

Introduction: The COVID-19 pandemic had a significant impact on pregnant women and infants. The Preg-CoV study examines the safety, immunogenicity, and optimal timing of COVID-19 vaccine doses administered during pregnancy aiming to inform tailored vaccination strategies for maternal and infant protection. The effect of maternal anti-spike SARS-CoV-2 IgG antibody levels at delivery on postnatal maternal and infant infection is reported.

Methods: The Preg-CoV study is a Phase II, multi-centre, hybrid randomised and observational platform study of pregnant women and their infants. From August 2021 to October 2022, participants were enrolled across 13 sites. Study participation was from time of consent during pregnancy to 12 months post delivery. Maternal blood samples were taken at delivery for anti-spike SARS-CoV-2 IgG antibody analysis by ELISA. Confirmed episodes of SARS-CoV-2 infection (COVID-19 nasopharyngeal self-test) were collected for mother and infant.

Results: 317 (309 evaluable) participants were recruited. Median age at enrolment was 34 years (interquartile range 30.4-36.7), gestational age (GA) 28.6 weeks [23.0-34.4], 54% had co-morbidities, 38% were SARS-CoV-2 seropositive, median birth GA was 39.4 weeks [38.9-40.6] and 35.9% were delivered by caesarean section. 178 participants met the criteria for population analysis of those who received one COVID-19 vaccine dose (3rd or 4th booster dose), during pregnancy. 56 (31%) reported a positive swab during their study participation. Of these, 31 (55%) had their positive swab after enrolment and before delivery. 25 (45%) had their positive swab after delivery. Of the 175 infants born to these participants, 13 (7%) had a reported positive swab during their study participation. The Kaplan Meier curve for maternal infection post delivery (figure 1) and infant infection (figure 2) demonstrates no evidence of a relationship between maternal anti-spike SARS-CoV-2 IgG antibody level at delivery and evidence of infection between the period after delivery and the final study visit.

Conclusions: Following a COVID-19 vaccine booster doses in pregnancy, there was no evidence of a relationship between maternal anti-spike SARS-CoV-2 IgG antibody level at delivery and subsequent infection rates in mothers or infants from delivery through to final study follow-up.

**50. Miss Emilee Gosnell**

Clinical and Sociodemographic Predictors of Hearing Aid Use in Infants Aged 0-2 with Permanent Childhood Hearing Loss: A Retrospective Cohort Single-Site Pilot Study

*Gosnell E, Mahon M, Rajasingam S, Vickers D*

Objectives: To explore patterns in hearing aid use times among infants aged 0-2 years at a single-site hospital. The results will inform a larger study to investigate which clinical and sociodemographic factors can influence hearing aid use in young children.

Design: Datalogging values alongside clinical and household sociodemographic information were collected from a retrospective review of hospital records including sex, average pure tone threshold, lateral configuration of use, speech intelligibility score, additional disabilities, Index of Multiple Deprivation, Income Decile, Education and Skills Decile, Income Deprivation Affecting Children Index (IDACI), ethnicity and home language.

Study sample: Records for 252 patients aged 0-2 years between 2005-2022 with permanent childhood hearing loss were reviewed. Ninety-six patients met the inclusion criteria.

Results: Datalogging values indicated a median use of 4.67 hours (3.0-7.3) per day across patients in the first two years post-fitting. Differences in datalogging according to Income Deprivation Affecting Children Index was significant (p=0.01), suggesting that infants from the more deprived groups (1-5) used their devices less.

Conclusion: Datalogging values are lower than expected and highlight that many families may struggle to achieve optimum usage in the early years post-fitting. Findings need to be verified on a larger scale through a multi-centre study.

**51. Mr Aurélien Guéroult**

Long-term outcomes of Fenestrated Endovascular Aneurysm Repair: a GLOBALSTAR registry stud

*Guéroult A*

Background: GLOBALSTAR is a registry of 1438 complex EVAR (UK, 2003-2022); it represents the largest mature dataset for FEVAR. The aims of this study are to report long-term outcomes for survival and freedom from re-intervention for FEVAR.

Methods: For this study of GLOBALSTAR, inclusion criteria were: all aneurysm morphologies, custom-made FEVAR. Exclusion criteria were: dissection, other complex EVAR techniques (BEVAR, ChEVAR). Time-to-event analyses were conducted for survival and freedom from re-intervention (FFR). A cox proportional hazards model was applied to survival for all pre-operative variables. A 10% Pocock threshold was applied to determine data maturity.

Results: 1067 patients were included in this analysis. Median age was 75.1 years [69.0-79.7 IQR] and 86.1% patients were male. This population had significant co-morbidities including 42.5% IHD and 74.6% hypertension. Data maturity reached 10 years and estimated survival [n= 1067] at 3, 5 and 10 years were 79.9% [77.5-82.4%, 95% CI], 64.2% [61.1-67.3%] and 34.0% [30.3-38.1%]. Median survival was 7.2 years for the whole cohort and >5 years for octogenarians. For FFR, data maturity reached 9 years and estimated FFR [n= 741] at 3, 5 and 9 years were 75.7% [72.4-79.1%], 70.0% [66.3-73.8%] and 64.6% [60.1-69.3%]. Mean time to re-intervention was 3.8 years.

Conclusions: These results are consistent with published contemporary FEVAR series and data maturity for survival is double that calculated for the meta-analysed literature. Octogenarian median survival beyond five years may support the use of FEVAR in this patient group.

**52. Dr Thomas Hart**

Kinematic Features of Voluntary and Involuntary Head Movements in Cervical Dystonia

*Hart T, Heideman L, Martino D, Beudel M, Sadnicka A, Morgante F*

Objective: To identify kinematic metrics that characterise and differentiate the motor manifestations of Cervical Dystonia (CD).

Background: Motor manifestations of CD include phasic torsional movements, painful tonic abnormal postures, and tremor, which combine to varying degrees within subjects and contribute to phenomenological heterogeneity. The current classification provides no formal definition of these terms and acknowledges that CD has not been consistently organised into distinct subtypes.

Kinematic analysis provides an objective and quantitative approach to describing these motor features.

Methods: CD subjects were recruited at least 3 months after their last botulinum toxin injection and compared with healthy controls. A wireless inertial measurement unit was used to record gyroscopic data pertaining to head movement. Voluntary movements were captured during head turns to the right and left side. Involuntary movements were captured holding a fixed neutral head position and in an unconstrained condition. Voluntary movement metrics included peak angular velocity, movement amplitude, movement smoothness, and asymmetry. Asymmetry represents within-subject direction differences for velocity ($\Delta$V), amplitude ($\Delta$A) and smoothness ($\Delta$S). Angular velocity of involuntary motion was analysed in time and frequency domains.

Results: 44 CD and 33 control subjects were enrolled. Voluntary movements showed reduced peak angular velocity ($p<0.001$), amplitude ($p<0.001$) and smoothness ($p<0.001$), with increased asymmetry ($\Delta$V: $p=0.02$; $\Delta$A: $p<0.001$; $\Delta$S: $p=0.004$). Cumulative involuntary movement was increased in all axes (pitch: 168.3 vs 43.8º; yaw: 256.9 vs 39.3º; roll: 151.5 vs 26.4º, all $p<0.001$). Power spectral density and position vector analysis revealed 3 patterns of involuntary movement: sinusoidal oscillations at 5.4±1.2 Hz affecting 73% of subjects, jerky oscillations at 2.9±0.7 Hz in 55%, and slow drift-saccade type movements at 0.6±0.4 Hz in 41%. 86.4% of subjects had least 1 involuntary movement pattern, with combinations frequently detectable within subjects.

Conclusions: Voluntary head movements in CD have impaired velocity, amplitude, smoothness, and symmetry. Several subtypes of involuntary movement are described with distinct kinematic patterns. This objective approach to appraising phenomenology has identified novel motor characteristics of a common and disabling movement disorder. This will aid classification, allow for quantification of treatment effects, and inform research into underlying disease mechanisms.

**53. Dr Thomas Hart**

Rapid Onset Kinematic Effects of Thalamic/Subthalamic DBS in Cervical Dystonia

*Hart T, Sadnicka A, Cociasu I, Ricciardi L, Baig F, Hart M, Edwards M, Pereira E, Morgante F*

Objective: To assess the effect of combined ventrolateral thalamus (VL-Th) and subthalamic nucleus (STN) stimulation in Cervical Dystonia (CD) using clinical and kinematic measurements.

Background: Deep brain stimulation (DBS) of the VL-Th and STN is effective for treating CD and dystonic head tremor, respectively. We hypothesized that combined VL-Th/STN DBS might improve kinematic components of CD, including head turning performance and involuntary movements.

Methods: Nine CD subjects were bilaterally implanted with an octopolar linear lead spanning from STN to VL-Th. They underwent clinical and kinematic assessment in two conditions: OFF STIM (with DBS turned off for 20 minutes) and ON STIM (with stimulation delivered according to subject's best DBS settings). Time from operation to assessment was 16.9+7.9 months. TWSTRS was used to rate clinical severity. Head motion was captured from the forehead with an inertial measurement unit. Voluntary movements were recorded during right and left head turns. Involuntary movements were captured while attempting to hold a fixed neutral head position and in an unconstrained condition. Kinematic metrics were compared OFF and ON STIM.

Results: TWSTRS significantly decreased in the ON STIM compared to the OFF STIM condition. Voluntary head turning movements ON STIM had increased mean amplitude ($p=0.004$) and

smoothness (p<0.001). 4/9 subjects showed improved peak angular velocity, but this did not reach significance at a group level. The ON STIM condition showed reduced range (p<0.001) and cumulative rotation (p<0.001) of involuntary movements. Spectral analysis of velocity data showed reduced power of involuntary movement ON STIM (p<0.001). Attenuation of several involuntary movement patterns was demonstrated, including high-amplitude drifts, rhythmic jerky oscillations and rhythmic sinusoidal oscillations.

Conclusions: Combined VL-Th/STN DBS improves smoothness and amplitude of voluntary head movements. Stimulation attenuates several distinct patterns, as well as the overall extent, of involuntary movement. Detectable kinematic improvements within a short time frame suggests rapid onset of treatment effect with stimulation of these targets. This study provides kinematic evidence that abnormal head turning and involuntary mobile components of CD can be successfully treated by dual targeting of the ventrolateral thalamus and the STN.

**54. Dr Thomas Hart**

Relationship between Non-Motor Symptoms, Kinematic Features, and Quality of Life in Cervical Dystonia

*Hart T, Heideman L, Martino D, Beudel M, Sadnicka A, Morgante F*

Objective: To assess the extent of non-motor symptoms (NMS) in Cervical Dystonia (CD) and investigate the interaction between NMS, kinematic metrics of motor severity, and health-related quality of life (HRQoL).

Background: NMS are prominent in CD and include neuropsychiatric symptoms, sleep impairment, pain, and fatigue. Multiple studies have demonstrated a high prevalence of NMS and a clear impact on HRQoL. However, the relationship between NMS and motor severity in CD remains ambiguous, as well as how these factors interact to affect HRQoL.

Methods: CD subjects were recruited at least 3 months after their last botulinum toxin injection and compared with controls. NMS were measured using the Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Scale (HARS), Pittsburgh Sleep Quality Index (PSQI) and the TWSTRS-2 Pain sub-scale. Kinematic metrics included peak velocity, amplitude, and smoothness of voluntary head turns, and the range and total cumulative extent of involuntary movement. HRQoL was measured using the Cervical Dystonia Impact Profile-58 (CDIP-58).

Results: 44 CD and 33 control subjects were enrolled. CD subjects showed significantly higher depression (p<0.001), anxiety (p<0.001), sleep impairment (p=0.002) and pain (p<0.001) scores. CDIP-58 was most strongly associated with pain ($\rho$=0.78, p<0.001) and HDRS ($\rho$=0.6, p<0.001), showing weaker correlations with HARS, PSQI, and involuntary movement. Kinematic metrics correlated with pain (smoothness-pain $\rho$=-0.4, p=0.02; cumulative involuntary movement-pain $\rho$=0.43, p=0.01), but not with other NMS scores.

Conclusions: Our study confirms the high burden of NMS in CD. The relationship between NMS, motor severity, and HRQoL is complex. Our data suggests that pain and depression have the highest impact on HRQoL. Motor severity and NMS severity appear to be relatively independent, with the exception of weak associations between kinematic metrics and pain. Multivariate analysis of a larger cohort is needed to properly explore these interactions.

**55. Mr George Hart**

Functional characterisation of pro-VWF-mStayGold, a new fluorescent reporter of Weibel Palade body exocytosis

*Hart G, Raguthasan N*

Weibel-Palade Bodies (WPBs) are the regulated secretory organelle of vascular endothelial cells, and contain Von Willebrand Factor (VWF), a protein essential for both primary and secondary haemostasis. Mutations in VWF cause the bleeding disorder Von Willebrand Disease (VWD), however, in about 30% of cases of VWD, VWF itself is normal. In these cases, it is thought that mutations in molecules that regulate WPB exocytosis are to blame.

To understand such cases, it is important to be able to directly analyse WPB exocytosis in living endothelial cells. Here we tested two new fluorescent reporters of WPB exocytosis based on a novel fluorescent protein called Staygold (SG). SG has potential advantages over current GFP based reporters; it is brighter and more photostable under blue light illumination. However, in its native form SG tends to dimerize, and this could cause protein aggregation when fused to VWF, impacting how VWF is stored within WPBs. A monomeric version (mSG; E138D) of the reporter has been made (VWFpp-monomeric StayGold (VWFpp-mSG)) and was tested here. To trigger WPB exocytosis we used the intracellular calcium-elevating hormone histamine, and simultaneously monitored both exocytosis and changes in intracellular [$Ca^{2}$+] using the fluorescent $Ca^{2}$+ indicator, fura-2. Our data will show that both VWFpp-SG and VWFpp-mSG function as useful reporters of WPB exocytosis in endothelial cells.

**56. Dr Sally Hayward**

Exploring the link between psychosocial stress, mental health, and tuberculosis: a mixed methods study

*Hayward S, Chong D, Townsend J, Kirwan D, Skolimowska K, Kutschenreuter J, Cusman R, Deal A, Rossanese M, Loader MC, Cosgrove C, Hargreaves S, Friedland J*

Background: Stress and mental illness are known to modulate immune function and infectious disease risk. Yet, the relationships between psychosocial stress, mental health and tuberculosis (TB) are poorly understood, despite the large global health impact of TB and its known links with social vulnerabilities. In Europe, migrants are at elevated risk of TB and certain mental illnesses compared with host populations. Therefore, we investigated the relationships between psychosocial stress, mental health, immune function and TB in migrants and non-migrants.

Methods: We undertook a mixed methods, cross-sectional study with newly-diagnosed TB patients at St George's Hospital, London, UK. Firstly, we explored experiences of psychosocial stress and migration through qualitative interviews, analysed through thematic analysis. Secondly, we examined associations between questionnaire measures of psychosocial factors/mental health (Perceived Stress Scale, UCLA 3-Item Loneliness Scale, Hospital Anxiety and Depression Scale) and a panel of pro-/anti-inflammatory biomarkers in patient plasma, measured by Luminex. Quantitative data were analysed by linear regression.

Results: Our qualitative data show that migrants with TB (n=23, mean age=34, 74% male) experience diverse psychosocial stressors prior to TB diagnosis/symptoms, which may be acute (e.g. bereavement), chronic (e.g. work) or related to prior adverse life events (e.g. migratory journey).

Factors fostering resilience include optimism and strong social support. Our quantitative data (n=40, mean age=40, 65% male, 90% foreign-born) show high levels of stress (67.5% high/severe or moderate), loneliness (42.5%), anxiety (42.5%) and depression (27.5%) among TB patients. Those with higher depression scores exhibit some elevated pro-inflammatory markers compared to those with lower scores: TNF-a ($R2=0.11$, $p<0.05$), IL-8 ($R2=0.11$, $p<0.05$) and MMP-7 ($R2=0.11$, $p<0.05$). Patients with higher loneliness scores show elevated MMP-7 levels ($R2=0.10$, $p<0.05$). Other measured biomarkers show no significant association.

Conclusions: Our study finds high stress and poor mental health among TB patients in the UK, and explores acute, chronic and life course stressors and protective factors fostering resilience. TB patients, in particular migrants, may benefit from integrated TB and mental health services. In addition, our data has identified potential inflammatory mediators that may underpin associations between mental illness and TB.

**57. Mrs Jia Hui Gan**

The feasibility, acceptability, safety, and effects of early weight bearing in humeral fractures – a scoping review

*Hui Gan J, Bearne L, Walters S, Room J, Booth G, Trompeter A, Nikoletou D*

Purpose: Rehabilitation programmes for humeral fractures often recommend non-weight bearing for varying durations, regardless of management approach. This study aims to summarise the extent and nature of the evidence for the feasibility, acceptability, safety, and effects of EWB in patients with humeral fractures.

Methods: Seven electronic data sources were searched to identified published (PUBMED, EMBASE, CINAHL) and unpublished (ClinicalTrials.gov, CENTRAL, NIHR Open Research, OpenGrey) literature that meeting our inclusion criteria: adults aged 18 or older, diagnosed with non-pathological causes of humeral fractures, EWB within 6-weeks, published in English, and grey literature in full-text. Independent data extraction was conducted by one reviewer with at least 50% independently extract by a second reviewer. Data were extracted using a priori protocol. Discrepancies were resolved via discussion, and additional reviewer arbitrated.

Results: 13,901 records were retrieved. Ten studies, involving 515 post-operative patients (mean age 39 years) and 351 healthcare professionals, were included. Overall EWB was found to be feasible in nine studies. Feasibility data highlighted two facilitators and five barriers. There was limited evidence regarding adherence to EWB. Acceptability was surveyed among orthopaedic surgeons, revealing EWB preference was based on surgery type, subspecialty, and postoperative polytrauma cases. No acceptability data was reported from patient's perspective. No safety issues arose from immediate weight bearing, except for two patients with lack of lower limbs who developed unsatisfactory postoperative outcomes from excessive EWB, against advice. Most of the unspecified positive effects of EWB were reported on disability level, pain, shoulder and elbow motion, and union.

Conclusion: This scoping review revealed that there is some evidence for the feasibility, safety, and effectiveness of EWB in humeral fractures following operative management only. EWB after some surgical approaches are acceptable to some sub-speciality of orthopaedic surgeons, but this is not universal among orthopaedic surgeons. Robust research studies using a core outcome set are

warranted to establish effective guidelines and clinical decision tools for the implementation of EWB after humeral fractures.

Impact: Findings of this review will be disseminated to clinical practitioners and policy makers through peer-reviewed publications, conferences, workshop, research reports and social media. This study will be crucial to healthcare professionals who are designing research studies in the area of EWB in humeral fractures and to the public advisory groups as a source of information about the existing literature gaps in this area.

**58. Ms Bryony Ishihara**

Neurophysiological markers of anxiety in Parkinson's Disease

*Ishihara B, Pegolo E, Hart T, Hart M, Pereira E, Howe F, Ricciardi L*

Background: Anxiety is a common non-motor symptom of Parkinson's Disease (PD) that is increasingly recognised to be at least partly linked to disease specific processes of PD, and not simply a psychological reaction to a chronic condition. However, its pathophysiology remains largely unknown. While neuroimaging studies have implicated the fear and limbic cortico-basal-thalamocortical circuits, there are few studies on the neurophysiological correlates of PD anxiety. The aim of this project is to identify neurophysiological (local field potential and EEG) markers of anxiety in PD.

Methods: Local field potential (LFP) from the subthalamic nucleus (STN) can be recorded from PD patients undergoing deep brain stimulation (DBS) treatment. We acquired 5-minute resting recordings of STN-LFP, EEG (covering frontal, central and parietal cortical regions), and ECG of 13 participants, 3-4 days following DBS electrode implantation. The power spectrum of the LFP data was calculated for low frequency theta (4-8 Hz) and alpha (8-12 Hz) bands, and phase coherence analysis was performed as a measure of the functional connectivity between the STN and cortical brain regions. All participants completed the Hamilton Anxiety Rating Scale (HARS) to measure the presence and severity of anxiety.

Results: There is a positive association between STN neural oscillatory power in the theta band and anxiety in PD, with higher theta power predicting more severe anxiety (linear mixed model, $p=0.031$). This local theta enhancement in anxious PD patients was accompanied by increased STN connectivity to parietal cortical regions in the same frequency band (linear mixed model, $p=0.005$).

Conclusion: Theta activity in the STN may contribute to symptoms of anxiety in PD, and may form part of a hyperconnected circuit with parietal regions of the brain to characterise a state of hypervigilance to threat.

**59. Miss Asha Isse Ali**

Breast Surgery at the St Georges Hospital Day Surgery Unit: The 23-hour in-patient admissions pathway

*Ali AI, Boutsikos G, Tang S*

Background: A minority of benign and oncoplastic breast procedures require delayed post-operative admission. The majority can be performed safely and patients discharged on the same day, with the appropriate safety-netting. Nationally, 70% of oncoplastic breast cases and 92% of benign cases are performed as day case procedures.

Recommendations from associations such as the British Association of Day Surgery focus on streamlining surgical care and minimising admission lengths where appropriate. This study examines the 23-Hour admission pathway for Breast Surgery at SGH Day Surgery Unit.

Aim: A retrospective study reviewing the 23-Hour admission pathway for Breast Surgery at SGH Day Surgery Unit over a period of 13 months.

Methods: Data collection was completed using electronic patient records and categorised into patient, treatment, and disease factors. All procedures performed between October 2021 and December 2022 were reviewed. Procedures included: wide local excision, mastectomy, therapeutic mammoplasty, sentinel node biopsy, axillary node clearance, re-excision of surgical margins, lumpectomy and needle localisation biopsy.

Results: A total of 83 procedures were performed. Most patients were discharged safely within 23-hours (82%). The remining 8% (15) required overnight admission. Reasons for admission included: social, post-op intravenous antibiotics and indicated regular post-op observations.

Five patients developed post-operative complications: wound infection (3), haematoma (1) and nipple necrosis (1). Due to involvement of surgical margins, 5 patients underwent further cavitectomy.

According to patient feedback, 95% rated the admission experience as good-excellent. One patient described the wait-time for administration of nanocolloid for axillary surgery an inconvenience.

The benefits of a newly proposed 23-hour short surgical stay include: shorter turnover between cases, availability of recovery beds, availability of nurse-led discharges, adequate scrub team skill set. Room for improvement included: limited space for consenting/examination, the inability to conduct team briefs prior to 8:30am and lack of Nuclear Medicine Serices on Sudays which delayed surgery for patients requiring sentinel node biopsies using nanocolloid tracers.

Conclusion: For a selective patient population, the 23-hour admissions pathway is a safe and suitable alternative to in-patient admission. This service has adequate surgical outcomes and positive patient satisfaction. Improvements in facilities and allied services can improve efficiency and patient satisfaction.

**60. Mr Jamie James**

Investigating the interplay between NKG2D ligands, gamma delta T cells and SARS-CoV-2 infected epithelial cells

*James J, Bodamn-Smith M, Groppelli E, Sharpe S, Salguero-Bodes J*

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the aetiological agent of the coronavirus-19 disease (COVID-19) pandemic. Despite the efficacy of spike glycoprotein-targeting vaccines against SARS-CoV-2, the emergence of variants of concern (VOCs) that evade vaccine and natural immunity have been a continuous threat to public health. There is therefore a need to research and elucidate other immune responses to SARS-CoV-2 that are not affected by immune-evasion mutations. Gamma delta T cells (γδ T cells) are an unconventional T cell that have both innate and adaptive immune response qualities, and are understudied in the context of SARS-CoV-2 infection. In the case of  influenza A virus (IAV) and SARS-CoV, γδ T cells have been shown to respond to these viral infections by, for example, killing infected cells in a CD107a-dependent manner.

Specifically, in IAV danger signals such as natural killer group 2 D (NKG2D) ligands are upregulated and activate γδ T cells via NKG2D. We therefore postulate that γδ T cells respond to SARS-CoV-2 infected cells in a similar manner. By using flow cytometry, we have investigated the expression profiles of two NKG2D ligands, MICA/B in SARS-CoV-2 infected cells of lung epithelial origin. Our data show that MICA/B are upregulated, and that this upregulation occurs specifically in cells with active viral replication. Now, using a co-culture assay, we are investigating if, as expected γδ T cells detect MICA/B upregulation on SARS-CoV-2 infected cells and respond by activating "cell-killing" pathways such as CD107a. Furthermore, we will also investigate if what we see in vitro is confirmed ex vivo by using Rhesus macaque tissue that are from non-human primates that have been challenged with SARS-CoV-2 in collaboration with our partners at UKHSA.

**61. Professor Heather Jarman**

The role of the Consultant Nurse and Consultant Practitioner in UK Emergency Departments?

*Jarman H, Mummery V*

Consultant nurses are clinical experts with responsibility for across four practice domains - leadership, research, education and advanced clinical practice. There is known to be variation in role implementation and lack of clarity on role preparation, definition and scope of practice. The Royal College of Emergency Medicine (RCEM) recommend that each Emergency Department will have at least one consultant nurse, but we do not know the extent to which these roles have been adopted or their impact on practice. We aimed to identify all consultant nurses and consultant practitioners working in emergency care in the UK, and to describe the nature and scope of their roles.

Methods: a cross-sectional national survey was distributed via clinical networks. Data collection was electronic and included demographic characteristics, experience, training, and domains and scope of practice. Characteristics were analysed using descriptive statistics, Categorical data, such as banding or proportion of time in each domain, are presented as number and percentage

Results: there were 37 respondents of which 51.35% were male. 86% were from a nursing background. Years of experience in professional roles totalled 952 with 299 years in consultant-level practice roles. Most time was spent in the expert practice domain and respondents indicated they had the most confidence in this area. Research was given the least time and where the respondents were least confident. More than 70% had no publications and more than 60% had not presented at a conference. There was good evidence of strategic leadership with 50% contributing to national guidelines and 70% participating in national or international committees.

Conclusions: despite workforce standards a small proportion of UK EDs have a consultant nurse. The is variability in how roles are configured but post holders are experienced senior clinicians making a significant contribution in the areas of learning and strategic leadership.

**62. Miss Hannah Johnson**

Use of Signal Detection Methods to Identify Associations Between Prenatal Medication Exposure and Subsequent Childhood Cancers: A Nordic Hypothesis-Generating Registry-Based Study

*Johnson H, ; Hjorth S, Morris J, Pottegård A, Leinonen M*

Background: Childhood cancer is an important contributor to childhood mortality in high income countries. Information on associations between childhood cancer and in-utero exposure is absent or limited for most medications. Signal detection methods identify medications where research should be focused but have not been applied to datasets containing prenatal medication exposures and childhood cancers.

Research Design and Methods: The aim of this study was to apply and evaluate four signal detection methods – incidence risk ratios (RR), the information component (IC), sequential probability ratio testing (SPRT), and Bayesian hierarchical models (BHM) - for identification of associations between medications dispensed during pregnancy and subsequent, incident diagnosis of childhood cancer using linked Nordic registry data. Signal detection results were compared to propensity score adjusted odds ratios from generalized linear models.

Results: Analysis was performed for 117 medication-cancer pairs with 5 or more observations. RR and IC had the greatest sensitivity (0.88 and 0.75). The IC had a greater specificity (0.97) than the RR (0.95).

Conclusions: The IC may be the most appropriate method for identifying signals within this type of data. Reported signals should not be considered sufficient evidence of causal association and must be followed-up by tailored investigations that consider confounding by indication.

**63. Dr Konstantinos Karampatsas**

Epidemiology of Group B Streptococcus: Maternal Colonisation and Infant Disease in Kampala, Uganda

*Kyohere M, Davies HG, Karampatsas K, Le Doare K*

Background: Child survival rates have improved globally, but neonatal mortality due to infections, such as Group B Streptococcus (GBS), remains a significant concern. The global burden of GBS-related morbidity and mortality is substantial, However, data from low and middle-income countries is lacking. Maternal vaccination during pregnancy could be a feasible strategy to address GBS-related disease burden.

Methods: We assessed maternal rectovaginal GBS colonization and neonatal disease rates in a prospective cohort of 6062 women-infant pairs. Surveillance for invasive infant bacterial infection occurred in parallel at two hospital sites. In a nested case-control study, we identified infants <90 days of age with invasive GBS disease (iGBS) (n=24) and healthy infants born to mothers colonized with GBS (n=72). We measured serotype-specific anti-capsular immunoglobulin G in cord blood/infant sera using a validated multiplex Luminex assay.

Results: We found a high incidence of iGBS (1.0 per 1,000 live births) within the first 90 days of life across the surveillance sites, associated with a high case fatality rate (18.2%). Maternal GBS colonization prevalence was consistent with other studies in the region (14.7%; 95% confidence interval 13.7-15.6%). IgG geometric mean concentrations were lower in cases than controls for

serotypes Ia (0.005 vs 0.12 µg/mL; p=0.05), III (0.011 vs 0.036 µg/mL; p=0.07) and in an aggregate analysis of all serotypes, (0.014 vs 0.05 µg/mL; p=0.02).

Conclusions: We found that Group B streptococcus is an important cause of neonatal and young infant disease in Uganda and confirmed that maternally derived antibodies were lower in EOGBS cases than in healthy exposed controls.

**64. Mr Michal Kawka**

Aneurysm CaRe – Pilot Randomised Controlled Trial of Cardiac Rehabilitation versus Standard Care after aortic aneurysm repair

*Kawka M, Budge JJR, Roy I, Bahia SS, Bown MJ, Holt PJE*

Background and aims: Abdominal and thoracic aortic aneurysms (A/TAA) are an important cause of mortality amongst the older population. The majority of deaths following A/TAA are caused by a heart attack or stroke, which can be prevented by cardiac rehabilitation (CR) – a multidisciplinary, biopsychosocial approach to the promotion cardiovascular disease recovery. However, it is unknown whether CR is feasible or acceptable to A/TAA patients, who are a older than those currently enrolling in CR.

Methods: This was a pilot, 1:1 randomised trial comparing CR to standard care (SC), following elective T/AAA repair, delivered in two UK tertiary care centres. Patients under the age of 50, suffering from connective tissue disorders, or deemed too unfit to participate in CR were excluded. Patients randomised to CR arm received a protocolised, 8 week regime of intensive medical risk factor reduction through supervised exercise, lifestyle modification, dietary interventions, and psychological assessment. The co-primary outcomes were the enrolment, with the hypothesis that 60% (95% CI 50.7% – 58.8%) of approached patients would be recruited, and the compliance to CR, with expected compliance to full regime of 70% (95% CI 55-84%). Secondary outcomes were major adverse cardiac events, biochemical cardiovascular markers, echocardiographic, lifestyle, and quality of life parameters. Data were analysed in R. This trial was supported by a British Heart Foundation Project Grant (PG/13/98/30490).

Results: Between September 2014 and September 2015, 159 patients were assessed for eligibility, with 97 being eligible, of whom 68 were randomised (70.1%) into SC (n=34) and CR (n=34). 21 patients attended all of the CR sessions (61.8%); 13 patients withdrew from CR group, with travel issues and personal commitments quoted as main factors. Amongst secondary outcomes, CR group maintained higher levels of physical activity at 36 weeks follow up (median 40 min vs 30 min, p = 0.042).

Discussion and conclusion: It is feasible to recruit patients after T/AAA surgery to structured CR programme, with 70.1% of approached patients enrolling in the study. Moreover, 81.0% of patients who began cardiac rehabilitation, completed all of the planned sessions. Novel approaches, including virtual, and video-based CR would help overcome barriers related to travel.

**65. Ms Rebecca Kimber**

Investigating the exerpeinces of peple with oral difficulties as a results of acquired facial palsy

*Kimber R, Calestani M, McRae J*

Introduction: It is estimated that 22,500 people experience peripheral facial palsy (PFP) in the UK per year. PFP results in unilateral facial weakness which can cause tightness, tension and reduced movement of the muscles, impacting on function. People with PFP often experience oral deficits (OD) including difficulty eating, drinking, communicating, smiling, managing saliva and creating a lip seal for leisure and vocational activities. There are no studies exploring the experiences of people living with PFP and OD.

Methods: This study aims to understand participants individual and shared experiences of OD and the impact on quality of life through qualitative methodology utilising an explorative design with phenomenological underpinnings. PPI were engaged to co-design the study. Purposive sampling was used to recruit participants through social media and charities. Focus groups were conducted to collect experiences. Reflexive thematic analysis was undertaken for data analysis.

Results: Thirteen participants, eight females and 5 males, with a mix of aetiologies took part. All were from white-British background, ages ranged from 24-66 years old and participants were geographically scattered in the UK. Three Focus groups were conducted virtually, lasting 90-120 minutes each. Five intersecting themes were derived from the data.

1. Experiences of mouth and lip difficulties
2. Experiences of other physical difficulties related to facial palsy
3. Living with and managing the symptoms of OD
4. The psychological impact of OD
5. Expectations for recovery and accessing care.

Conclusions: People with PFP experience OD as a consequence of their facial nerve injury. Experiences vary based on the persons interactions with their environment, vocation and personality. OD had a significant impact on the participants psychological well-being- and participation. Experiences of interactions with the National Health Service and Health Care Professionals impacted on care. The results of this study allow greater insight into the patient experiences of OD which will directly impact on clinical practice, support current research exploring OD and provide a platform for future research.

**66. Ms Julia Kutschenreuter**

Leucine-rich alpha-2 glycoprotein-1 drives lung remodelling in Tuberculosis via PI3K signalling

*Kutschenreuter J, Loader MC, Kirwan DE, Cusman R, Gilman RH, Friedland JS, Chong DLW*

Background: 10 million people are currently ill with Tuberculosis (TB), and are often left with significantly reduced lung function, a feature of post-tuberculosis lung disease (PTLD). The mechanisms driving PTLD are unknown, although neutrophils play a key role in TB immunopathology. Leucine-rich α2 glycoprotein-1 (LRG1) was proposed as a biomarker for active TB, but its cellular source and role are unknown. It may contribute to tissue remodelling by acting on

fibroblasts, the main structural cell in the lungs. We investigated whether LRG1 drives lung remodelling in TB, contributing to PTLD.

Methods: Serum LRG1 was measured by ELISA in a Perviuan cohort of TB patients (n=64) and healthy controls (n=51) at diagnosis and after 45 days of treatment. LRG1 expression was assessed in lymph node biopsies from TB patients by immunohistochemistry. Control neutrophils were infected for 4h with Mycobacterium tuberculosis (Mtb, at a 1:1 ratio) and secreted LRG1 measured. Primary human lung fibroblasts (PHLF, in later experiments pre-treated with a PI3K inhibitor for 1h) were stimulated with LRG1, and collagen production assessed by confocal microscopy. Secretion of inflammatory and tissue remodelling mediators were quantified by Luminex, and phosphorylated signalling proteins detected by Western blot.

Results: LRG1 serum concentrations in TB patients were significantly higher than in healthy controls (61.6±34.8 vs. 20.5±14.1µg/ml, $p<0.0001$). LRG1 concentrations decreased significantly after 45 days of anti-mycobacterial treatment ($p<0.0001$). Intracellular and extracellular LRG1 expression was detected in granulomatous TB lymph node tissue. Mtb-infection led to LRG1 secretion by neutrophils (1.3 vs. 0.24 ng/ml, $p=0.0159$). LRG1 stimulated IL-6, IL-13, GM-CSF, MMP-7, and MMP-8 secretion from PHLF ($p<0.05$). Furthermore, LRG1 significantly increased phosphorylation of AKT and extracellular collagen I deposition, a fibrotic marker, from PHLF ($p=0.0003$), which was significantly decreased upon inhibition of PI3K signalling.

Conclusions: Serum LRG1 concentrations are elevated in TB patients and decrease significantly during treatment, representing a novel biomarker for active TB disease. Neutrophils secrete LRG1 in response to Mtb infection, and LRG1 drives collagen production and expression of tissue remodelling mediators in fibroblasts via the PI3K/AKT signalling pathway. Targeting LRG1 may represent a novel host-directed therapy to prevent tissue remodelling in PTLD.

**67. Dr Mary Kyohere**

Increasing Maternal Immunisation Awareness, by Working with Women Influencers in Kawempe Division, Uganda

*Kyohere M, Nalubega P, Ssemere H, Ssali A, Le Doare K*

Background: WHO recommends two doses of Td injections during any pregnancy to realize full protection. However, WHO data in 2022 indicated that only 59.2% of pregnant women received TT2 in Uganda, indicating ineffective coverage and compromised protection for women and their newborns. A major driver of low uptake of TT vaccinations is lack of awareness of importance of maternal immunisation. This project set out to 1)create awareness on vaccine-preventable diseases, maternal immunization benefits, and vaccination safety, 2)determine effectiveness of maternal immunisation campaigns and ascertain whether there is increased awareness 3)assess stakeholder's acceptability of project interventions' delivery methods, and effectiveness of training on community influencers.

Methods: Twenty community influencers from ten parishes surrounding a major maternal-child health facility were trained on maternal vaccination using Uganda Ministry of Health Vaccination handbook, and did a door-to-door campaign, distributing t-shirts portraying key messages aimed at raising awareness. They helped co-create video and audio messages, that were shown in antenatal waiting areas, during community engagement sessions and broadcast over three radio stations. Three radio talk shows addressed questions around maternal immunisation and debunked myths.

Ten community engagement sessions were held with pre- and post-film Q&A sessions, to assess existing knowledge and learning among community members.

Results: Door-to-door campaign reached 900+, community engagement sessions involved 430+ community members. Audio and video messages were well received; 63% had heard radio broadcasts and were able to quote benefits of maternal vaccination. There was increased knowledge displayed by the end of the community engagement sessions. Male involvement among the influencers was appreciated as pregnancy and maternal health are widely viewed as women's issues.

Conclusion: Audio and video messaging campaigns are acceptable methods of public engagement and the involvement of men in health campaigns can help improve uptake of maternal vaccination.

**68. Miss Katie Latham**

An Unexpected Function of The Previously Uncharacterised HCMV protein UL2.

*Latham K, Goodbourn S, Strang B*

Human cytomegalovirus (HCMV) is a widespread pathogen that causes life-altering clinical symptoms in immunocompromised individuals. HCMV has the largest herpesvirus genome but there remains a large number of genes yet to be characterised, including those in the region UL2-11. Notably, UL2 has not been characterised to belong to any known family of HCMV proteins, but due to its size of only 59kDa it can be classified as a microprotein. Additionally, UL2 remains conserved across all mammalian strains of CMV, suggesting its importance. Therefore, this project aimed to characterise the HCMV protein UL2 and determine its function during infection. Initially, viral titre experiments with a single gene KO mutant in comparison to wildtype virus were performed to investigate the effect on viral growth of the presence/absence of UL2. This showed no difference in the reproductive pattern or final viral titre of the UL2-KO compared to wildtype virus. In parallel, infections with the UL2-KO mutant and wildtype were performed to examine temporal HCMV proteins by western blotting. This resulted in no reduction in the expression of immediate-early or early proteins, but a decrease in the expression of the late protein pp28 (UL99) in adult fibroblasts was observed in the absence of UL2. To characterise this further we performed yeast two-hybrid assays and confocal microscopy to investigate the interaction between UL2 and pp28. The yeast two-hybrid assays concluded no direct protein-protein interaction between UL2 and pp28. However, the confocal microscopy showed an increase in the frequency of assembly compartment complexes from which pp28 is an integral component. Our findings demonstrate an effect on pp28 by UL2 whereby a decrease in expression is observed in infected cell lysate by western blotting but an increase in the number of assembly compartments observed in cell by microscopy. We also determined this effect was by an indirect mechanism as UL2 and pp28 were found to not directly bind in isolation. Although a greater understanding is required of the relationship between detection of pp28 in different methods, our findings represent a novel mechanism wherein a viral microprotein indirectly affects formation of viral assembly compartments.

**69. Miss Skye Lau**

The influence of G protein-coupled Receptor Kinases on CGRP-mediated Relaxations in Rat Cerebral Arteries

*Lau S, Greenwood IA*

Calcitonin gene-related peptide (CGRP) is a neuropeptide with potent vasodilatory effects. The CGRP receptor, a class B GPCR, undergoes desensitisation and internalisation via G protein coupled-receptor kinases (GRK)-mediated phosphorylation, which recruits ß-arrestins. This prevents G-protein binding and facilitates receptor internalisation through clathrin-coated pits, leading to either receptor recycling or lysosomal degradation. This study aimed to investigate the role of GRKs in CGRP-induced relaxations in basilar arteries.

The expression of GRK2-6 and ß-arrestin 1 and 2 genes was quantified by RT-qPCR in rat cerebral and mesenteric arteries. CGRP effects were assessed via wire myography on pre-contracted arteries from male Wistar rats, with GRK2/3 inhibitor (compound 101) and GRK5 inhibitor (compound 707). Concentration-response curves were plotted logarithmically, with values expressed as mean ± SEM.

Our results showed that 10nM CGRP induced more sustained relaxation in mesenteric arteries compared to basilar arteries. In contrast, basilar arteries exhibited a transient relaxation response, diminishing after 5-10 minutes (n=5). Compounds 101 and 707 significantly enhanced and prolonged CGRP-evoked relaxations in basilar arteries (n=5). GRK2-6 and ß-arrestin 1 and 2 gene expression was confirmed in both vascular beds with a greater relative transcript abundance of GRK5 and ß-arrestin 2 in cerebral arteries (n=3).

In conclusion, this study highlights the involvement of GRK2, GRK3, and GRK5 in modulating CGRP-mediated relaxations in cerebral arteries.

**70. Mr Hamin Lee**

Characterising MRPL44(L156R) Transgenic Mouse Model: Insights into Mitochondrial Disorder Pathogenesis and Sex-Dependent Responses

*Lee H, Pittman A, Cooper S, Carroll C*

Background: A subset of primary mitochondrial disorders arises from recessive mutations in the mitochondrial ribosomal (mitoribosome), including the large subunit gene MRPL44. This study focuses on the L156R missense variant, shared by all nine reported patients with a pathogenic MRPL44 mutation, leading to a multisystemic clinical presentation involving the heart and liver.

In this study, a novel CRISPR-generated transgenic knock-in mouse model of L156R variant in MRPL44 was investigated as an animal model for mitochondrial disorders.

Methods: Heart, liver, brain, muscle and kidneys were harvested from young (1 and 3months) and mature (6 and 12 months) MRPL44 (L156R) and wildtype mice. They were processed for histopathology and molecular analyses of mitochondrial structure, content and function. Additionally, RNA sequencing was performed for evaluating the cellular gene expression response to mitoribosome dysfunction.

Results: The L156R mutation destabilised the MRPL44 protein, impacting mitoribosomal large subunit assembly. This resulted in mitochondrial translation defects, leading to concomitant

Complex I + Complex IV Oxidative Phosphorylation (OXPHOS) deficiency. Despite the marked biochemical deficiency, mild tissue pathology was observed, indicating compensatory pathways activation, in line with evidence of increased mitochondrial biogenesis. Additionally, the MRPL44(L156R) mutation induced sex specific phenotypes, with the females having more severe OXPHOS and mitoribosome deficiency. RNA sequencing unveiled sex-dependent bidirectional responses in mitochondria-related genes.

Conclusion: Our findings establish the MRPL44(L156R) mouse model as a promising tool for studying mitochondrial diseases, emphasising the significance of sex specificity in these disorders.

**71. Dr Fiona Leggat**

Process evaluation of a personalised self-management support intervention for people living with Long Covid

*Leggat FJ, Torrens-Burton A, Sevdalis N, Domeney A, Parson, J, Busse M, Jones F*

Background: The development and evaluation of rehabilitation interventions designed to support people with Long Covid (LC) remains an important ongoing priority. Many people with LC experience episodic, debilitating symptoms which can reduce their ability to engage in physical and social activity. The Long CovId personalised Self-managemenT support co-design and EvaluatioN (LISTEN) trial co-designed and evaluated a personalised self-management support intervention to support people to live better with LC.

Aim: This poster reports on the LISTEN process evaluation which sought to explore the context, implementation, mechanisms of impact and reported outcomes from the LISTEN intervention, in comparison with usual LC services accessed within the National Health Service (NHS).

Methods: The mixed methods process evaluation was nested within a 2-arm randomised controlled trial. Between September 2022 and January 2024, data were collected from sites in England and Wales. To assess fidelity, observations of healthcare practitioners (HCPs) delivering the intervention were conducted. Implementation science measures, focussed on intervention feasibility, acceptability and appropriateness, were gathered from HCPs and intervention participants. A subset of participants and HCPs further participated in semi-structured interviews and focus groups. Using a convergent design, data sources were analysed independently and subsequently integrated using the Consolidated Framework for Implementation Research v2.

Findings: Thirty-six HCPs participated in the process evaluation, 197 intervention participants completed implementation science measures, and 49 participants from both trial arms participated in semi-structured interviews. Six integrated cross-cutting themes were constructed across all data sources: ‘Delivery during uncertainty and ambiguity’, ‘Diversity and consistency of usual care, ‘Drivers for self-care and the impact of self-generated expertise’, ‘Appropriate if unexpected support’, ‘Personalisation at the core of success’ and ‘A spectrum of individual change’. These themes illustrate links between the context, implementation, mechanisms of impact and reported outcomes.

Conclusion: The LISTEN intervention is an appropriate, feasible intervention for participants and HCPs. With HCP training and ongoing support, the intervention can be delivered with high fidelity. Access, receipt, and perceptions of NHS LC services was variable. Personalised interventions such as

LISTEN, are acceptable, can foster favourable impacts on confidence, knowledge, and activity, and are strongly recommended for integration within NHS LC rehabilitation.

**72. Dr Fiona Leggat**

Building bridges: Co-designing a co-design process to develop self-management support for stroke survivors in the Philippines

*Leggat FJ, Otter P, Ballard-Ridley S, Jones F*

Background: About 500,000 Filipinos will be affected by stroke at any point in time, with an estimated US$350 million to $1·2 billion needed to meet the cost of medical care. Most of the cost is borne out-of-pocket by patients and their families, with limited use of healthcare by lower and middle-income groups. There is a lack of established community-based care facilities in the Philippines, and qualified staff to deliver rehabilitation are scarce. The Tulong, Ugnayan ng Lingap At gabaY (TULAY) project, funded by the NIHR Global Health programme, aims to address this lack of provision, and co-design and implement a sustainable self-management community-based programme for stroke survivors, contextualised for the Philippines.

Aim: This poster reports on the current progress of the co-design process, with a focus on the successes, challenges and learnings from adapting, co-designing and applying an existing UK co-design process in the Philippines.

Methods: Informed by Bridges Self-Management (Bridges), a participatory experience-based co-design (EBCD) methodology will be adapted and applied across six sites spanning municipalities in Luzon, Visayas and Mindanao. Co-design meetings will engage multiple stakeholders, including stroke survivors and their families. To support the adaptation and use of EBCD, the Philippines teams' will attend weekly co-design coaching sessions provided from FL, FJ and Bridges. Semi-structured interviews with Philippines and Bridges team members supporting the co-design, and field notes from coaching sessions will be used to capture their experiences. Data will be analysed using thematic analysis to understand successes, challenges, solutions and learning from the co-design processes.

Results: The first site, Las Piñas, in Luzon, begun their co-design process in Autumn 2024. Preliminary themes from field notes have highlighted challenges with terminology (e.g., self-management and co-design), difficulties managing difficult conversations (e.g., stories of depression), expectations of information-giving and navigating power dynamics.

Conclusions: The five remaining co-design processes be ongoing until mid-2025. Co-design meetings will continue to be undertaken with stroke survivors, their families, healthcare staff and village workers until contextualised, sustainable self-management resources are developed. A full implementation evaluation of the self-management support resources will be completed by 2026.

**73. Dr Alejandra Letelier**

Inequalities in Wellbeing Around Becoming a Young Carer in the UK

*Lacey R, Letelier A, Xue B, McMunn A*

Introduction: Caring responsibilities can profoundly affect young carers' wellbeing. This paper adopts a longitudinal approach to comprehensively analyse both the immediate and long-term effects of becoming a young carer.

Objective: To investigate the longitudinal impact of becoming a young carer on wellbeing compared to peers who are not carers, examining how this effect varies by care intensity (weekly hours), gender, ethnicity, and socioeconomic status.

Methods: Data from the UK Household Longitudinal Study (2009-2023) were used, focusing on individuals aged 10-25 across Waves 1-13. Wellbeing was measured via self-reported life satisfaction and self-esteem. Carers were matched with non-carers using Propensity Score Matching. Linear piecewise growth curve modelling was applied to examine wellbeing trajectories pre-, during, and post-caring. The analysis included 4,202 individuals, stratified by care intensity, gender, ethnicity, and household income.

Results: Wellbeing declined at the transition to care, with a more pronounced decrease observed in young carers compared to non-carers. High-intensity carers reported lower life satisfaction and self-esteem than low-intensity carers, a trend that persisted post-transition. Declines were observed for both males and females, with no significant gender differences. White carers reported lower wellbeing than white non-carers, while carers from other ethnic groups showed similar levels of wellbeing to non-carers during and after the transition. Carers from lower-income households also reported reduced wellbeing at the transition to care.

Conclusion: Young carers experience a marked decline in wellbeing during the transition into caregiving, more so than non-carers, with the effect particularly pronounced for those providing intense care and those from socioeconomically disadvantaged backgrounds.

**74. Dr Leonie Lewis**

Demographic representation in clinical trials of vaccine preventable diseases at St George's Vaccine Institute: a quantitative analysis

*Lewis L, Evans L, Radia K, Gregory B, Chan T, Galiza E*

Background: Representative populations in clinical trials of vaccine preventable diseases are vital in establishing efficacy of vaccines across patient groups and in identifying important differences in efficacy and safety outcomes.

Objective: To investigate whether the recruitment of participants to clinical trials of vaccine preventable diseases at St George's Vaccine Institute (SGVI), Centre for Neonatal and Paediatric Infection, part of City St George's, University of London represents the demographics of Greater London as the wider area.

Methods: A retrospective cohort study of participants recruited to vaccine clinical trials at SGVI was conducted. Demographic data including ethnicity, Index of Multiple Deprivation (IMD), and distance to study site were reviewed. Participant ethnicity data was compared to ethnicity data for Greater

London based on the 2021 census. IMD data was captured by 2019 UK IMD postcode data, classified into quintiles for statistical analysis, and compared to IMD data for Greater London.

Results: The demographic data of 1460 participants recruited to fifteen vaccine clinical trials between 2020 and 2023 was assessed. Ethnicity data was available for 1245 participants. 87.1% of participants were white compared to 53.8% of the Greater London population. 12.4% of participants were from BAME groups compared to 46.2% of the Greater London population. Demographic postcode data was available for 555 participants - 3.7% of study participants were in IMD quintile 1 (most deprived) compared to 16.3% of the local population (OR 0.44; 95% CI:0.29 to 0.68; p=0.0002). Conversely 33.3% of study participants were in IMD quintile 5 (least deprived) compared to 11.7% of the local population (OR 7.99; 95% CI 6.69 to 9.52; p<0.0001). Average distance from place of residence to study site location was 6.12 miles, and 4.56 miles when 5% of outliers were removed.

Conclusions: Participants in vaccine clinical trials at SGVI are not representative of the demographics of the wider area. Participants were disproportionately recruited from white ethnic and higher socioeconomic status populations. Inequalities in socioeconomic and geographic factors may influence recruitment. This has implications for healthcare equity and generalisability of clinical trial results. There is a need for continued awareness and new approaches in designing studies that reflect population diversity.

**75. Ms Elizabeth Limb**

Tuberculosis and increased incidence of cardiovascular disease: a cohort study using UK and US electronic health records.

*Limb ES, Khakharia A, Carey IM, De Wilde S, Chaudhry UAR, Bowen L, Harris T, Auld SC, Phillips LS, Cook DG, Magee MJ, Critchley JA*

Background: Tuberculosis (TB) has been the leading cause of infectious disease mortality globally, with about 1.5 million deaths annually. Limited evidence suggests elevated risks of cardiovascular disease (CVD) among people diagnosed with TB disease, although existing studies have not adjusted for pre-existing CVD risk and may also be affected by selection biases or residual confounding.

Methods: Cohort analyses used 2000-2020 electronic health data from the United Kingdom (Clinical Practice Research Datalink) and United States (Veterans Health Administration). Adults with incident TB disease (UK n=15,820; US n=2,121) and no CVD history 2-years before TB diagnosis were matched (age, sex, ethnicity/race, health-care practice) with up to 10 people without TB. Participants were followed +/- 2 years of TB diagnosis, the main outcome was incident CVD events. Five analysis periods were defined: baseline (1-2 years before TB diagnosis), pre-acute (3-12 months before), acute (+/- 3 months of TB diagnosis), post-acute (3-12 months after), post-TB (1-2 years after). Poisson regression models, adjusting for covariates (socio-economic deprivation, body mass index, smoking, co-morbidities, prescribing of statins or anti-hypertensives) estimated incident rate ratios (IRR) in each period for CVD events in people with TB compared to those without and also adjusted for baseline differences.

Results: In both UK and US cohorts, CVD incidence was consistently higher in people with TB compared to those without TB throughout the two years before and after TB diagnosis. Patterns were similar in both cohorts, although CVD incidence rates were higher in the US data, likely due to the different age-sex profile. The IRR was significantly higher for the acute period: UK IRR=2.7 (95%CI

2.1, 3.4), US IRR=4.0 (2.7-5.9). After adjusting for differences at baseline (1-2 years before diagnosis), rate ratios remained high in the acute period: UK 1.6 (1.2-2.1), US 3.2 (2.2-4.4).

Conclusions: The rate of incident CVD events close to date of TB diagnosis was 3-4 times higher in patients with TB disease compared with similar patients without TB. After adjusting baseline differences in CVD incidence, rates were still 2-3 times higher. Enhancing CVD screening and risk management may improve long-term outcomes in people with TB.

**76. Ms Katy Mackey**

Prevalence of sexually transmitted infections in migrants: a policy analysis and systematic review

*Mackey K, Morais B, Al-Sharabi I, Mayaud P, Pescarini JM, Hargreaves S*, Sanchez Clemente N**

Introduction: Sexually transmitted infections (STIs) are a major public health concern. While migrants are disproportionately impacted by HIV and other blood-borne viruses, research on the prevalence of STIs among migrants is limited. STIs are not yet routinely included in host countries' initial health assessments or screening of migrant populations and migrants may face significant barriers in accessing essential sexual health services. Further research is necessary to understand the impact of STIs on migrant groups and develop best practices for sexual health service providers.

Methods: First, I conducted a policy analysis on UK policy and strategy documents related to sexual health and migrant health. Resources published in the last ten years were analysed for the content related to migrants' sexual health. Secondly, I conducted a systematic review to explore the prevalence of STIs in migrant groups globally. Studies from 2014 to 2024 were searched in MEDLINE, Embase and Ovid Global Health without language limitation. Narrative synthesis was conducted to analyse study settings, populations studied, prevalence by infection, relative risk and barriers and facilitators of migrants' access to sexual health services.

Results: Of the 25 included resources on sexual health policy in the UK, only 11 make any reference to migration and only four recommend specific provisions for migrants. 119 studies were included in the narrative analysis of the systematic review. The most studied infection was syphilis. The majority of studies did not include a comparison group. Of the studies that did include native-born populations as comparators, two thirds found that migrants had a higher prevalence of STIs, while almost a quarter found a lower prevalence among migrants.

Conclusion: Migrants are currently poorly considered within UK sexual health and STI prevention policy. A lack of quantitative data on STI prevalence within this population impedes evidence-based policy making.

**77. Dr Chinedu Maduakor**

7T MRI Study of Small Vessel Damage and Cognitive Impact in Adults with Sickle Cell Disease

*Maduakor C, Benjamin P, Cleary J, Rhodes E, Doogan C, Isaacs J, Hainsworth A*

Sickle Cell Disease (SCD) affects approximately 17,000 individuals in the UK and is characterized by an autosomal recessive mutation in the haemoglobin beta gene (HBB). Severe forms of SCD, such as HbSS and HbSß0 genotypes, are associated with significant complications, including vascular fragility and cerebrovascular events that contribute to cognitive decline and disability. Although cognitive

impairment in children with SCD has been well documented, there is limited research on its impact in adults. As the life expectancy for individuals with SCD increases, understanding the progression of neurovascular complications in adults is essential for improving their quality of life and functional outcomes.

This study utilises ultra-high-resolution 7 Tesla (7T) MRI to examine early microvascular changes in adults with severe SCD, specifically targeting small vessel morphology, blood flow abnormalities, and microinfarctions.

We hypothesise that abnormal small vessel morphology, ischaemic damage, and cognitive impairment will be more prevalent in adults with severe SCD compared to healthy controls.

Our proof-of-concept design involves two participant groups:

1. A control group of 15 adults aged 18-50 with no known health conditions or recent transfusions, not meeting standard MRI exclusion criteria.

2. A patient group of 15 adults aged 18-50 with severe sickle cell disease (defined by HbSS/HbSß0 genotypes) also not meeting standard MRI exclusion criteria.

At St George's University Hospital, an established multidisciplinary team (MDT) service already provides specialised care for over 300 SCD patients, addressing neurological complications and stroke risks through a weekly neurovascular clinic. The MDT team includes neuro-radiologists, neurologists, and haematologists, who collaboratively deliver timely and comprehensive care for both acute and chronic neurovascular cases. Through this structured pathway, patients receive individualised treatment plans that incorporate transfusions or tailored interventions based on neuroimaging and cognitive assessments.

Integrating our MDT framework with this research study will allow us to evaluate neuroimaging and cognitive screening tools for identifying SCD patients at high risk of cognitive decline. Our findings aim to support early intervention pathways and model optimal neurovascular care in SCD, underscoring the value of a tailored, interdisciplinary approach for managing complex, lifelong impacts of SCD on neurological health.

**78. Dr Natasha Matthews**

Emergency care without borders: a scoping review of migrant health in the Emergency Department

*Matthews NR, Jarman H*

Aims and objectives: Today, migrants comprise at least 10% of the European Region's population, leading to diverse and complex healthcare needs. Vulnerable migrants, including refugees and asylum seekers, are particularly exposed to health challenges such as chronic diseases, mental health issues, maternity-related complications, and communicable diseases. Migrants commonly face barriers to healthcare, such as legal status, interpreter shortages, and limited guidance on accessing healthcare, leading to poorer health outcomes compared to host communities. Recognising the unique health challenges these populations face is crucial for developing effective and equitable emergency care services. Whilst migrant health literature is growing, the representation of migrant health research in emergency care is not yet known.

Methods: We conducted a scoping review to determine the scope and type of literature relating to migrant populations in European Emergency Departments (EDs). MEDLINE and PUBMED databases

were searched using keywords “migrant” and “Emergency Department” or “Emergency Room.” All papers published before June 2024 were reviewed, and non-English language papers were excluded. The papers were categorised by study characteristics and analysed for themes by two reviewers.

Results and conclusion: Thirty-two papers met the inclusion criteria, 26 of which were published from 2017 onwards. The majority were from Switzerland (9), the UK (4), Germany (3), Greece (3), Italy (3) and Spain (3). The literature focused on three predominant themes: health service and ED utilisation, clinical outcomes and quality of care, and the use of interpretation services and communication challenges. There was large variability in definitions used for migrant populations.

The literature on migrant populations in the ED is limited but highlights barriers such as language difficulties, limited access to care, and higher rates of chronic and acute conditions compared to the host population. The studies also consistently highlight the importance of interpreter services and tailored healthcare provision for migrants. More comprehensive research is needed to address these gaps and inform policy and practices to ensure equitable healthcare.

**79. Mr Michael Mills**

Magnetic Resonance Lymphangiography of Healthy Individuals

*Mills M, Pearce J, Ho B, Gordon K, Ostergaard P, Howe FA*

Background: Contrast Enhanced Magnetic Resonance Lymphangiography (MRL) is increasingly employed to depict lymphatic vasculature in people with lymphoedema. However, few reports have investigated these vessels in non-oedematous individuals. Nor, despite its increased use , has there been a thorough investigation of how contrast agent (CA) injection protocol affects image appearance. We have performed MRL in the legs of individuals without a history of lymphatic disease to establish normal lymphatic appearance, the dynamics of CA uptake and distribution, and have begun to explore how changes in CA administration may affect these.

Methods: Images from 17 healthy individuals (10 female) who underwent MRL of their lower limbs using a 3.0 T Philips magnetic resonance imaging scanner were assessed. All participants were imaged before and after forefoot injections of a Gadolinium based CA. For two individuals (1 female), imaging was repeated with CA injected into the 1st and 4th interdigital spaces, lateral midfoot and medial and lateral aspects of the rear of the foot. Instances of lymphatic drainage via any of four established anatomical drainage routes were recorded for each limb and, for a subset of lymphatic vessels, their diameter and tortuosity were estimated.

Results: Following forefoot CA injection, lymphatic vessels following the anteromedial pathway were routinely observed. An average of 2.18 ± 0.92 lymphatic vessels of diameter 2.47 ± 0.49 mm were measured as crossing the anterior ankle. In seven limbs, vessels following the anterolateral pathways were observed. No vessels traversing the posterior of the legs were seen.

In the two participants with alternative injection sites, lymphatic vessels travelling up the posterior of their legs were additionally visualised.

Conclusions: Contrast-enhanced MRL reliably depicts the lymphatic vessels in the legs of healthy controls. Following interdigital contrast injection, anteromedial drainage appears dominant. Posterior lymphatic drainage may additionally be observed following CA injections to locations in the foot more commonly employed for indocyanine green fluorescence imaging. Quantitative measures related to lymphatic vessel size and tortuosity rate are obtainable. However, automatic methods to

detect and segment vessels are required to ensure accurate and reproducible analysis, and reduce the analysis time burden.

**80. Mrs Sile Molloy**

Illuminating the full spectrum of cryptococcal disease through linked clinical trial, cohort and surveillance studies

*Molloy SF, Berghammer-Bohmer R, Thombrayil A, Adams J, Comins K, Nel J, Tsitsi M, Bremer M, Verhagen D, Kabanda D,6 Maphalala L, Mfinanga S, Lesikari S, Ladislaus N, Mosses A, Makoko N, Edkins L, Fatti I, Halley-Stott R, Meiring S, Quan V, Mashau R, Lawre*

Background: Understanding pathophysiology and outcomes associated with each stage on the spectrum of cryptococcal disease is essential for optimising the management of patients with AIDS.

Methods: Data from three cohorts of patients at different stages of HIV-associated cryptococcal disease were described at the same sites in South Africa (SA) and Tanzania: 1) asymptomatic cryptococcal antigenaemia (EFFECT phase III trial), 2) subclinical cryptococcal meningitis (CM) (subEFFECT prospective cohort study), 3) symptomatic CM (surveillance study, SA; prospective cohort study, Tanzania).

Results: Data for 322 individuals with asymptomatic cryptococcal antigenaemia [trial data not currently available], 28 subclinical CM and 188 symptomatic CM were collected from November 2022 to June 2024 (recruitment is ongoing).

Subclinical CM cohort: Median age was 41 years (IQR: 31-49) with 50% (14/28) male and 67.9% (19/28) ART experienced. Seventeen baseline opening pressures were recorded; median 17cm H2O (IQR: 16-21cm H2O). Following treatment, overall mortality was 42.9% (12/28). Of those with appropriate follow-up data, 2-week, 10-week and 6-month mortality 8.0% (2/25), 43.5% (10/23) and 63.2% (12/19), respectively. 75% (9/12) died as inpatients with a median time to death of 33 days (IQR: 18-70 days).

Symptomatic CM cohort: Median age was 39 years (IQR: 34-45) with 64.9% (122/188) male and 59.6% (102/171) ART experienced. Overall mortality was 45.2% (85/188). Of those with appropriate follow-up data, 2-week, 10-week and 6-month mortality was 23.9% (44/184), 48.7% (75/154) and 63.4% (85/134), respectively. 87.1% (74/85) died as inpatients with a median time to death of 14 days (IQR: 3-30 days).

Discussion: These cohorts spanning the cryptococcal disease spectrum will yield important comparable data to inform future management, particularly considering whether subclinical CM requires inpatient treatment. Current descriptive findings indicate that deaths among this subclinical CM cohort are not usually directly attributable to cryptococcal disease.

**81. Mrs Sile Molloy**

EFFECT - Fluconazole plus flucytosine vs. fluconazole alone for cryptococcal antigen-positive patients identified through screening: A phase III randomised controlled trial

*Molloy SF, Govender NP, Comins K, Mfinanga S, Meintjes G, Lesikari S, Eriksson M, Adams J, Nel J, Moosa MY, Wilson D, Tsitsi M, Black J, Kyazze D, Alam N, Variava E*

Background: Cryptococcal meningitis (CM) is the commonest form of meningitis in sub-Saharan Africa (SSA), accounting for 15%-20% of all AIDS-related deaths. Screening patients with advanced HIV disease to detect cryptococcal antigen (CrAg) in the blood and treatment of CrAg-positive patients in advance of severe cryptococcal disease represents a practical and cost-effective approach to reducing mortality. However, current pre-emptive treatment with fluconazole alone may be suboptimal with a substantial number of patients going on to develop cryptococcal meningitis and die. The EFFECT trial aims to assess the effectiveness of a combined treatment of fluconazole plus flucytosine (a drug combination recently shown to be effective for inpatients with CM) in this patient cohort.

Methods: The EFFECT trial is a phase III, multi-centre, open-label, 1:1 randomised treatment trial embedded into existing CrAg screening programmes at 13 sites in South Africa, Tanzania and Vietnam. The primary objective it to determine whether combination treatment of fluconazole plus flucytosine for 2 weeks will be superior to standard treatment of fluconazole alone in reducing 6-month all-cause mortality for CrAg-positive individuals with advanced HIV disease.

Results to date: The trial opened to recruitment at all African sites in Nov 2022. Vietnam sites will open Q1 2025 following receipt of all approvals. To date, 378 participants have been recruited (332 in SA and 46 in Tanzania). Recruitment will continue until October 2025, followed by 6-month follow-up.

Discussion: Demonstrating the effectiveness of the addition of flucytosine to the fluconazole treatment currently in use for this patient cohort could have an important global impact on the reduction of advanced HIV mortality as has been seen for CM inpatients.

**82. Mr Cameron Moss**

Functional paraplegia and anaesthesia: A review of two cases from a physiotherapy service.

*Moss C, Higgins R, Teodoro T, Nielsen G.*

Objective: To identify and discuss the clinical characteristics and treatment outcomes of two people presenting to physiotherapy with functional paraplegia and anaesthesia in the lower limbs.

Background: Scan-negative cauda equina syndrome is a relatively common presentation, with symptoms experienced in the absence of compression on imaging [1]. Less common are people with functional neurological disorder (FND) presenting with symptoms involving bladder/ bowel dysfunction, and a complete absence of voluntary movement and sensory perception in both lower limbs. In our FND physiotherapy service, two patients with these symptoms presented over 12 months. Symptom onset was after a functional seizure for person A, and following complications post decompressive spinal surgery for person B. Both had experienced past mental health difficulties, and had completed previous inpatient rehabilitation without experiencing any improvement.

Methods: Review of two people who presented to a specialist physiotherapy service for FND. Treatment followed physiotherapy consensus recommendations [2]. Treatment adjuncts included functional electrical stimulation, an electric standing frame, and a tilt-table. Outcomes were collected using the Clinical Global Impression Scale (CGI), Berg Balance Scale (BBS), and Functional Mobility Scale (FMS).

Results: Both people had similar demographics, predisposing, precipitating, and perpetuating factors. They presented with significant non-dermatomal somatosensory loss and absent movement in the lower limbs not explained by neurophysiological testing. Both had a positive Spinal Injury Centre Test for functional weakness. Mechanical vibration and pain pressure thresholds were not detected. They had absent sensation for bladder or bowel movement. After intensive outpatient physiotherapy treatment, person B regained sitting balance, but the CGI and FMS were unchanged in both people. Neither person regained movement nor sensory perception of their lower limbs.

Conclusion: Functional weakness and sensory loss are common in FND, and scan-negative cauda equina syndrome can share these symptoms. However, the experience of paraplegia and anaesthesia in both lower limbs are rare. This small sample size limits generalisability, however, we suggest that in these cases the combination of a medical triggering event, the absence of movement and sensation in the lower limbs, and past psychological comorbidity contributed to the resistance of these symptoms to rehabilitation.

References

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**83. Miss Ruby Moy**

Structural variants dysregulating FOXC2 cause Lymphoedema Distichiasis Syndrome?

*Moy R, Dobbins S, Mansour S, Pagnamenta A, Noble A, Birdsey G, Martin-Almedina S, Ostergaard P*

Primary Lymphoedema (PL) is a rare lifelong disabling condition caused by underlying genetic defects leading to lymphatic dysfunction. These defects lead to lymph fluid retention in the affected limb(s). Lymphoedema distichiasis syndrome (LDS) is an autosomal dominant inherited form of PL, typically with distichiasis (abnormality of the eyelashes) present from birth and pubertal onset of lower limb lymphoedema. Whilst LDS presentation is variable both within and between families, the genetic basis is homogenous with 95% of patients harbouring heterozygous, pathogenic variants in the FOXC2 gene (Mansour et al, 2005). Despite this, there are still several patients that do not have a variant within the coding region of FOXC2. Investigating whole genome sequencing of four new LDS families recruited to the 100,000 Genomes Project, we identified they each have structural variants (SVs) in the noncoding region of FOXC2.

In this work, we use Decipher to investigate variation surrounding FOXC2 as well as combining data sets such as ATAC-seq and ChIP-seq from lymphatic endothelial cells. It is likely that these distal SVs delete or disrupt cis-regulatory elements controlling the expression of FOXC2, therefore we can

utilize these datasets to look for regions that could possibly be enhancers of FOXC2 in the regions of our SVs, as well as previously reported SVs (Butler et al, 2012, Le Collen et al, 2022).

Our findings suggest that small deletions ~1500kb that do not include the FOXC2 gene can cause LDS. We found that there are numerous cis-regulatory elements covering this region with several different transcription factors binding. However, there is a region that is shared between most of the SVs containing an enhancer which binds PROX1, a transcription factor essential for lymphatic development. Future work will involve investigating whether this enhancer is active using a luciferase assay.

This work highlights the importance of looking for variants outside of the coding regions of the causative gene. The establishment of additional genetic diagnosis will lead to appropriate referrals for disease management and genetic counselling for these families and could inform the development of novel or more effective therapies.

**84. Miss Rahil Muhanna Isar**

Characterisation of the interaction between activated αIIbβ3 and SLC44A2

*Isar RM, Caroline G, Greenwood IA, Crawley J, Salles-Crawley I*

Background: Venous thrombosis (VT) is a leading cause of morbidity and mortality worldwide. Although the major risk factors for VT are well understood, the mechanisms driving VT development remain poorly characterised. We recently demonstrated that in binding to von Willebrand Factor platelets become primed to present activated αIIbβ3 that in turn binds to neutrophil SLC44A2. This transduces intraneutrophil signals that promote the formation of prothrombotic neutrophil extracellular traps – a precursor to VT development. In support of this, a common single-nucleotide polymorphism (rs2288904-A) in SLC44A2 results in an R154Q substitution in the SLC44A2 extracellular domain 1 (ED1). This disrupts the interaction with activated αIIbβ3 and protects against VT. However, the molecular mechanisms of αIIbβ3 interaction with SLC44A2 remains unclear.

Aims: To characterise the binding of activated αIIbβ3 to SLC44A2 and investigate the role of SLC44A2 in neutrophils.

Methods: SLC44A2 ED1 was recombinantly expressed and purified to homogeneity. Slc44a2-/- mice were immunised with SLC44A2 ED1 and resulting mAbs were screened for binding recombinant SLC44A2 ED1 and full length human and murine SLC44A2. Alphafold predicted four regions (P1-4) in SLC44A2 ED1 with putative amino acids potentially involved in αIIbβ3 binding. The binding of αIIbβ3 to SLC44A2 WT/P1-4 was assessed under flow conditions using VWF-bound platelets.

Results: 44 mAbs demonstrated strong reactivity to human SLC44A2 ED1 in ELISA, with 11 also cross-reacting with mouse SLC44A2 ED1. Further screening identified those mAbs that also recognised full length human and mouse SLC44A2 on the surface of cells. SLC44A2 (WT and P1-4) were successfully transfected in HEK293T cells, and ongoing experiments are evaluating the αIIbβ3-SLC44A2 interaction under flow conditions.

Conclusion: We generated high affinity mAbs against SLC44A2 ED1. These will help us characterise SLC44A2 cellular physiology and understand how the αIIbβ3-SLC44A2 interaction drives neutrophil extracellular trap formation.

**85. Miss Vicky Mummery**

Evaluating a practitioner-led rapid 'see and assess' model for non-urgent patients in the Emergency Department

*Mummery V, Jarman H*

The increasing patient workload in UK Emergency Departments (ED) is well documented. To meet this demand several strategies have been proposed to improve patient flow and increase the functional capacity (process and turnaround times) of EDs, including rapid assessment models and use of senior decision makers at the 'front door'.

To address a local challenge of flow in non-urgent patients, we introduced an early assessment and diagnostic pathway for adult patients with minor injuries and illness led by Emergency Practitioners (EPs). We evaluated the impact of this model on the time to see clinician, time to interventions and 'left without being seen' (LWBS) rates in this group of patients in a large London ED.

Methods: a pre- and post-implementation study using retrospective data was undertaken. Data were collected for 2-weeks during the pre-implementation period in June 2023 and 2-weeks in August 2023 after the EP-model initiation. Variables included time to clinician, x-ray, analgesics and referral, and LWBS rates.

Independent sample t-tests were completed on pre- and post-implementation data to review differences between groups with significance set at $p<0.001$.

Results: analysis was of 1032 and 1031 patients (pre- and post-implementation respectively). Mean reductions in time to clinician, bloods, and specialty referral were observed comparing pre-and post-implementation phases. Statistically significant reductions were noted in time to x-ray and discharge/admission decision. Conversely, mean time to analgesia increased. LWBS decreased by 2.32% between groups.

Conclusions: the time reductions in this work align with findings from previous studies of doctor-led rapid assessment models and supports the efficacy of this model in improving functional capacity in the ED.

**86. Miss Ayesha Naeem**

Visualising the function of glutamine transporter ASCT2 in cancer cell lines ?

*Naeem A, Hughes H, Carter T, Török K*

The most prevalent amino acid in human is glutamine, essential for cellular metabolism, protein synthesis, and energy production. These activities depend on its absorption into cells, which is principally carried out via the Alanine Serine Cysteine Transporter 2 (ASCT2). There are few techniques to track ASCT2's activity and mechanism in cellular systems, despite the fact that its significance in cancer biology is becoming increasingly apparent. Optical methods, specifically Fluorescence Lifetime Imaging Microscopy (FLIM) and Förster Resonance Energy Transfer (FRET), are used in this work to investigate ASCT2 function by tracking real-time conformational changes and protein-protein interactions during glutamine absorption.

The first step in the research was to choose the right fluorescent proteins (FPs) to use in FRET, a technique that tracks conformational changes in ASCT2 based on the proximity of two fluorophores.

By choosing FRET pairs with an appropriate Förster distance, dynamic mechanisms associated with ASCT2 function were found, and the system was verified by the successful expression of these FPs in both cancer and healthy cells. Moreover, when co-expressed with ASCT2 constructs, intracellular glutamine sensors were added to track glutamine input and revealed novel results. These results were supported by FLIM, which demonstrated fluorescence lifetime linked to glutamine uptake and ASCT2 activity.

This work provides important information about the function of ASCT2-mediated glutamine transport in cancer metabolism by demonstrating the effectiveness of FRET- and FLIM-based methods. These results lay the groundwork for future studies that specifically target ASCT2 in cancer therapy, which might result in the development of novel methods to interfere with the metabolic requirements of cancer cells.

**87. Dr Shabir Najmudin**

Experimental localization of metal-binding sites reveals the role of metal ions in type II DNA topoisomerases

*Najmudin S, Wang B, Pan XS, Mykhaylyk V, Orr C, Wagner A, Govada L, Chayen, Fisher LM, Sanderson MR*

Metal ions have important roles in supporting the catalytic activity of DNA-regulating enzymes such as topoisomerases (topos). Bacterial type II topos, gyrases and topo IV, are primary drug targets for fluoroquinolones, a class of clinically relevant antibacterials requiring metal ions for efficient drug binding. While the presence of metal ions in topos has been elucidated in biochemical studies, accurate location and assignment of metal ions in structural studies have historically posed significant challenges. Recent advances in X-ray crystallography address these limitations by extending the experimental capabilities into the long-wavelength range, exploiting the anomalous contrast from light elements of biological relevance. This breakthrough enables us to confirm experimentally the locations of Mg2+ in the fluoroquinolone-stabilized Streptococcus pneumoniae topo IV complex. Moreover, we can unambiguously identify the presence of K+ and Cl- ions in the complex with one pair of K+ ions functioning as an additional intersubunit bridge. Overall, our data extend current knowledge on the functional and structural roles of metal ions in type II topos.

**88. Dr Miriam Nantamu**

Comparison of community and hospital Antibiotic use practices, Susceptibility and resisTance and determinants of care seeking among patients with Urinary Tract Infections (CAST-UTI)

*Nantamu M, Ekusai D, Tuheirwe H, Enomut JR, Sharon N, Kirabo PE, Gobba S, Kajumbula H, Kitutu F, Kapisi J, Moore C*

Introduction: Despite the establishment of the WHO Global Antimicrobial Resistance Surveillance System (WHO-GLASS) and other surveillance systems and data gathering exercises, there is a noticeable gap in detailed, community-level data. Virtually no data exists on antibiotic use and its association with AMR, thus hindering context-specific interventions to address AMR.

The primary challenge is the scarcity of micro-level data on antibiotic dispensing practices and their impact on the emergence of resistant bacterial strains outside of hospitals. Our research bridges this

gap by exploring the nexus between antibiotic resistance and treatment practices, human behaviour, and socioeconomic factors, to shed light on the drivers of AMR in the community.

We focus on uncomplicated urinary tract infections (uUTIs), a frequent reason for pharmacy visits in Uganda, to understand where patients go when they have a UTI, and which antibiotics they are dispensed at community drug retail outlets (CDROs)

Materials and Methods: Attendants at the CDROs/clinics and hospital OPDs within the boundaries of Namuwongo and Muyenga in Kampala are eligible to enrol. Participants are being recruited for qualitative research using convenience sampling to understand the patient pathway and how they manage uUTIs in the community using a semi-structured qualitative interview guide.

Results: The patient journey is complex, shaped by co-morbidities alongside uUTIs, strong therapeutic relationships, perceived seriousness of the UTIs, treatment failures, and referral for further laboratory tests when resistance is suspected. Patients seek care at one or more facilities at different points along the treatment pathway depending on the treatment outcomes, ability to pay the out-of-pocket costs, and access to antibiotics and laboratory testing services.

Reported treatment failures and assumed resistance are blamed on self-medication, misuse, overuse of antibiotics, misdiagnoses, over/under-prescribing antibiotics, and prescribing second-line parenteral antibiotics for uUTIs. Antibiotic prescription relied on symptoms, test results when performed, available antibiotics, suspected resistance, treatment failure, affordability of tests and treatments, and sometimes patient choice.

Positive treatment outcomes were linked with patient follow-up, providing holistic care, altruism, health education, compliance with medical advice, and access to appropriate antibiotics and tests.

Conclusions: From this small sample at the beginning of our study, we can see patterns emerging.

**89. Miss Andisheh Niakan**

“What makes osteoarthritis painful? Understanding the mechanisms of pain and tissue damage induced by bone marrow lesions in osteoarthritis”

*Niakan A, Chikh A, Westaby J, Sofat N*

Osteoarthritis (OA) is the most prevalent form of arthritis worldwide and is a leading cause of chronic pain and disability. OA is characterised by complex disorders of the whole joint, involving structural defects of hyaline articular cartilage, loss of intact subchondral bone, tissue hypertrophy and increasing vascularity in the synovium. Currently, there is no effective treatment to alleviate OA symptoms and prevent disease progression.

Joint pain is the hallmark symptom of OA. Advanced imaging techniques like MRI have indicated that the presence and severity of pain are associated with specific features of OA, including synovitis, cartilage degradation, bone marrow lesions (BMLs), and osteophyte formation. BMLs are a very early biomarker of joint damage in OA and are associated with structural change, lost osteochondral integrity, fibrosis, cysts, and de novo cartilage within subchondral bone.

Our group previously performed a whole transcriptomic analysis of OA-BML regions, which showed upregulated expression of genes involved in neurogenesis, pain sensitisation, chemokine and cytokine signalling pathways, and cartilage remodelling pathways. In the current study, we are

investigating further some of the most upregulated genes from the microarray study in both human cell lines and BML tissues.

We have used various techniques, including qPCR, western blotting and immunocytochemistry to reveal the expression profile of the genes of interest at mRNA and protein levels in osteoblasts. Our data showed overexpression of several candidate genes, such as STMN2, THBS4, VEGFA, NF-κB, COL16A1, and MMP13 in differentiated osteoblasts. The expression of some genes, including NYAP2, LHX2, and RANKL were significantly downregulated during osteoblast differentiation. In addition, our data showed upregulated expression of proteins, including STMN2, THBS4, and MMP13 in differentiated osteoblasts, suggesting that these proteins might be involved in osteoblast differentiation, bone formation and remodelling.

The significantly altered gene expressions in osteoblasts may lead to changes in the subchondral bone microenvironment, which triggers pain. Therefore, several candidate biomarkers such as THBS4, STMN2, and MMP13, as well as molecules involved in different signalling pathways like RANKL and NF-κB might have the potential to be used for therapeutic targeting in OA.

**90. Mr Jack Nicholls**

Identification of novel genes involved in fovea formation

*Nicholls J, Cavodeassi F, Pittman A, Gestri G, Monfries C, Adjei M*

The fovea is a specialised retinal structure which is responsible for high acuity vision (1). The development of the fovea is well described, however; little is known about the genetic network and molecular mechanisms that underlie this process (2). This lack of knowledge makes it challenging for ophthalmologists to provide a genetic diagnosis for patients suffering from foveal hypoplasia, a congenital malformation, which is characterised by an underdeveloped fovea and poor visual acuity (2). Zebrafish, like humans, possess a similar high acuity area making them an excellent model to study foveal development (3,4). In a previous collaboration between St George's and UCL a zebrafish line which lacks a high acuity area and simulates foveal hypoplasia was generated (4). Through bulk RNA sequencing, this model has produced a list of candidate genes potentially contributing to fovea development. An in-depth investigation of these genes should identify which are involved in fovea formation and which have potential foveal hypoplasia variants. During my PhD I will use in-situ hybridisation and hybridisation chain reaction assays to visualise the expression patterns of several candidate genes within the developing zebrafish retina. Candidate genes enriched within the high acuity area will be targeted and knocked out using CRISPR Cas9. These knockout embryos will be developed into larval stages and subjected to behavioural tests to assess their visual acuity (5,6). The first target of this experimental pipeline is the gene ahrrb. ahrrb is a strong candidate due to it being the top downregulated gene from the transcriptomics analysis and it potentially having a role in repressed retinoic acid signalling, a process known to contribute to high acuity area development (2,7,8,9). Further investigation of ahrrb and other candidate genes will improve our understanding on fovea formation and help foveal hypoplasia patients currently lacking a genetic diagnosis.

References:

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3) PMID: 32473094

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8) PMID: 28817646

9) PMID: 28648799

**91. Dr Aileen O'BRIEN**

A Controlled Trial of a Virtual Reality Intervention in Students for Anxiety

*O'Brien A, Bell D, Smith J, Mantovani N, bin Fauzi N, Abbott M, Railton J, Collinson A, White S, Riches S*

Introduction: Virtual reality Hypnotherapy (VRH) describes the combination of a VR experience combined with audio hypnotherapy. There is some evidence that hypnotherapy can be highly effective when combined with VR for anxiety. There is a well documented crisis in student mental health in the UK and internationally and Universities are struggling to address this. A VR hypnotherapy based app was trialled in 15 SGUL students in 2022 and feedback was positive with no adverse effects.

Setting and methods: After further cocreation of the app with 30 students, an unblinded randomised controlled trial of 97 students was performed in November 2024 comparing VR hypnotherapy over five days with the same experience watched on a smartphone. All participants completed a number of wellbeing scales repeated two weeks post trial. Before and after each session participants were also asked to complete simple Visual Analogue Scales asking how stressed, happy, sad, calm, and anxious they were (0 to 10).

Results: There were no adverse incidents or side effects. Both VR and video group participants showed some pre-to-post session improvements measures. Overall VAS change scores were significantly greater for participants experiencing VR than those receiving the video intervention. VR group participants reported significantly reduced perceived stress from pre-intervention to follow-up at two weeks, while there were no significant changes in the video group. This appears to demonstrate the superiority of the immersive VR experience in producing sustained improvements in stress levels. In the VR group, over half the sample said the experience made them feel 'calmer' or 'more relaxed'. In the video experience overall the comments were similar to the VR feedback but more 'muted'.

Discussion: The students were receptive to the VR experience . Initial qualitative feedback was very positive and initial VAS improvements superior in the VR group. These results are very encouraging but highlight the need to compare the VR experience with other VR calming experiences to establish and to measure longer-term effectiveness and impact of the VR experience.

**92. Dr Sharon Ocansey**

An Audit of the R136 Primary Lymphoedema Gene Panel: October 2019-February 2024

*Ocansey S, Sritharan R, Riches K, Mansour*

Background/Objectives: Primary lymphoedema is a lymphatic anomaly due to a presumed genetic developmental fault in the structure or function of lymph conducting pathways.

Research has identified several causal genes associated with the development of primary lymphoedema. In the era of increasing developments in genomic therapeutics, identification of a molecular diagnosis is critical for this phenotypically heterogenous condition.

The St George's classification algorithm of primary lymphatic anomalies was established in an endeavour to guide a clearer categorisation of phenotypes and enable to discovery of further casual genes.

The NHS Genomic Medicine Service offers R136 panel testing for  genes associated with Primary lymphoedema. The aim of this audit was to identify which patient groups are most likely to carry clinically actionable variants in these genes.

Methods: A 5-year retrospective audit was performed. This reviewed the outcome of R136 panel testing for all patients who were seen within specialist lymphoedema clinics at St George's Hospital, Nottingham University Hospitals, and University Hospitals of Derby and Burton between October 2019 and February 2024. Exclusion criteria included results of cascade testing following the identification of a familial variant, diagnoses of secondary lymphoedema and where data was insufficient.

Results: Data for 264 patients were included in the final analysis. Over one-third (36%) of patients seen in the clinic had a family history of primary lymphoedema. Most patients (73%) were classified as 'late onset lymphoedema'.

Overall, a molecular diagnosis was made in 14% (38/264) all the patients. Clinically actionable variants were identified in a greater proportion of individuals with a positive family history (22%) compared to those with no previous family history (9%). The vast majority of causal variants (97%) were identified in individuals aged 0-20 years. No clinically actionable variants were identified in the 43 individuals categorised as 'late-onset unilateral leg lymphoedema'.

Conclusion/Recommendations: The findings of this audit were presented at the Paediatric & Primary Lymphoedema Rare Disease Collaborative Network Meeting. A consensus was agreed to discontinue R136 panel testing towards patients categorised as 'late-onset lymphoedema'. It is clear from this audit that there are still several genes that have not yet been identified.

**93. Miss Love Onwuzuruike**

Transgenic Domestic Pigs for research in Vascular Contributions to Cognitive Impairment and Dementia

*Onwuzuruike L, Hainsworth A, Lillico S, Meijles D, Ramesh M, Ascione R, Benjamin P, Berry C, Bridges LR, Cash D, Clutton R, Daniel C, Gao B, Collaborator R*

Background: Cardiovascular disease is a primary contributor to vascular dementia and most clinical dementia cases, encapsulated within the concept of vascular contributions to cognitive impairment and dementia (VCID). Endothelin-1 (ET1), a potent endogenous peptide, which induces vasoconstriction and fibrosis in small arteries and is implicated in microvascular disease and VCID. Currently, few experimental animal models are available to study VCID. Pigs, as large-brained mammals, possess a gyrencephalic brain and substantial subcortical white matter, making them valuable for such research.

Method: We engineered domestic pigs with additional copies of the ET1-encoding gene EDN1, controlled by a tet-on promoter, using lentiviral injection into blastocysts. Transgene expression was induced for up to 8 days in young adults via oral doxycycline.

Results: Both ET1-overexpressing and control animals were studied (n=6,3F/3M, mean±SD age 184±61 days and n=5, 3F/2M, 149±41 days respectively). Doxycycline treatment led to varied transgene expression at the mRNA level, with antibody labeling showing a range of ET1 abundance in brain and heart tissues. Heart weight was 460±106g in ET1-overexpressing pigs and 394±25g in controls. Brain weight was 104±14.4g in ET1-overexpressing pigs and 101±9.0g in the controls. Phenotypes relevant to inflammation and blood vessel fibrosis will be reported.

Conclusion: Inducing EDN1 expression in adult domestic pigs results in ET1 overexpression, which is well-tolerated for up to 8 days.

**94. Dr Alistair Paterson**

Predictors of intra-articular steroid injection response in knee Osteoarthritis – a multi-centre clinical trial

*Paterson A, Feather K, Lambarth A, Siebachmeyer, Ejindu, Howe, Rudnicka, Ezeonyeji, Ramsden, Sofat*

Background: The prevalence of knee osteoarthritis (OA) is rising, with 5.4 million UK patients affected in 2023. Patients can develop pain and disability that worsens with time. Intra-articular corticosteroid injections (IACI) can reduce pain and inflammation in OA, though efficacy and duration of benefit are variable. To better stratify future patients, we aimed to identify factors that influence IACI response in knee OA.

Methods: Participants with knee OA were recruited in this prospective multi-centre trial. At baseline, demographics, painDETECT and Western Ontario and McMasters Universities Arthritis Index (WOMAC) were collected. A painDETECT score =19 was classified as “sensitised” to pain. Clinical or ultrasound-guided IACI was undertaken with synovitis/effusion classified as present/absent. Knee radiographs were Kellgren-Lawrence (KL) graded by two Musculoskeletal Consultant Radiologists. Questionnaires were repeated at 3 months. IACI response was defined as a 20% improvement from the baseline WOMAC pain score. Univariate and multivariate logistic regression was conducted in R.

Clinical expertise and statistical principles guided variable selection for multivariate models, with Firth's correction used to mitigate biased coefficient estimation. We assessed predictive accuracy using the average area under the receiver operating characteristic (AUROC) across leave-one-out cross-validation (LOOCV) resamples.

Results: Of 92 patients recruited, 88 (96%) had IACI, with 28 (42%) participants responding. The multivariate model included 50 participants with complete data. Of these, 19 (38%) responded. The final model included age, gender, pain sensitisation, baseline WOMAC pain score and KLG (LOOCV AUROC 0.76). Age (per 10-year increase) was a significant predictor of response in both univariate (OR 2.15, p=0.0072) and multivariate analysis (OR 2.20, p=0.024). Pain sensitisation was a negative predictor of response in univariate analysis (OR 0.24, p=0.044); this finding was not statistically significant in multivariate analysis (OR 0.28, p=0.12). Synovitis/effusion did not significantly predict response in univariate or multivariate models.

Conclusion: Our study demonstrates that IACI response in knee OA may be predicted by clinical and radiological parameters. We found older patients without pain sensitisation had an increased likelihood of response. Further work to validate our findings could allow for stratification of OA care, cost saving and better resource distribution.

**95. Dr Michael Perkin**

Rescue peanut oral immunotherapy in infants in an NHS paediatric allergy service: our experience

*Wells R, Fenton S, Murgasova D, Oyelade B, Pattenden L, Primett M, Thomas LV, Vaughan S, Perkin MR*

Background: Peanut oral immunotherapy (POIT) has been shown to be an effective treatment for peanut allergy in multiple studies. Data have indicated that treatment is safer and more effective in younger children. In June 2023 we introduced rescue POIT as a treatment option for all peanut allergic infants presenting to our service.

Methods: We developed guidelines, a standard operating procedure, a patient information sheet and consent form for initiating POIT in infants (<12 months of age). In June 2023 we started offering POIT as routine clinical practice. The protocol uses real food and six in-hospital updosing appointments at monthly intervals. A food challenge will be offered after 6 months maintenance treatment. Information about each individual patient is kept on a secure hospital database.

Results:

- Between June 2023 and August 2024, 20 infants offered POIT

- 17 patients started POIT, 3 parents declined treatment

- Age 7-11 months (median 10 months)

- M: F 11:6

- Ethnicity: 8 White British, 3 White (other), 1 Asian Indian, 4 Mixed ethnic groups, 2 Black

- 5 infants have completed all updose appointments and are on maintenance 320mg peanut protein daily (Fig. 2)

- 11 infants are currently updosing (Fig. 2)

- 1 infant discontinued treatment within a week due to parental ill health

- No severe allergic reactions, no AAIs administered

- 41% (7 of 17 patients) reported at least one possible reaction

- 15 mild allergic reactions reported in the approx. 3,100 doses (reaction rate 0.4%)

- 33 contacts from parents via e mail over the 14-month period

Conclusions:

- Rescue POIT with six updose appointments at monthly intervals is a practical treatment for use in the NHS

- No severe reactions have been observed during updose and maintenance in our patients

- Feedback from parents has been extremely positive

- Appointments for updosing have impacted the waiting list for food challenges

- Moving forward, we have applied to NIHR for a RCT of infant POIT across 12 NHS services

**96. Dr Michael Perkin**

Diagnostic Accuracy of CoMiSS in detecting challenge-proven Cow's Milk Allergy in the EAT study cohort

*Pandiri A, Navaratnam P, Marrs T, Logan K, Craven J, Flohr C, Radulovic S, Vincent R, Ridd M, Lack G, Boyle R, Perkin MR*

Background: Cow's milk allergy (CMA) affects ~1% of infants but can be difficult to diagnose due to non-specific symptoms, leading to over-diagnosis. Cow's Milk-related Symptom Score (CoMiSS) is an industry-sponsored tool that quantifies crying, regurgitation, stool changes, skin and respiratory symptoms to calculate a score, with 10 or more suggesting high likelihood of CMA. This study aimed to understand the diagnostic performance of CoMiSS in identifying CMA in infants.

Methodology: This was a secondary analysis of the Enquiring About Tolerance (EAT) study which confirmed CMA in participants through gold-standard blinded food challenges & clinicians. CoMiSS scores were calculated using EAT monthly symptom questionnaire data for 1303 healthy breastfed infants while blinded to CMA status of infants. Linear regression was used to explore association between infant CoMiSS scores and age in months. Diagnostic performance measures of CoMiSS in identifying EAT-confirmed CMA were calculated to assess diagnostic accuracy.

Results: For every EAT-confirmed CMA infant, CoMiSS labelled ~48 healthy infants as possible CMA. CoMiSS scores decrease as monthly age increases. CoMiSS is a non-specific tool, especially when detecting Non-IgE-CMA where diagnosis is most challenging.

**97. Mr Alexander Phillips**

A specialist physiotherapy programme for adults with functional neurological disorder: a service evaluation and exploratory analysis.

*Phillips; Nielsen; Holt; Moss; Mountain; Higgins*

Background: Evidence for the benefit of physiotherapy for FND has grown in the recent past leading to the development of specialist services in the UK. Research is needed to guide successful implementation of the evidence and to understand which patients benefit most from this intervention.

Objective: To describe the patient characteristics and evaluate the treatment outcomes of a specialised Functional Neurological Disorder (FND) physiotherapy programme at a London hospital. This service offers intensive blocks of physiotherapy, informed by treatment principles recommended by expert consensus.

Methods: This is a single-centred retrospective cohort study of 100 consecutive patients who have completed a block of specialist physiotherapy. Treatment outcomes are described by comparing outcome measures assessed at the start and end of the programme. Results are preliminary with further outcomes to be collected and analysed.

Results: Patients were mostly female (76%), the mean symptom duration was 5.3 years (SD 4.9), and, gait disorder was the most common presentation (42%). The majority received eight treatment sessions over five consecutive days. The patients improved by a median of 10 points on the Berg Balance Scale, and were 3.7 seconds faster on the 10-Meter Walk Test. Furthermore, 81.6% reported symptom improvement on the Clinical Global Impressions Scale. In a preliminary analysis, we explore the relationship between clinical characteristics and treatment outcome.

Conclusions: This adds to the evidence that specialist physiotherapy services can provide valuable intervention for selected people with FND. More research is needed to guide treatment triage decisions.

**98. Mr Alexander Phillips**

Evaluation of a novel Functional Neurological Disorder (FND) Care Advisor service

*Phillips, Moss, Novak's, Teodoro, Nielsen, Coebergh*

Introduction: The FND Care Advisor (FNDCA) is a service designed to support the management of people living with FND across southwest London and Surrey. It aims to be a central point of contact for patients, health and social care professionals, and to facilitate coordinated personalised care across the integrated care system, especially for cases were complex or long-term symptom management is required. Furthermore, the service provides direct contact for people with FND to promote self-management skills and to collaborate on personalised care plans based on recommendations from the multidisciplinary team.

Methods: Since the commencement of the service in November 2023, it has been collecting data on referrals, patient related contacts and interactions with healthcare teams as well as feedback from patients and clinicians. Case studies are used to demonstrate impact on patient outcomes and experiences.

Results: In the first six months, the FNDCA received 110 referrals from specialists, hospitals and community teams. This led to 416 patient related actions including 16 inpatient in-reach sessions for complex admissions across multiple hospitals. The service has visited 17 different NHS providers across the region and has provided 13 FND specific trainings to healthcare teams.

Case study: A young woman was referred with a recent diagnosis of FND. She had multiple A&E attendances and a 30-day admission to a district hospital. She had uncertainty about her diagnosis, complex mental health needs, and distrust in healthcare. The FND care advisor provided a point of contact and weekly phone calls to support post discharge. The role provided education on FND and functional seizures, encouraged attendance of regular GP appointments, and helped follow up referrals to chronic pain, mental health and dietetics. There has been a slow improvement in symptoms, no further hospital admissions since the involvement of a care advisor and positive feedback from this person and her family.

Conclusion: The FNDCA is demonstrating its impact through direct personalised care and improved integration of health care services to meet individual needs. Case studies suggest cost saving by reduction in healthcare usage, improved patient outcomes, and enhanced communication between healthcare professionals.

**99. Miss Matilda Pitt**

A simple score-based strategy to improve equity of the UK biennial diabetic eye screening protocol among people deemed low risk

*Pitt M, Olvera-Barrios A, Anderson J, Bolter L, Chambers R, Warwick A, Mann S, Webster L, Fajtl J, Barman S, Egan C, Tufail A, Rudnicka AR, Owen CG*

Introduction: Biennial, as opposed to annual, screening for diabetic retinopathy was recently introduced for those considered “low risk” within the UK. This study aims to examine the impact annual vs biennial screening has on equitable risk of diagnosis of sight-threatening diabetic retinopathy (STDR) among people at “low risk” and develop an amelioration protocol.

Research Design and Methods: There were 105,083 people with no diabetic retinopathy detected on two consecutive screening visits in the North East London Diabetic Eye Screening Programme (DESP) who were identified (January 2012-September 2023), and linked to electronic health records (EHR). Characteristics associated with subsequent STDR diagnosis were identified (including age, sex, ethnicity, and diabetes duration) and logistic regression performed to identify people for annual screening, using DESP available variables, and from EHR. Simulations of the biennial screening protocol, and protocols using the logistic models and a simplified points model, were implemented and the relative risk of STDR per appointment compared amongst different population sub-groups. Results were validated in the South East London DESP.

Results: Among the “low risk” participants, there were 3,694 incident STDR cases over a mean duration of 5.0 (SD 3.4) years. Under biennial screening, almost all groups would have had a significantly higher risk of STDR diagnosis compared with people aged over 40 years of white ethnicity living with diabetes for <10 years. Compared to biennial screening, a simplified protocol based on age, diabetes duration and ethnicity reduced the number of delayed STDR from 39% to 25%, with more equitable performance and modest impact on appointment numbers (46% vs 57% of annual appointments, respectively).

Conclusions: A simple, clinically deliverable, personalised protocol to offer annual or biennial screening would provide more equitable risk of STDR diagnosis per appointment.

**100. Priyanka Pradhan**

Deep Brain Stimulation: To Prehab or not to prehab, that is the question!

*Pradhan P, Leake A, Ricciardi L, Paviour D, Pereira E, Betteridge S, Morgante F*

Deep brain stimulation (DBS) is an elective neurosurgical procedure and is the gold standard treatment used for improving the motor symptoms of a high percentage of people living with Parkinson's Disease. There are number of medically validated inclusion and exclusion criteria for those undergoing consideration of DBS. Inclusion for consideration would be a good response to levodopa, relatively intact cognition, and stable mood with no indices of significant previous mood disturbance. This is due to the occurrence of a number of suicides following DBS. Poor levodopa response, evidence of cortical dysfunction and significant mood disturbance would qualify as exclusion criteria.

More recently the issue around patient expectation management has been explored in terms of post-surgical outcome and adjustment to living with DBS. How do we, as specialist MDT prepare patients and their families for this life changing neurosurgical intervention and help them get the most out of DBS? In order to do this, a Neuropsychological prehab programme was set up to to meet the pre-surgical needs and identify potential post-surgical needs of patients following DBS.

Patients and partners were invited to a Neuropsychology group workshop prior to their DBS surgery. The workshop comprised of two weekly 90 minute sessions and were run online. Session content included 'living with Parkinson's Disease the DBS process, what DBS can and can't help, hopes and fears, and living with DBS'. Quantitative mood, QoL and carer burden measures were given to both patients and their partners before the sessions and a qualitative questionnaire looking at satisfaction was given after completion of the sessions.

Currently results are qualitative and preliminary. Both patients and partners qualitatively reported that they found the pre-DBS workshop beneficial and world recommend it to others going through the process. We currently collecting data on DBS candidates that have attend both the pre-surgical and post surgical workshops to compare their quality of life, psychological adjustment, stress, anxiety and depression. For partners, we are looking at stress, anxiety and depression along with carer burden.

There is a clinical need for patients and their partners to undergo a pre-hab process as this helps with expectation management which improves patient and partner satisfaction and increases understanding and engagement with the post surgical process.

**101. Miss Nangitha Raguthasan**

Functional characterisation of pro-VWF-mStayGold, a new fluorescent reporter of Weibel Palade body exocytosis.

*Hart G and Raguthasan N*

Weibel-Palade Bodies (WPBs) are the regulated secretory organelle of vascular endothelial cells, and contain Von Willebrand Factor (VWF), a protein essential for both primary and secondary haemostasis. Mutations in VWF cause the bleeding disorder Von Willebrand Disease (VWD), however, in about 30% of cases of VWD, VWF itself is normal. In these cases, it is thought that mutations in molecules that regulate WPB exocytosis are to blame.

To understand such cases, it is important to be able to directly analyse WPB exocytosis in living endothelial cells. Here we tested two new fluorescent reporters of WPB exocytosis based on a novel fluorescent protein called Staygold (SG). SG has potential advantages over current GFP based reporters; it is brighter and more photostable under blue light illumination. However, in its native form SG tends to dimerize, and this could cause protein aggregation when fused to VWF, impacting how VWF is stored within WPBs. A monomeric version (mSG; E138D) of the reporter has been made (VWFpp-monomeric StayGold (VWFpp-mSG)) and was tested here. To trigger WPB exocytosis we used the intracellular calcium-elevating hormone histamine, and simultaneously monitored both exocytosis and changes in intracellular [$Ca^{2}$+] using the fluorescent $Ca^{2}$+ indicator, fura-2. Our data will show that both VWFpp-SG and VWFpp-mSG function as useful reporters of WPB exocytosis in endothelial cells.

**102. Miss Rezbieara Rahman**

From Genomes to Phenomes: Discovering DMPK Repeat Expansions in Genomics England as a Gateway for Future PheWAS

*Rahman R; Matthews E; Behr E; Futema M*

Background: Myotonic Dystrophy Type 1 (DM1) is an autosomal dominant disorder caused by an expansion of a CTG repeat sequence in the DMPK gene. Healthy individuals typically carry 5-37 repeats, while those in the premutation range (38-49 repeats) may be asymptomatic, risk intergenerational repeat expansion. Pathogenic expansions (>50 repeats) lead to DM1's multisystemic manifestations and noted for its remarkable variability. Although these clinical features are well-documented, the broader impact of DMPK expansions in large-scale populations, particularly across different genetic ancestries, remains underexplored. Leveraging the Genomics England (GEL) Research Environment with extensive whole-genome sequencing (WGS) data, we aim to (1) identify DMPK repeat expansions in GEL data, classifying them into cohorts, (2) compare repeat length distributions across ancestries, and (3) establish a genotype-phenotype dataset linking individuals to phenotypes using Human Phenotype Ontology (HPO) terms. Thus, laying the groundwork for a future phenome-wide association study (PheWAS) utilising this data. This research represents the start of the first application of an HPO-based PheWAS in a DM1 context.

Methods: Employing Expansion Hunter, a tool for targeted detection and quantification of repeat expansions, we analysed a total of 80,110 WGS GEL samples for DMPK expansions. We then built our groups, categorising participants into normal (<37 repeats), premutation (38-49 repeats), and pathogenic (>50 repeats) cohorts. To assess ancestry-based patterns, we performed appropriate

statistical analyses to determine differences in repeat distributions across ancestry groups. A robust HPO-linked dataset is under development to support the planned PheWAS.

Results: Expansion Hunter analyses of 80,110 genomes identified 78 participants with >50 repeats (pathogenic), 183 with 38-49 repeats (premutation), and 79,849 with <37 repeats (normal). Statistical tests revealed significant ancestry-based differences between pathogenic vs. normal cohorts ($p=0.038$) and premutation vs. normal cohorts ($p=0.003$), $p<0.05$. All participants have been linked to their HPO-terms, in preparation for the PheWAS.

Conclusions: In summary, we identified DMPK expansions, classifying participants into annotated cohorts, revealing ancestry-based differences. Thus, paving the way for the first study to employ a PheWAS, focusing on DMPK repeat lengths, using HPO terms to explore pleiotropic effects. Underscoring an underexplored area of DM1 research, deepening our understanding of DMPK expansions across populations.

**103. Dr Sharenja Ratnakumar**

Phosphodiesterase 4 regulates monocyte-dependent fibroblast activity in Mycobacterium tuberculosis (Mtb) infection

*Ratnakumar*, Chong*, Porter, Friedland*

Introduction: Tuberculosis (TB) infects around a third of the world's population and even after recovery, up to 94% patients have clinically significant lung fibrosis. Fibrotic lung tissue is characterised by the increased presence of differentiated fibroblasts expressing a-smooth muscle actin (aSMA) and excessive deposition of extracellular matrix proteins. During Mycobacterium tuberculosis (Mtb) infection, cyclic adenosine monophosphate (cAMP) is a key regulator of the interface between inflammation and fibrosis and modulated by nucleotide phosphodiesterases (PDE). PDE4 (subtypes A-D) are highly upregulated during TB and so we investigated the hypothesis that PDE4-dependent events drive the development of chronic fibrosis in TB.

Methods: Primary human lung fibroblasts (PHLFs) were stimulated with media, 1 ng/ml TGFb (positive control), or media from Mtb-infected monocytes (CoMTB) or from un-infected monocytes (CoMCon) for 72 h. Expression of aSMA was detected by immunofluorescent microscopy and DAPI nuclear co-staining; quantification of aSMA mean stain area was assessed using ImageJ software. Supernatants were collected at 72 h and profibrotic mediators PDGF-BB and TGFb quantified by ELISA. RNA was extracted and cDNA reverse transcribed for qRT-PCR analysis of pde4a-d expression.

Results: PHLFs treated with CoMTB but not CoMCon enhanced aSMA expression compared to media alone, leading to differentiation into myofibroblasts, a key effector cell in fibrosis ($p=0.011$). CoMTB-stimulated PHLFs secrete significantly more PDGF-BB than fibroblasts treated with CoMCon (73.63pg/ml vs. 35.85 pg/ml, $p<0.01$). CoMTB-stimulated PHLFs secrete increased concentrations of TGFb1 compared to PHLFs stimulated by CoMCon (748.8 pg/ml vs 552.0 pg/ml, $p<0.05$). Stimulation of PHLF with CoMTB results in upregulation of pde4a-d, compared to CoMCon ($p<0.05$ in all subtypes). Pre-treatment of PHLF with PDE4 inhibitor decreases PDE4 mRNA expression and TGFb secretion.

Conclusion: Fibroblasts activated by Mtb-infected human monocytes secrete pro-fibrotic mediators in a PDE4-dependent manner. PDE4 may be a potential target for host directed therapy in TB treatment, thus reducing the mortality and morbidity associated with TB disease.

**104. Ms Violeta Rojeab**

Urbanization and health inequalities in Ecuador: an analysis using national data

*Rojeab; Cis Ster; Cooper;  Dundas*

Background: Urbanization is accelerating globally, with projections suggesting that 68% of the world's population will reside in urban areas by 2050. In low- and middle-income countries such as Ecuador, urban growth generally proceeds without adequate planning resulting in urban populations living without inadequate infrastructure, and in conditions of overcrowding and informality, with their consequent challenges for health outcomes including increasing inequality and a growing burden of chronic NCDs.

In Ecuador, a rapid pace of urbanization from the 1950s saw the urban population surpassing the rural population in 1980. NCDs have become increasingly prevalent, accounting for a significant proportion of deaths. A significant knowledge gap exists with respect to how urbanicity and the process of urbanization affects health outcomes and associated axes of inequalities in the context of Ecuador.

Objective: To create an urbanicity index to investigate the extent how urbanicity and the process of urbanization are associated with health outcomes and health inequalities in Ecuador.

Methods: The research will analyse data from eight censuses conducted since 1950 to model and evaluate an administrative urbanicity index, and spatio-temporal trends of urbanisation in Ecuador, focusing on inequalities related to age, gender, and ethnicity. Methods will include principal components analysis, cluster analysis, time series portfolio, and geospatial and spatio-temporal modelling.

Results: We mapped changes in urban/rural populations and administrative boundaries in Ecuador since 1950, analysed evolving concepts and their implications for population data analysis. We identified key variables from census databases that might be included in an urbanicity index and identified key health outcomes relevant to the Ecuadorian context. We studied and visualised historical population characteristics, population spatial distribution, and household attributes.

Conclusions: This will be the first extensive national study in Ecuador to explore health outcomes in relation to urbanization. The results are expected to advise targeted policies aimed at reducing health inequalities and provide a better understanding of the effects of urbanization on health. This study highlights the urgent need in Ecuador for analyses of systematically collected data to monitor and address changing trends in health, identify potential causes, and design strategies to improve health and reduce health inequalities

**105. Miss Isabelle Rose**

Targeting of Gene Therapies to Specific Cell-types of the Airway Epithelia can improve Functional Outcomes

*Rose I, Baines D*

Cystic Fibrosis (CF) is an autosomal recessive disease caused by mutation within the cystic fibrosis transmembrane conductance regulator (CFTR) gene. CFTR is required for chloride and bicarbonate secretion into luminal spaces of the epithelia throughout the body, and so it considered a multi-organ disease. CFTR is an attractive target for gene editing approaches as corrective editing of 5-20%

of alleles can restore sufficient function to prevent symptomatic CF and respiratory decline. For gene editing to be effective, the heterogeneity of cell-types present in the epithelial landscape need to be considered. This is because there are cell-specific differences in expression of CFTR and its function, with some cells differing in propensity for chloride secretion into luminal spaces.

To explore the activity of CFTR in CF and non-CF airway cells in vitro, plasmid constructs were developed to express a halide-sensitive yellow fluorescent protein (hsYFP) in specific airway cell-types which can be used to measure CFTR activity. These were transfected into human nasal airway cells using Lipofectamine 3000 and using directed Homology-Independent Targeted Integration (HITI), were edited into a genomic safe-harbour site known as AAVS1. Three different cellular reporter lines were constructed FOXJ1-hsYFP (ciliated cells), MUC5AC-hsYFP (secretory cells), and ASCL3-hsYFP (ionocytes). These have been used to identify cell-types abundant CFTR and comparing quantity to quenching speed and capacity to identify potential gene editing targets. Directing editing to cell-types with both high abundance and function of CFTR may be beneficial during in vivo experiments.

Cell specific hsYFP was determined by co-staining with anti-GFP and an antibody directed to a cell specific epitope. RT-qPCR was used to correlate expression of the cell-type marker with hsYFP levels. hsYFP fluorescent quenching was achieved using iodine exchange quenching assay. Imaging was obtained using Nikon A1R and ImageExpress Pico. Iodide quenching indicated a mean change in relative fluorescence of 1318.7±221.2 in cells expressing MUC5AC-hsYFP, compared to a significantly larger change of 1536.5±173.1 in cells expressing FOXJ1-hsYFP. Quenching was also prolonged in MUC5AC-hsYFP cells, indicating that these cells may be less metabolically active in comparison to FOXJ1-hsYFP cells (n=3). These data indicate that targeting of editing machinery to ciliated may elicit the greatest effect on CFTR channel function in the airways.

**106. Miss Isabelle Rose**

Adenine Base Editing for the Cystic Fibrosis Variant G542X

*Rose I, Greenwood M, Biggart M, Baumlin N, Hart S, Tarran R, Baines D*

The Cystic Fibrosis (CF) causing variant G542X (GGA>TGA) results in premature termination of translation of the cystic fibrosis transmembrane regulator (CFTR) protein, and nonsense-mediated decay of the CFTR mRNA resulting in almost complete loss of functional CFTR protein expression. Currently available CF modulator therapies cannot be used to treat this variant, but an Adenine Base Editor (ABE) and guide RNA combination can convert the G542X stop codon to G542R, a variant which retains about 30% of WT activity and is amenable to CFTR triple modulator therapy (Elexacaftor-Tezacaftor-Ivacaftor ETI).

Plasmid DNA encoding this ABE and guide RNA with GFP were encapsulated in lipid-based nanocomplexes, which have reduced immunogenicity and high cellular uptake, and were delivered to human airway epithelial cells (HAECs) harbouring the G542X CFTR variant. Transfected cells were identified by analysing GFP fluorescence. Ion transport was measured as short circuit current (Isc) across resistive epithelial monolayers. Airway Surface Liquid (ASL) height was visualised using Texas-red dextran as a soluble fluorescent label of volume, and perfluorocarbon-77 to prevent fluid evaporation. CFTR was activated using vasoactive intestinal peptide (VIP)(100 nM, basolateral), and changes were calculated from XZ scans taken at regular intervals. ASL pH was measured using pHrodo-dextran pH-sensitive fluorescent labelling normalised to a pH-insensitive in situ control.

48 hours post transfection, next-generation sequencing showed 17% of alleles had been edited from G542X to G542R. Isc measurements showed that even as little as 17% of editing restored CFTR activity to ~60 % that of normal levels when in combination with modulators. CFTRInh-172 inhibitable current was ~four-fold greater in ETI treated G542R compared to G542X samples (p=0.015, n = 6). Transfected cells were sorted using fluorescence-activated cell sorting to concentrate the population of edited cells. VIP stimulated changes in ASL height indicated that edited and sorted cell monolayers displayed wild-type like airway hydration. Additionally, VIP stimulated changes in ASL pH were positively correlated to the proportion of G542R cells, suggesting that bicarbonate transport was also being restored by correction of G542X to G542R CFTR protein.

This data provides proof-of-concept for restoration of anion transport by gene editing of G542X.

**107. Miss Amber Saleem**

Examining the extent of under-reporting of infection-related mortality in people with Type 1 Diabetes

*Saleem A*

Background: This study investigates the under-reporting of infection-related mortality among individuals with Type 1 diabetes (T1D). Infection is a common cause of hospitalization, yet its role as a contributing factor to mortality is often overlooked in death certifications. Understanding the extent of this under-reporting is critical for improving health outcomes and addressing treatable infections that may contribute to mortality.

Methods: Utilizing anonymized linked primary care data from the Clinical Practice Research Datalink (CPRD), this study analyzed 2,401 deaths occurring between 2015 and 2019. Deaths were categorized by International Classification of Diseases (ICD-10) codes to determine both underlying and contributing causes related to infections. The analysis focused on variations by age, sex, and socio-economic deprivation, employing descriptive statistics to calculate proportions and 95% confidence intervals.

Results: Findings revealed that 12% of deaths among individuals with T1D were attributed to infections as the underlying cause, while 14% were identified as contributing causes. Older adults (=60 years) exhibited a higher likelihood of infections as the underlying cause (15%), and women showed a greater proportion of infection-related deaths classified as contributing causes (16%). Additionally, infection-related mortality was most pronounced in areas of higher socio-economic deprivation. Respiratory infections, particularly lower respiratory tract infections, emerged as the most common underlying cause, accounting for 74% of cases. Sepsis was documented as the underlying cause in 5% of deaths but was noted as a contributing cause in 20%.

Conclusion: This study highlights a significant gap in the recognition of infection-related mortality among individuals with T1D, suggesting that nearly half of such deaths may be overlooked when only considering underlying causes. These findings emphasize the importance of refining death certification processes to better acknowledge the impact of infections. Future research should further investigate the influence of demographic factors, such as gender and socio-economic status, on infection-related mortality to enhance understanding and management of this critical health issue.

**108. Mr Rahul Shah**

Dopamine modulates subthalamic nucleus laser-evoked thermal potentials in Parkinson's disease

*Shah, Nair, Ishihara, Hart, Ricciardi, Morgante, Pereira*

Background and aims: The role of dopamine (DA) in acute and chronic pain is still uncertain. Animal studies suggest DA and subthalamic nucleus (STN) activity can modulate spinal nociception. We used laser-evoked thermal pain to investigate dopaminergic modulation of STN pain-related neural activity in humans.

Methods: We recorded brain activity (local field potentials [LFP] and electroencephalogram [EEG]) from externalised deep brain stimulation (DBS) electrodes and scalp vertex (Cz EEG) during bilateral hand laser thermal stimuli in 4 patients undergoing staged surgery for Parkinson's disease (day 4-5 post-implant), both off medication (OFF-MED) and 1hr post L-dopa administration (ON-MED). A DEKA Stimul 1340 Nd:YAP laser was used, patient self-reported pain score was documented and at least 10 painful events were recorded per hand. DBS electrode contact positions were reconstructed in Lead-DBS (lead-dbs.org) and classified into ipsilateral or contralateral STN. EEG and LFP signals were preprocessed, then epoched around laser timestamp (-1 to +2s). Evoked-responses were calculated using 500ms pre-event baseline period and averaged for each anatomical zone. There was no significant difference in mean pain score in OFF-MED vs ON-MED trials.

Results: We confirmed the LEP waveform in subcortical structures compared to Cz was temporally similar, though clearer in the LFP. Thermal pain produced LEPs in contralateral and ipsilateral DBS electrodes in both OFF-MED and ON-MED states. Paired t-test was used to compare overall normalised LEP waveforms 0-2s which were significantly different between OFF-MED and ON-MED states in Cz, Ipsilateral STN and contralateral STN ($p<0.0001$). Time-Frequency analysis suggests pain-evoked very high gamma and high frequency oscillations are significantly modulated by OFF-MED vs ON-MED state, particularly in the contralateral STN ($p<0.0001$). Ipsilateral and contralateral STN only differed in alpha band evoked response (and marginally in high gamma).

Conclusions: To our knowledge, this is the first reported electrophysiological evidence of dopaminergic state modulating acute pain processing in humans. Further investigation to understand how this correlates with experienced pain, other types of acute pain (e.g. mechanical) and whether similar effects may underlie dopamine responsiveness in non-PD chronic pain conditions is indicated.

**109. Dr Mohammad Sharif Razai**

Navigating Vaccination in Pregnancy: Qualitative Study in 21 Ethnically Diverse Pregnant Women

*Razai, Ussher, Goldsmith, Hargreaves, Pippa Oakeshott*

Background: Vaccination during pregnancy is crucial for safeguarding maternal and neonatal health, but vaccination rates remain suboptimal, especially in women from Black and Asian ethnic minorities. We explored the perspectives and decision-making processes of pregnant women regarding uptake of the three recommended vaccines in pregnancy: Influenza, Pertussis (whooping cough) and COVID-19. We also explored women's attitudes to taking part in vaccine trials during pregnancy and the use of artificial intelligence (AI) to obtain information on vaccines.

Methods: In 2023, we conducted in-depth telephone interviews with ethnically diverse pregnant women in the Greater London area using convenience and snowball sampling. The interviews focused on participants' views on vaccination during pregnancy, participation in vaccine trials, information-seeking behaviours, and attitudes to emerging technologies for health information. Interviews were transcribed verbatim and thematically analysed. The data collection and analysis were conducted alongside the iterative development of the topic guide and coding framework, with key themes emerging through collaborative team discussions.

Results: Twenty one pregnant women aged 20-39 were interviewed of whom 67% were from ethnic minorities and 29% were from migrant backgrounds. Half the participants (53%) reported hesitancy towards at least one of the vaccines. The analysis revealed several themes: concerns about vaccine safety, particularly regarding newer vaccines due to lack of long-term data; reliance on healthcare professionals for guidance, balanced with personal research; and a strong desire for clear and comprehensive information specifically tailored to pregnant women. Pregnant women reported insufficient information, explanation, or recommendation by midwives. Additionally, there was widespread refusal regarding participation in vaccine trials; and mixed responses to the use of AI (such as chatbots) for obtaining vaccine information.

Conclusions: Pregnant women's vaccination decisions are complex and require clear, unambiguous communication from healthcare providers, especially midwives, to address their specific concerns. Although information obtained via AI can be useful, responses were mixed.

**110. Dr Annalisa Sheehan**

Road traffic flow and environmental noise modelling for the Equal-Life project

*Sheehan, Jephcote, Gulliver*

Environmental noise is one of the key exposures in exposome studies of cognition and mental health in the Equal-Life project. To estimate noise levels at the quietest and noisiest facades for 11 cohorts in 8 different European countries, we required detailed geographical data including accurate data on traffic flows. Data on traffic flows is, however, mostly restricted to selected major roads where available. To address this limitation and advance the state-of-the-art, we aimed to predict traffic flows on all residential roads, to provide a geographically dense basis for noise modelling. To do this, we developed a ‘baseline’ statistical (Generalised Linear Mixed Methods) traffic model for England by selecting 300 traffic counts sites to develop a model and 300 traffic counts sites for model evaluation stratified by road type and urbanicity. Key variables in the model were the residential population count within a 5-minute drive time and distance to the nearest major road junction. The model for England explained 70% of the variability in annual average daily traffic (AADT) using the independent (i.e., held-out) traffic counts sites. Using traffic counts from Barcelona and Copenhagen, the traffic model transferred well with up to 17% lower explained variability in AADT than for England. We therefore used the CNOSSOS-EU traffic methodology to estimate long-term residential noise levels for daytime (LDAY; 0700-1900 hours), evening (LEVE; 1900-2300 hours), nighttime LNIGHT (2300-0700 hours), and the 24-hour, day-evening-night metric LDEN. This resulted in ~500,000 modelled locations (i.e., individuals) for use in the project and future use via cohorts.

**111. Dr Keira Skolimowska**

Platelets drive neutrophil-mediated neuroinflammation in TB meningitis

*Skolimowska, Reid, De Swardt, Chong, Kutschenreuter, Kirwan, Davis, Wasserman, Wilkinson, Friedland*

Introduction: Neutrophils drive inflammation and poor outcome in TB meningitis (TBM) yet mechanisms are poorly understood. Platelets are critical components of the immune response that link haemostatic and inflammatory pathways through aggregating with immune cells, such as neutrophils. In TBM, neutrophils infiltrate the central nervous system where they interact with astrocytes, key regulators of brain inflammation. We characterised platelet-neutrophil aggregation (PNA) in TBM patients and defined platelet-dependent effects on neutrophil immune responses to M.tuberculosis (M.tb). In addition, we investigated how neutrophil-platelet interplay drives astrocyte immune activation in the context of M.tb infection.

Methods: Clinical samples were collected from TBM patients enrolled into a phase III clinical trial and from people living with HIV (PLWH) and healthy donors (HD) in South Africa. PNA (%) were quantified by flow cytometry and visualised using Imaging flow cytometry. Secreted mediators in plasma were quantified using Luminex bead array. Cellular co-culture using M.tb-infected neutrophils +/- platelets was utilised to explore platelet-dependent effects on neutrophil and astrocyte immune responses.

Results: PNA were significantly elevated in TBM vs. comparator groups. Moreover, the number of neutrophil-bound platelets correlated with disease severity. Neutrophil-derived MMP-8, a collagenase associated with matrix destruction in TB, and IL-8, a chemoattractant for neutrophils, were elevated in TBM vs PLWH and associated with death. Plasma MMP-8 and IL-8 positively correlated with circulating PNA. M.tb-infection of neutrophils in co-culture with autologous platelets significantly increased IL-8 secretion compared to M.tb infection of neutrophils alone which functionally resulted in increased neutrophil chemotaxis. Blocking neutrophil PSGL-1, the ligand for platelet P-Selectin, significantly reduced neutrophil IL-8 secretion in response to M.tb.

Platelets were identified in CSF from TBM patients and CSF platelet-secreted mediators associated with more severe disease. S100B, a marker of astrocyte injury, was detected in the CSF and plasma from TBM patients, associated with more severe disease at presentation and death. Conditioned media from M.tb-infected neutrophils in co-culture with platelets induced an neurotoxic astrocyte phenotype.

Conclusion: Platelets circulate in complexes with neutrophils in TBM, influencing neutrophil immune responses and astrocyte phenotype, suggesting a role in TBM immunopathology.

**112. Dr Adam Sparow**

The interaction of BCG with B cells

*Sparrow A*

We have developed a mycobacterial infection model which has revealed that B and T lymphocytes interact directly with BCG GFP. The interaction of B cells with mycobacteria has not been extensively studied. We sought to better characterise this interaction. Microscopy was used to visualise the infection of B cells with BCG GFP. This revealed that BCG GFP binds to the external surface of B cells. There was no evidence of BCG establishing intracellular infections within B cells.

Further investigation revealed the mechanism by which B cells and BCG interact. Antibodies contribute to the attachment of BCG to B cells. There was no evidence that phagocytosis or macropinocytosis were necessary for the interaction of B cells and BCG GFP. The complement component C1q did not impact the infection of B cells.

The functional effect of BCG binding to B cells was unknown. This study determined that BCG exerts a profound suppressive effect on the function of B cells. In RAJI B cells, BCG infection led to reduced expression of the markers for chemotaxis and proliferation. Antibody production was suppressed along with the expression of HLA DR and costimulatory molecules. In tonsillar B cells infected with BCG, chemotaxis and antigen presentation markers were suppressed, but the B cells were still capable of responding to the infection with enhanced proliferation and antibody production. The mechanism by which BCG suppresses B cells has not yet been resolved but this work showed that it was not due to B cell death or anergy.

These findings may offer insight into the limited efficacy of the BCG vaccine and be useful in the development of a more effective TB vaccine.

**113. Mr Ian Storey**

Evaluating the predictive capabilities of deep learning generated diffusion parameters in glioma

*Storey, IR., Barrick, TR., Howe, FA*

Introduction: Quantitative parameters obtained from mathematical fitting of diffusion magnetic resonance imaging (dMRI) data have the potential to operate as minimally invasive biomarkers in the categorisation of gliomas into tumour grades and genetic subtypes. This has a use case in providing earlier diagnosis and treatment selection compared to the current clinical standard of biopsy, which is a surgical intervention, and histo-genetic testing which incurs a significant time delay for diagnosis. Mathematically derived diffusion parameters such as from the quasi-diffusion MRI technique (QDI) developed at SGUL, are repeatable but prone to noise and artefacts typically found in dMRI data. Deep learning techniques such as the fully connected neural networks (FCN) configured for non-linear regression are capable of estimating diffusion model parameters from dMRI, can mitigate the effects of noise, and provide visually enhanced images compared to those from direct mathematical derivation.

Method: An FCN was trained on 5 healthy volunteer and 7 brain tumour datasets where target images included very high quality QDI images (30-minute MRI scan), with the aim to derive improved image quality from clinically acceptable QDI images (a 2.5 minute MRI scan). K-means clustering was applied to QDI parameter maps from the direct mathematical model and compared with that from

QDI maps using an FCN. We obtained 6 clusters within the whole tumour region, with each cluster representing tissue of similar microstructure. We derived the percentage volume of each cluster for each tumour which were used in a Mann-Whitney U-test to evaluate for differences between low- and high-grade tumours. The 2 most significantly different clusters were used in a receiver operator curve (ROC) and linear discriminant (LDA) analysis to evaluate LGG and HGG classification accuracy.

Results: It was found that cluster labels obtained from both the FCN and QDI mathematical model provide separation between LGG and HGG. FCN obtained the highest AUC at 0.946 compared to QDI (0.839 AUC) in ROC analysis. In LDA the FCN obtained 73.3% cross-validation accuracy whilst QDI obtained 80% cross-validation accuracy. This research shows promising results in the use of an FCN and the QDI mathematical model parameters in a role as a biomarker for glioma grade.

**114. Dr Sarah Sturrock**

Clinical prediction models to diagnose neonatal sepsis in low-income and middle-income countries: a scoping review

*Neal S, Sturrock S, Musorowegomo D, Gannon H, Zaman M, Cortina-Borja M, Le Doare K, Heys M, Chimhini G, Fitzgerald F*

Background: Neonatal sepsis is a leading cause of neonatal morbidity and mortality. This burden is felt disproportionately by neonates in low- and middle-income countries where access to laboratory diagnostics and specialist care is limited. Clinical prediction models (CPMs) for neonatal sepsis can improve diagnostic accuracy, facilitating earlier treatment for cases and avoiding antibiotic overuse. However, no previous review has synthesised the evidence surrounding the types of CPMs validated in low- and middle-income countries.

Methods: We performed a scoping review of CPMs for neonatal sepsis diagnosis using Ovid MEDLINE, Ovid Embase, Scopus, Web of Science, Global Index Medicus, and the Cochrane Library. Any study reporting validation of a new or existing CPM for neonatal sepsis (sepsis occurring <28 days of life) in a low- or middle-income country as defined by the World Bank was included. Studies were excluded where neonates could not be separated from a larger paediatric population or where factors included in the CPM were not described. Studies were selected by two independent researchers.

Results: From 4024 unique records, we included 52 studies validating 35 distinct models. Most studies were set in neonatal intensive or special care units in middle-income countries and included neonates already suspected of sepsis, with only 3 studies set in the WHO African region. Three quarters of models were only validated in one study, and only 11 models did not use any laboratory parameters.

Conclusions: Our review highlights several literature gaps, particularly a paucity of studies validating models in the lowest-income areas where sepsis is most prevalent, and models for the general, undifferentiated neonatal population that do not require laboratory facilities. Furthermore, heterogeneity in study populations, definitions of sepsis and classification thresholds prevents meaningful comparison between studies of the same models and may hinder progress towards useful diagnostic tools.

**115. Miss Lorena Symes**

Investigating the presence of polyresistance in Candida isolates obtained from ICU patients

*Symes L*

Candida spp are fungal pathogens which cause serious infections, especially in immunocompromised individuals. Exposure to antifungals, Candida species including C.albicans, C. glabrata and C. parapsilosis have developed resistance against drugs including fluconazole and anidulafungin. Polyresistance in Candida is where multiple populations of the same species present in a sample having varying minimum inhibitory concentration (MIC). Current research has shown that multiple-colony MIC testing increases the probability of identifying polyresistant populations within a sample. Multiple-colony MIC testing of serial clinical samples for either fluconazole or anidulafungin found two isolates from 4002 C.parapsilosis which were possibly polyresistant for fluconazole, species identification confirmed that they belonged to C. parapsilosis and were polyresistant. The polyresistant isolates underwent PCR and genetic analysis to identify the presence of mutations on the ERG 11 gene. Results from PCR analysis found possible presence of mutations on ERG 11 gene in one isolate, yet further genetic analysis is required to confirm this. Direct multiple-colony MIC testing of clinical swabs from newly recruited patients for both fluconazole and anidulafungin found one isolate with possible polyresistance for fluconazole. Species identification confirmed that the resistant isolate belonged to the same species as the other isolates tested and therefore confirmed the presence of polyresistance in the sample. This is the first time clinical swabs have directly been tested for the presence of polyresistance in the sample and been successful. We confirm the presence of polyresistance for fluconazole in clinical Candida samples, with multiple-colony testing being a successful method in identifying polyresistance.

**116. Dr Natasha Thorn**

Development of a serocorrelate of protection against invasive infant Group B streptococcal disease: A prospective case control study

*Thorn N, Karampatsas K, Kyohere M, Cochet M, Rouse N, Hall T, Beach S, Daniel O, Bentley E, Peacock J, Walker K, Khalil A, Daniels J, Plumb J, Andrews N, Le Doare K, Heath PT*

Introduction, Background and Aims: Group B streptococcus (GBS) is a leading cause of neonatal infection and meningitis. Despite intrapartum antibiotic prophylaxis, a vaccine is a long-standing unmet need. Licensure of current vaccine candidates is problematic; defining a correlate of protection will enable this pathway. This study aims to: 1. provide data on the relationship between antibody and infant invasive GBS (iGBS) risk by estimating the odds ratio of iGBS for antibody concentrations above various thresholds for different serotypes (ST), 2. determine whether acute disease antibody concentrations can predict cord blood antibody concentrations.

Methods: A multicentre, prospective, case control study, embedded within a cluster randomised GBS testing trial. Cord blood samples are collected prospectively. Cases are iGBS occurring within 90 days of life, controls are those testing GBS rectovaginal swab-positive in pregnancy whose infants do not develop iGBS. Consent is gained to retrieve cord blood, relevant GBS isolates, clinical data and for cases, infant serum. Sample size is 170 cases of iGBS (100 of serotype III) of which 50 with matched cord blood, and 1000 controls (300 of serotype III). Isolates undergo whole genome sequencing to determine serotype and Alpha-like protein (Alp) type. Specific anti-GBS IgG is quantified against capsular serotype and Alp via standardised immunoassays. Opsonophagocytic

killing assay (OPkA) titres will be measured. Geometric means calculated for cases and controls will be compared by t-test or Kruskall Wallis. Logistic regression will estimate the odds of disease at increasing antibody threshold concentrations.

Results: 57 sites are participating; recruitment is ongoing. To date, 201 infant GBS cases (19 with associated cord blood) and 398 controls are recruited (305 with cord blood). See Table 1 for interim study population description. Sample analysis is near completion and data analysis is soon to begin.

Conclusions: Despite recruitment challenges, this ongoing study promises important data to define a GBS serocorrelate of protection and to further the licensure of GBS vaccines, a much-needed global health intervention.

**117. Mrs Luz Toribio**

Differential monocyte activation by diagnostic neurocysticercosis antigens: inflammatory and tissue remodelling responses

*Toribio LM, Chong D, Garcia HH, Friedland JS.*

Background: Neurocysticercosis (NCC), caused by Taenia solium, is a parasitic infection of the central nervous system and the most prevalent cause of acquired epilepsy globally. Parasitic cyst degeneration can lead to neuroinflammation and tissue remodelling. Monocytes play a key role in early immune responses, secreting cytokines and matrix metalloproteinases (MMPs) to drive inflammation and tissue remodelling. However, the role of monocytes in NCC are not fully understood.

Aim: To investigate the effect of diagnostic NCC antigens on monocyte-induced inflammation and tissue remodelling.

Methods: Human monocytes were stimulated with diagnostic antigen LLGP, a mixture of seven purified parasitic glycoproteins, or individual antigens (rGP50, rT24H and 8kDa antigens) for 4-72h. RT-PCR and ELISA were used to measured gene expression and secretion of cytokines (TNF-a, IL-1, IL-6, IL-8) and MMPs (MMP-1, and -9), along with functionality assay to evaluate MMP enzymatic activity.

Results: Monocyte stimulation with LLGP antigen mixture induced significant increase in gene expression and secretion of IL-6, IL-8, MMP-1 and MMP-9 (all $p<0.05$). Functionality assay confirmed elevated collagenase and gelatinase activity of MMP-1 and -9, respectively. Interestingly when testing individual antigens found in LLGP, rGP50 stimulated a similar response to LLGP, whereas rT24H induced significant more TNF-a and IL-1ß expression ($p=0.0015$). No significant difference was found for secretion or gene expression of IL-8 between LLGP and individual antigens ($p=0.096$). rGP50 and rT24H also stimulated high secretion of active MMP-1 and -9 from monocytes. 8kDa family antigens did not exhibit pro-inflammatory responses in monocytes. Additionally, 8kDa antigens obtained the lowest MMP-1 responses when compared to unstimulated cells (54.73 vs. 33.61pg/ml).

Conclusion: LLGP induce inflammatory responses and is an important activator of tissue remodelling responses in NCC. Individual antigens contribute differentially to monocyte activation in NCC, with rT24H driving inflammation and 8kDa antigens showing minimal effects. By characterising and understanding these cellular interactions, potential biomarkers for early therapeutic intervention can be proposed to mitigate the detrimental effects of the host response and improving clinical

outcomes for patients affected by NCC. Future research will explore the cellular pathways underlying these inflammatory and tissue remodeling processes.

**118. Dr Andy Tran**

A Novel Self-adjuvanting Mucosal Vaccine for Tuberculosis (TB)

*Tran AC, Kim MY, Vergara EJ, Paul MJ, Bursnall D, Das M, Pearl JE, Cooper AM, Relic R*

Tuberculoisis (TB) predominantly affects the lungs, and is caused by Mycobacterium tuberculosis (Mtb). Despite being among the oldest known human pathogens, there is currently only one licensed vaccine against TB, Bacille Calmette Geurin (BCG), which offers some highly variable levels of protection against pulmonary TB in adults. With the increasing burden of drug resistant TB and acute shortfalls in TB management programmes as a result of COVID-19, it is imperative that we continue to develop new and more effective vaccines against TB.

We propose that the "next generation" of TB vaccines should be focused on mucosal delivery, to offer increased efficacy against TB compared to BCG, in addition to a lower cost and ease of administration on low-middle income settings where TB is most prevalent. In this project, we developed a novel vaccine candidate, TB-PCF, a recombinant polymeric construct consisting of the mucosal molecular adjuvant CTB, Mtb antigens ESAT6 and CFP10, and IgG Fc. PCF differs from most protein-subunit vaccine formulations in that the molecular adjuvant is expressed with antigens on a single chain. This can dramatically accelerate quality control and clinical development by reducing the number of discrete components required in a vaccine candidate.

We tested the PCF vaccine platform in vitro to determine cell binding and activation, polymerisation and optimisation of aerosol delivery of the protein. Furthermore, the immunogenicity of PCF in the mouse model was tested by immunising mice with PCF via the subcutaneous and intranasal routes, followed by immunological readouts including mucosal and systemic antibody responses, T cell responses and lung resident memory cells. Finally, the efficacy of TB-PCF was assessed in a novel modified mycobacterial growth inhibition assay as well as a low-dose aerosol TB challenge model in mice. The early promising results for the TB-PCF vaccine candidate warrant investigation of this platform with new and novel TB antigens, and further preclinical and clinical development.

**119. Mr Chris Tung**

High-Fidelity 3D-Printed Anatomical Models: Advancing Precision in Surgical Training and Clinical Simulation

*Tung, Chen*

The integration of 3D printing in neurosurgical training represents a significant advancement in the practice of complex, high-stakes procedures, creating a controlled, reproducible environment that enhances skill development. This study describes the development and validation of high-fidelity, anatomically precise 3D-printed brain models designed specifically for neurosurgical training and simulation. By utilizing advanced imaging modalities, including high-resolution MRI and CT scans, combined with precision 3D printing technologies, we created models that closely replicate intricate cerebral anatomy, capturing essential structures such as vascular networks, neural pathways, and

cranial landmarks. These models, generated from patient-specific imaging, offer an accurate, customized alternative to cadaveric specimens, aligning closely with real clinical anatomy.

Our models were employed at the Queen Square Simulation Centre at the National Hospital for Neurology and Neurosurgery (NHNN) as part of the Lateral Skull Base Approaches Course. This course provides neurosurgical and ENT trainees with hands-on experience in critical lateral skull base approaches, including retrosigmoid, middle fossa, and translabyrinthine techniques. Feedback from surgeons and trainees has been overwhelmingly positive, indicating the models' effectiveness in simulating complex anatomy and providing essential tactile feedback for skill acquisition. Additionally, individual models have been customized for surgeons to use in preoperative planning for complex cases, allowing them to familiarize themselves with unique anatomical variations specific to each patient.

We rigorously evaluated the models for anatomical accuracy, material realism, and procedural effectiveness, demonstrating that they provide enhanced tactile feedback and realistic anatomical landmarks, both of which are crucial for developing the spatial awareness and motor skills fundamental to neurosurgical proficiency. Comparative assessments with traditional training models revealed that these 3D-printed models offer a more cost-effective, accessible, and scalable solution, enabling a higher degree of personalization and reproducibility in training.

Our findings underscore the potential of 3D-printed models as an advanced tool in neurosurgical education. By offering a patient-specific, anatomically accurate, and economically viable alternative to cadaveric specimens, this approach supports improved skill acquisition, reduces intraoperative error rates, and ultimately enhances patient outcomes. The scalability and precision of this model align with the increasing demand for realistic, customized training solutions within neurosurgery.

**120. Dr Charlotte Wahlich**

Building excellence in participatory research at City St George's, University of London

*Wahlich C, Jones F*

Participatory research (PR) encompasses research designs, methods, and frameworks that use systematic inquiry in direct collaboration with those affected by an issue being studied for the purpose of action or change. PR engages those who are not necessarily trained in research but belong to or represent the interests of the people who are the focus of the research (Vaughen et al 2020). Researchers utilising a PR approach often choose research methods and tools that can be conducted in a participatory, democratic manner that values genuine and meaningful participation in the research process. Participatory research is now widely used, but seldom described or evaluated in detail. Done well PR can align the goals of the research with the end-user much more closely and cut down on research waste and provide greater value for money for funders (Slattery et al., 2020). This project aims to create and curate resources on PR methods, drawing from exemplary applications across City St George's, University of London (CSG) and Bridges Self-Management to share expertise and exemplars in PR. PR involves direct collaboration with affected communities to facilitate action and change, enhancing the alignment between research goals and end-user needs. This study will conduct semi-structured interviews with ten researchers, from CSG and Bridges, who have successfully implemented PR methods in their projects over the past five years. Participant recruitment will leverage existing networks and institutional communications, employing a snowball sampling strategy. Interviews will be conducted on Zoom, transcribed and thematically analysed to

identify key reoccurring themes. Analysis is ongoing but we aim to present the key findings from our interviews at Research Day. This initiative seeks to enrich understanding and application of participatory methods. The findings will inform the development of training materials and resources for staff, promoting effective use of participatory approaches in research.

**121. Dr Michael Waight**

Evaluating Heart Digital Twins in Guiding Catheter Ablation for Ventricular Tachycardia

*Waight M, Li A, Prakosa A, Trayanova N, Saba M.*

Introduction: Catheter ablation of scar-dependent ventricular tachycardia (VT) is frequently hampered by haemodynamic instability, long procedure duration and high recurrence rates. MRI-based personalised heart digital twins may overcome these challenges by non-invasively predicting VT circuits and optimum ablation lesion sites. In this combined clinical and digital twin study, we investigated the relationship between digital twin-predicted substrate abnormalities, VT circuits and optimum ablation lesion sets with their invasively mapped counterparts during clinical VT ablation.

Methods: 18 patients with scar-dependent VT underwent digital twin creation based on pre-procedural, contrast-enhanced cardiac MRI. Using rapid pacing protocols, VT was simulated and ablation targets derived which would terminate all possible VTs in the models. Patients subsequently underwent invasive VT ablation including targeting of abnormal electrograms, diastolic activity during VT and labelling of sites of VT termination with ablation. Digital twin-predicted VT circuits and ablation lesions were compared to their invasive clinical counterparts.

Results: 7699 invasive electrograms were analysed. All electrograms abnormalities were more frequently observed within digital twin predicted areas compared to non-predicted areas. An electrogram abnormality was seen in 1116/2822 (39.5%) of predicted electrograms compared to 1108/4877 (27.2%) of non-predicted electrograms ($p < 0.001$). Electrogram duration was significantly longer in the predicted areas (77.5ms [± 25.8ms] vs 65.7ms (± 20.2ms], $p < 0.001$. During VT, mid-diastolic potentials (a marker of the VT isthmus) were recorded in 16/43 (37.2%) of induced VTs. 13/16 (81.3%) of MDPs were located within 5mm of a digital twin-predicted area vs 3/16 (18.8%) which were remote ($p < 0.001$). A total of 709 clinical radiofrequency lesions were delivered to terminate VT, of which 426/709 (60.1%) were within 5mm of a digital twin-predicted target site.

Conclusions: Heart digital twin VT circuits and ablation targets accurately predict their respective clinical counterparts. Our findings demonstrate the immense potential of digital twin technology in guiding catheter ablation for scar-dependent VT.

**122. Dr Rae Wake**

Illuminating the full spectrum of cryptococcal disease through linked clinical trial, cohort and surveillance studies

*Molloy SF, Berghammer-Bohmer R, Thombrayil A, Adams J, Comins K, Nel J, Tsitsi M, Bremer M, Verhagen D, Kabanda D,6 Maphalala L, Mfinanga S, Lesikari S, Ladislaus N, Mosses A, Makoko N, Edkins L, Fatti I, Halley-Stott R, Meiring S, Quan V, Mashau R, Lawre*

Background: Understanding pathophysiology and outcomes associated with each stage on the spectrum of cryptococcal disease is essential for optimising the management of patients with AIDS.

Methods: Data from three cohorts of patients at different stages of HIV-associated cryptococcal disease were described at the same sites in South Africa (SA) and Tanzania: 1) asymptomatic cryptococcal antigenaemia (EFFECT phase III trial), 2) subclinical cryptococcal meningitis (CM) (subEFFECT prospective cohort study), 3) symptomatic CM (surveillance study, SA; prospective cohort study, Tanzania).

Results: Data for 322 individuals with asymptomatic cryptococcal antigenaemia [trial data not currently available], 28 subclinical CM and 188 symptomatic CM were collected from November 2022 to June 2024 (recruitment is ongoing).

Subclinical CM cohort: Median age was 41 years (IQR: 31-49) with 50% (14/28) male and 67.9% (19/28) ART experienced. Seventeen baseline opening pressures were recorded; median 17cm H2O (IQR: 16-21cm H2O). Following treatment, overall mortality was 42.9% (12/28). Of those with appropriate follow-up data, 2-week, 10-week and 6-month mortality 8.0% (2/25), 43.5% (10/23) and 63.2% (12/19), respectively. 75% (9/12) died as inpatients with a median time to death of 33 days (IQR: 18-70 days).

Symptomatic CM cohort: Median age was 39 years (IQR: 34-45) with 64.9% (122/188) male and 59.6% (102/171) ART experienced. Overall mortality was 45.2% (85/188). Of those with appropriate follow-up data, 2-week, 10-week and 6-month mortality was 23.9% (44/184), 48.7% (75/154) and 63.4% (85/134), respectively. 87.1% (74/85) died as inpatients with a median time to death of 14 days (IQR: 3-30 days).

Discussion: These cohorts spanning the cryptococcal disease spectrum will yield important comparable data to inform future management, particularly considering whether subclinical CM requires inpatient treatment. Current descriptive findings indicate that deaths among this subclinical CM cohort are not usually directly attributable to cryptococcal disease.

**123. Dr Rae Wake**

Fluconazole plus flucytosine vs. fluconazole alone for cryptococcal antigen-positive patients identified through screening: A phase III randomised controlled trial

*Molloy, Govender, Comins, Mfinanga, Meintjes, Lesikari, Eriksson, Adams, Nel, Moosa, Wilson, Tsitsi, Black, Kyazze, Alam, Variava,*

Background: Cryptococcal meningitis (CM) is the commonest form of meningitis in sub-Saharan Africa (SSA), accounting for 15%-20% of all AIDS-related deaths. Screening patients with advanced HIV disease to detect cryptococcal antigen (CrAg) in the blood and treatment of CrAg-positive patients in advance of severe cryptococcal disease represents a practical and cost-effective approach to reducing mortality. However, current pre-emptive treatment with fluconazole alone may be suboptimal with a substantial number of patients going on to develop cryptococcal meningitis and die. The EFFECT trial aims to assess the effectiveness of a combined treatment of fluconazole plus flucytosine (a drug combination recently shown to be effective for inpatients with CM) in this patient cohort.

Methods: The EFFECT trial is a phase III, multi-centre, open-label, 1:1 randomised treatment trial embedded into existing CrAg screening programmes at 13 sites in South Africa, Tanzania and Vietnam. The primary objective it to determine whether combination treatment of fluconazole plus

flucytosine for 2 weeks will be superior to standard treatment of fluconazole alone in reducing 6-month all-cause mortality for CrAg-positive individuals with advanced HIV disease.

Results to date: The trial opened to recruitment at all African sites in Nov 2022. Vietnam sites will open Q1 2025 following receipt of all approvals. To date, 378 participants have been recruited (332 in SA and 46 in Tanzania). Recruitment will continue until October 2025, followed by 6-month follow-up.

Discussion: Demonstrating the effectiveness of the addition of flucytosine to the fluconazole treatment currently in use for this patient cohort could have an important global impact on the reduction of advanced HIV mortality as has been seen for CM inpatients.

**124. Mr Maximilian Wallat**

Antimicrobial resistance (AMR) gene transfer between clinical methicillin-resistant staphylococcus aureus (MRSA) isolates

*Wallat M, Lindsay J, Knight G, Holt K*

Aim: To identify mechanisms used by clinical Methicillin Resistant Staphylococcus aureus (MRSA) isolates to exchange antimicrobial resistance (AMR) genes, and determine if efficient gene transfer is associated with epidemiological success of clinical MRSA populations.

Background: Whilst MRSA core genomes are relatively stable and lineage specific, they possess diverse accessory genomes, including AMR genes. MRSA are able to exchange genes rapidly in vivo via bacteriophage-mediated generalised transduction. This facilitates adaptation to new niches and selection pressures such as antimicrobial exposure within hours of colonisation.

MRSA populations vary by geographical region, each usually dominated by a few epidemiologically successful clones, which can change over time. Why these clones become dominant and shift over time is unknown. The ability to dynamically shuffle AMR genes may influence which strains become dominant. Understanding mechanisms of gene transfer between clinical MRSA isolates will help us predict and control the emergence and spread of resistant and successful MRSA populations.

Methods: Using a European clinical MRSA isolate collection of epidemiologically successful and unsuccessful isolates that have been whole genome sequenced (WGS), we developed an in vitro model of AMR gene transfer between clinical MRSA isolates under competitive conditions to uncover patterns of gene transfer between strains. Bioinformatic analyses screened isolates for lineage and AMR profiles in clinical MRSA isolates.

Results: When co-culturing clinical MRSA isolates in a competitive gene transfer assay, gene transfer was more common with erythromycin-gentamicin pairings than with erythromycin-tetracycline pairings. Some lineages (CC8) frequently exchanged genes within and between lineage, whilst others (CC1) seldom exchanged with tested partners. Bacteriophage transduction was responsible for the majority of AMR gene transfer among clinical MRSA isolates, however carriage of phi7 bacteriophage is associated with blocking of gene transfer in non-CC8 cocultures.

Conclusions: Combining AMR gene transfer phenotype with genomic data uncovers patterns of efficient and stable AMR gene transfer in clinical MRSA isolates. Future work will identify genetic components responsible for horizontal gene transfer (HGT), including barriers to gene transfer, and mobile genetic elements such as plasmids and bacteriophage. We expect to enhance understanding

of phage-driven AMR gene transfer dynamics among clinical MRSA populations. A better understanding of these mechanisms will help us predict how AMR bacteria survive, adapt and spread.

**125. Miss Brianna Watson**

GPIba intracellular tail impacts on GPVI-mediated signalling by influencing GPVI-shedding upon activation and filamin binding

*Watson, Greenwood, Ahnström, Crawley, Salles-Crawley*

Introduction: Glycoprotein (GP) Iba and GPVI are two key platelet surface receptors involved in haemostasis and thrombosis. We have recently demonstrated that the intracellular domain of GPIba plays a role in GPVI-mediated signalling events leading to reduced platelet activation and spreading after CRP stimulation and platelet aggregate formation under flow on collagen surfaces. The aim of this project is to underpin the molecular mechanisms of this GPIba-GPVI crosstalk.

Methods: Platelets from GPIba+/+ and GpIbαΔsig/Δsigmice (lacking the last 24 amino acids of GPIba intracellular tail) were stimulated with collagen related peptide (CRP-XL) and phosphorylation levels of signalling molecules assessed by western-blot. Immunoprecipitation was used to identify signalling molecules that associate with the GPIba intracellular tail upon GPVI activation. GPVI shedding and phosphatidylserine (PS) exposure in GpIbαΔsig/Δsigplatelets was assessed via flow cytometry. Thrombin generation was performed using calibrated automated thrombography assay.

Results: GpIbαΔsig/Δsigplatelets had reduced tyrosine-phosphorylation of SYK, LAT and reduced PKC activity after CRP activation compared to GpIba+/+ platelets but unchanged phosphorylated levels of Src, Lyn and Btk tyrosine kinases. GPIba from GpIbαΔsig/Δsigplatelets demonstrated reduced ability to bind filamin and PI3K compared to GpIba+/+ platelets. GPVI-mediated signalling defect in GpIbαΔsig/Δsig platelets was also accompanied with increased GPVI shedding (40%) compared to GpIba+/+ platelets upon CRP stimulation. GpIbαΔsig/Δsig and GpIba+/+ platelets had similar ability to become procoagulant and generate thrombin.

Conclusion: Our data suggest the GPVI-mediated defect occurs downstream of Src family kinases leading to reduced tyrosine-mediated signalling of major kinases such as SYK, LAT and PKC. This defect may be linked to increased GPVI shedding together with reduced ability of GpIbαΔsig/Δsig platelets to bind filamin, both important for GPVI-mediated signalling. The reduced, but not totally abrogated, PI3k and GPIba binding seen in GpIbαΔsig/Δsig platelets suggests an additional, previously unknown PI3K binding site in the GPIba intracellular tail. Together these data provide new insight into platelet signalling mechanisms in haemostasis and thrombosis. Work to identify additional binding partners of the tail of GPIba and how this influences platelet activation and thrombus formation is ongoing.

**126. Dr Sarah White**

Examining the measurement of severity of intimate partner violence: a narrative synthesis

*White S., Bearne L., Sweeney A., Mantovani N.*

Introduction: After completion of a systematic review which aimed to establish the prevalence of intimate partner violence (IPV) and its association with mental health outcomes we identified potential weaknesses in how IPV severity was measured (White et al., 2022). The aim of this synthesis was to investigate limitations in existing measures used to assess severity of IPV.

Methods: We conducted a narrative synthesis of 76 studies which were a subsample of the studies identified in study mentioned above. We identified IPV measures used in at least five studies, focusing on inconsistencies from how the measures had been intended to be used, both in structure of tool and response formats used which together led to variations in severity score calculation.

Results: Twenty-two different measures of IPV were used across the 76 studies in our sample. Thirteen studies (17%) utilized two IPV measures, and nine studies (12%) used three IPV measures. The Revised Conflict Tactics Scale was the most frequently used measure, with 35 studies (45%) employing it to measure at least one type of IPV. Measures of intimate partner violence were often modified from their original, potentially impacting on the reliability and validity of these measures. The operationalization of violence severity varied across studies and we found a lack of consistency in applying validated methods for scoring instruments to determine abuse severity.

Discussion: To achieve a comprehensive understanding of the mechanism by which IPV severity is related to mental health it may be time to take an alternative approach to measuring IPV severity. No IPV measures assessed the acceptability of the content to people who have experienced IPV. This is an important omission with significant consequences for the validity of the evidence base.

**127. Miss Kathryn Willis Kathryn Willis**

Development and feasibility testing of an intervention to prevent potentially harmful skincare practices during infancy

*Willis KM, Ussher M, Perkin MR*

Eczema is a dry, itchy skin condition affecting 15% of infants and young children, with a disproportionately high burden on children from ethnic minorities. Eczema has a significant impact on quality of life and is not currently preventable or curable. Whilst genetic factors which damage the skin barrier play a part in eczema emerging, the increase in eczema during the twentieth century means environmental factors must also be a contributor to skin barrier impairment. In infants, these environmental factors include how often babies are bathed, how long baths last, the use of soap products, and the temperature of the water.

The BabyBathe study is exploring whether it would be feasible to conduct a large, definitive trial to examine whether advising families to bathe their babies less often might stop babies developing eczema. This intervention, aimed at persuading families to change their baby bathing routine, has been co-designed with families and healthcare professionals.

The feasibility trial aims to recruit 125 pregnant women to be randomly assigned to either the new baby bathing intervention or to routine NHS advice. Recruitment opened in December 2023, and as of 31st October 2024, 92 families have been recruited. Evaluative interviews with intervention

families have begun to establish the ease and acceptability of the intervention. Preliminary data from the feasibility trial and evaluative interviews will be presented in this poster.

**128. Dr Stephen Woolford**

Preliminary results from The Hidden Workload Study: a national mixed methods analysis of local demographics and general practice workload.

*Woolford SJ, Jones F, Harris T.*

Background: When analysing general practice workload, routinely collected NHS data does not capture “hidden” work, such as administrative and supervisory tasks, or personal experiences of workload in relation to local communities. Furthermore, clinician’s planned work schedules are increasingly not representative of their actual daily workload.

Aims: To accurately describe all tasks undertaken during a general practice clinician's workday, other than and including direct patient contacts, and explore how local demographics affects clinicians’ workload.

Methods: The Primary care Academic CollaboraTive's collaborative research approach and mixed methodology is being utilised. All general practice clinicians in England (i.e., not only doctors) are eligible for recruitment. Participants record their planned work schedule and then their actual work (including clinical, administrative, and supervisory tasks) using timers on a randomly allocated workday in late 2024/early 2025. Practice demographic data will be collected from NHS Fingertips data profiles. 15-20 participants from a variety of clinical roles will be interviewed during the same period, exploring lived experience of workload and how local demographics affect workload.

Results: As of October 2024, 367 general practice clinicians have been recruited (GP partner: 152 [41.4%], salaried GP:90 [24.5%], GP trainee:60 [16.3%], other clinical role:65 [17.8%]). All participants to date have been allocated a data collection day in November 2024. 223 participants (60.8%) have additionally agreed to be approached for interview, with 14 interviews planned between October and November 2024. We will present preliminary findings from the study, comparing planned with real workload, describing workload according to practice demographics, and emerging interview themes.

Discussion: This is the first study to accurately describe national general practice workload in relation to local demographics and synthesise results with qualitative data from participants. This will form a contemporary analysis of general practice workload, informing future workforce and service provision planning. Recruitment is ongoing and further data collection is planned for early 2025.

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