

St. George's, University of London Research day 2019

Poster Abstracts

1. Miss Fahimah Amini

Investigating the use of dried blood spots in the measurement of antibodies against *Bordetella pertussis* virulence factors

Amini F, Erick A, Hall T and Le Doare K

Background: In 2014, the WHO estimated that *Bordetella pertussis*, a respiratory pathogen, affected 24.1 million children under-fives worldwide. Although, licensed pertussis vaccines are available, there has been a resurgence of *B. pertussis* noted in many countries. Infants younger than three months are the most affected age group, mainly because of their underdeveloped immune systems. Methods: A multiplex immunoassay (MIA) was used to compare the antibody titres against five *B. pertussis* virulence factors (BVF) in eleven paired DBS and serum samples and in recently and previously vaccinated individuals. Results: IgG concentrations against BVFs in paired DBS-serum samples demonstrated a good correlation ($r^2=0.99$). The mean IgG difference against the five BVFs observed in vaccinated individuals were not statistically significant (p-value range: 0.36-0.89). Conclusion: The correlation of antibodies in DBS-serum samples is strong and thus DBS can be utilised in surveillance and vaccine studies. However, our results and the literature review highlighted the imperative of correct storage of this valuable resource.

2. Miss Hafssa Anfishi

Investigating effectiveness of wild type and optimised codon CFTR transport in Cystic Fibrosis mutations

Anfishi H, Woodall M, Baines DL

The monogenetic nature of CF alongside the relative accessibility of the lungs to nebulisers makes the disease an obvious candidate for gene therapy. Recent developments of drugs targeting CF such as Kalydeco and triple combination Tezacaftor therapy has proved to be very effective at restoring dysfunctional CFTR protein, but they may not take into consideration the decreased expression of CFTR proteins in CF patients with class I mutations which accounts for approximately 10% of all CF cases. Gene therapy presents as a potential therapeutic option in such occurrences where both wild type (WT) and codon-optimised CFTR have shown to increase the expression of functional CFTR proteins in class I mutations. In this project, codon optimised and enhanced CFTRs will be compared against WT CFTR to determine which is more effective in increasing the expression and activity of the protein for recovery in class I CF mutations. This will be performed by investigating protein expression and observing protein transport within the cell by FRAP to determine whether they are transported effectively to the cell membrane. The results may provide deepened insight into the mechanism of class I mutations and gene therapy.

3. Dr Tarek Antonios

Late Effects of Hypertensive Disorders of Pregnancy on Central Blood Pressure, Microcirculation and Cardiovascular Diseases: A Cross-Sectional Case Control Study

Ayushi Singh, Elisa Allievi, Mihari De Soysa, Rhoda Cookey-Bresi, Roberta Angheleanu, Tarek Antonios

Introduction: The risk of cardiovascular disease (CVD) increases in women with a history of hypertensive disorders of pregnancy (HDP). Although the mechanisms exploring this association are poorly understood, a reduction in skin capillary density or capillary rarefaction (CR), has been proposed in its pathogenesis. CR precedes the onset of pre-eclampsia (PE) and essential hypertension. A total of 86 non-pregnant women were studied (age 37 ± 6 y), 44 had a previous history of PE (age 37 ± 9 y), 29 had history of gestational hypertension (GH) (age 37 ± 6 y) and 13 were healthy controls (age 35 ± 5 y). We measured central systolic blood pressure (cSBP), aortic augmentation index (AIx), pulse pressure (PP) and capillary density on the dorsum of the middle finger using intra-vital capillaroscopy. Results: GH group had higher cSBP, SBP, DBP and PP compared to controls. GH also had a higher SBP and PP compared to PE. Moreover, PE group had higher cSBP compared to controls. No significant differences were seen in AIx or capillary density between groups. Conclusions: Women with a history of GH are more likely to have systemic arterial stiffness, raised cSBP, PP and SBP, compared to women with history of PE and healthy controls.

4. Dr Natalicia de Jesus Antunes

Mycophenolic Acid therapeutic drug monitoring by LC-TOF-MS

Antunes NJ, Ince NLR, Raymond JA, Kipper K, Couchman L, Holt D, and Johnston A

This study developed and validated, for the first time, a liquid chromatography and time-of-flight mass spectrometry (LC-TOF-MS) detection to measure mycophenolic acid (MPA) to quantify the drug in patient samples as part of the routine therapeutic drug monitoring service. MPA was extracted from 50 µL human plasma by protein precipitation, using sulindac as internal standard (IS). Analyte and IS were monitored on a LC-TOF-MS. The method was used to evaluate the drug level in plasma of patients (n=15) to therapeutic drug monitoring. The retention time was 2.33 min and 2.31 min for MPA and sulindac, respectively, and no carry-over was observed. Lower limit of quantification (LLOQ) of MPA was 0.1 µg/mL. The within and between assay reproducibility results were within the assay acceptance criteria. MPA demonstrated stability in plasma after 6 days at room temperature and at 4°C, 4 days in the auto-sampler at 10°C, 5 months at -20°C and after 3 freeze/thaw cycles, with accuracy ranging from 91.56% to 100.62%. The patient's samples quantification was comparable to the previous method. This method showed satisfactory analytical performances for the determination of MPA in plasma over the calibration range of 0.1 µg/mL to 15.0µg/mL.

5. Miss Sandy Ayoub

Loss-of-function variants in TBC1D32 underlie syndromic hypopituitarism

Hietamäki J, Gregory LC, Ayoub S, Iivonen AP, Vaaralahti K, Liu X, Brandstack N, Buckton AJ, Laine T, Käsäkoski J, Hero M, Miettinen PJ, Varjosalo M, Wakeling E, Dattan M, Raivio T.

PURPOSE To describe patients with syndromic hypopituitarism due to biallelic loss-of-function variants in TBC1D32, a gene implicated in Sonic hedgehog signaling **METHODS** Genome sequencing was applied to a Finnish family of two siblings with panhypopituitarism, absent anterior pituitary, and mild craniofacial dysmorphism, and to a Pakistani family with a proband with growth hormone deficiency, anterior pituitary hypoplasia, and developmental delay. Expression profiling of TBC1D32 in human fetal brain was performed through in situ hybridization. Stable and dynamic protein-protein interaction partners of TBC1D32 were investigated in HEK cells followed by mass spectrometry analyses **RESULTS** The Finnish patients harboured compound heterozygous loss-of-function variants (c.1165_1166dup, p.Gln390Phefs*32, and c.2151del, p.Lys717Asnfs*29) in TBC1D32; the Pakistani proband carried a known pathogenic homozygous TBC1D32 splice-site variant c.1372+1G>A (p.Arg411_Gly458del); as did a fetus with cleft lip and intestinal malrotation from a terminated pregnancy. TBC1D32 was expressed in the developing hypothalamus, Rathke's pouch and the hindbrain. TBC1D32 interacted with proteins implicated in cilium assembly, Shh signaling and brain development.

6. Dr Alexis Bailey

Does long term inhalation of nicotine containing electronic cigarette vapour cause toxicity in vivo?

Zhuikova E, Goldsmith N, Marczylo T and Bailey A

E cigarettes have proved to be very popular as a smoking cessation aid. Evidence so far from short term studies in humans, including our Horizon 2020 SmokeFreeBrain study, found significant harm reduction from switching from smoking to e-cigarette use and promising smoking cessation rates. Nonetheless the potential hazards of long-term inhalation of e-cigarettes are unknown and have not been investigated so far. Our objective was 1) To investigate the potential neurotoxicity and the neuroadaptive consequences of long term inhaled nicotine from e-cigarette fluid in an in vivo model of e-cigarette vapour inhalation; 2) To investigate the effect of long term inhalation of nicotine containing e-cigarette vapour on toxicity biomarkers in biofluids and organ toxicity. Adult male mice were exposed via nose-only inhalation to e-cigarette aerosol (0%, 0.6% or 1.8% nicotine) or air only for 3 hours every day for 16 days. Animals were restrained in multi-chambered systems connected to an E-Cigarette aerosol generator, enabling the simultaneous delivery of 3 different aerosols and filtered air. A wide range of tissues/biofluids were collected. This is the first inhalation exposure study to e-cigarette vapour carried out in rodents in the UK

7. Miss Mohani-Preet Kaur Bajaj

Clinical risk factors for microstructural brain damage

Bajaj M-P.K., Ruickbie S.V., Burrage D.R., Spilling C.A., Dodd J.W., Jones P.W., Baker E.H., Barrick T.R.

Chronic smoking is a significant risk factor for respiratory, cardiovascular and cerebrovascular diseases. Neuropathological mechanisms are unclear. FEV1, oxygen saturations (SaO2), high sensitivity C-reactive protein (hsCRP), mean arterial pressure and brain natriuretic peptide (BNP) were measured in 100 smokers. Brain tissue microstructural health (fractional anisotropy) and ultrastructural damage (mean diffusivity), were analysed on a voxel-by-voxel basis using tract-based spatial statistics. Greater lung function and arterial oxygenation was significantly associated with greater tissue microstructure and reduced ultrastructural damage in white matter tracts globally. Increased systemic inflammation was associated with reduced tissue microstructure, no associations were found with ultrastructural damage. Greater blood pressure was associated with reduced tissue microstructure and increased tissue ultrastructural damage. No associations were found with BNP. All statistics were corrected for age, sex and multiple comparisons. The association between microstructural white matter damage and pulmonary, inflammatory and cardiovascular biomarkers raises the possibility of a multifactorial pathogenesis leading to brain disease.

8. Mr Samuel Baldwin

Sex-dependent differences of vascular Kv7 channels

Samuel Baldwin, Vincenzo Barrese, Iain Greenwood

As vascular smooth muscle cells contract, blood vessels narrow reducing blood flow and increasing total peripheral resistance. VSMC contraction is achieved by an increase in intracellular calcium, which is dictated by VSMC membrane potential and thus voltage gated calcium channels (VGCC)Po. Kv7 channels are shown to regulate VSMC membrane potential at rest, their activity mediates VSMCs hyperpolarization deterring VGCC opening and vasoconstriction. Kv7 channels also contribute to an array of receptor mediated responses and are degraded in hypertension, contributing to a hypertensive phenotype. However, the wealth of current literature focuses predominantly on males. Thus we have compared KCNQ expression and function in arteries from male and female Wistar rats. We have characterized transcript expression patterns of all isoforms of KCNQ/B-auxiliary subunit KCNE via qPCR, demonstrated the effect of efficacy of Kv7 activators S-1 and ML277 to relax constricted vessels as well as the contribution of Kv7 channels to thromboxane A2 receptor mediated vasoconstriction. Our data indicates a sex-dependent post transcription difference in KCNQ regulation resulting in a cycle dependent shift in potency of Kv7 activator mediated relaxation.

9. Dr Thomas Barrick

Quasi-Diffusion Magnetic Resonance Imaging (QDI): a fast, high b-value diffusion imaging technique

Thomas R. Barrick, Catherine A. Spilling, Carson Ingo, Jeremy Madigan, Jeremy D. Isaacs, Philip Rich, Timothy L. Jones, Richard L. Magin, Matt G. Hall, Franklyn A. Howe

There is a clinical need for fast, high contrast, diffusion magnetic resonance imaging (dMRI) techniques that are sensitive to changes in tissue structure and provide diagnostic signatures at the early stages of disease. Here we describe a new way to minimise the acquisition of multi-shell b-value diffusion data, Quasi-Diffusion MRI (QDI). QDI is based on a special case of the Continuous Time Random Walk (CTRW) model of diffusion dynamics and assumes presence of non-Gaussian diffusion properties within tissue microstructure. We present a framework for multi-directional diffusion gradient acquisition and data processing that allows computation of Quasi-Diffusion-Weighted Imaging (QDWI) and Quasi-Diffusion Tensor Imaging (QDTI) maps. We show that QDI provides excellent healthy and pathological tissue contrast using standard clinical MRI gradients in short acquisition times of between 1 and 4 minutes.

10. Samantha Baskerville

Manifestations of Otolithic Dysfunction: A Scoping Review

Baskerville, S

Introduction: Evidence suggests that dizziness affects 35% of adults over forty with the most common cause of vertigo being vestibular in origin. Vertigo is a disabling and costly condition and despite advances in vestibular research there remains clear diagnostic criteria for insult to the otolith organ of the vestibular system. Aim: To scope, identify and evaluate the evidence supporting current understanding of otolithic dysfunction manifestations as a precursor to the subsequent development of diagnostic criteria for the condition. Methods: A scoping review was undertaken following modified PRISMA guidelines (Tricco et al, 2018) Results: 34 articles were sourced, located and charted into the a priori charting form. The range of evidence found was predominantly research articles which were quantitative and cross sectional in nature. The quality of evidence overall was limited due to small patient numbers and poor methodological approaches. Conclusion: These results conclude that there is not currently sufficient evidence base to build a diagnostic tool for otolithic dysfunction. It supports clinical practice utilising SVV and SVH routinely alongside in-depth history taking and VRBQ self-report questionnaire.

11. Miss Clare Benson

Investigating Rho dysregulation in Adams-Oliver syndrome as a model of vascular development.

Benson CE, Osborn D, Southgate L

Adams-Oliver syndrome (AOS) is a genetically heterogeneous developmental disorder, predominantly characterised by scalp, limb and vascular anomalies. Of the six causal genes identified to date, DOCK6 and ARHGAP31 encode regulators of the Rho GTPase pathway. To investigate the overarching hypothesis that AOS is caused by disrupted vascularisation, this project aims to examine the molecular mechanisms underlying perturbed vasculogenesis using a combined approach to model Rho-related AOS in vitro (vascular cell culture) and in vivo (zebrafish). Initial experiments sought to characterise dock6 and arhgap31 during zebrafish embryogenesis. Quantitative PCR analysis confirmed these genes are expressed in the early stages of vascularisation. Whole-mount in situ hybridisation in zebrafish embryos demonstrated localisation of dock6 and arhgap31 to the regions affected in AOS, indicating a correlation with the human phenotype. Furthermore, morpholino-targeted knockdown of dock6 generated AOS-like features including cardiovascular and eye defects. This approach will elucidate the healthy physiological functions of DOCK6 and ARHGAP31 during vascularisation, and provide key insights into the pathological mechanism of vascular disruption in AOS.

12. Mr Rohan Bhate

Research priorities for the future health of multiples and their families: The Global Twins and Multiples Priority Setting Partnership

Lam. J.R , Bhate. R , Khalil. A

Objectives: The Global Twins and Multiples Priority Setting Partnership (PSP) sought to identify the top ten research priorities to reduce twins and multiples' risks and improve health outcomes for families of multiples. Methods: The PSP followed the James Lind Alliance method. An initial survey identified unanswered questions; these questions were verified as true unanswered questions. A second survey prioritised only the unanswered quantitative questions and created a short-list of unanswered questions for a final workshop. Results: A sample of 1,120 multiples, parents, clinicians and, researchers globally suggested 2,891 questions. These were divided into those answerable by quantitative and qualitative research. Of the questions answerable by quantitative research, 89 were verified as true unanswered. A final face-to-face workshop determined ten research questions to be a priority. Conclusion: Despite evidence that multiples are at increased risks of ailments and that there are burdens on the families of multiples, attention to address these issues is lacking. We believe these priorities, derived from a collaborative participatory and multidisciplinary approach provide credible direction for those driving research forward.

13. Mr Matthew Biggart

Effect of hyperglycaemia on peptide composition of in vitro airway surface liquid.

Biggart MGS, Ling X, Simpson N, Gani J, Chen X, Wrobel J, Hilpert K, Tarran R & Baines DL.

The airway surface liquid (ASL), a protective layer secreted by the airway epithelium, represents the first line of defence against inhaled infectious material. It contains a complex array of proteins and peptides that aid the neutralisation and removal of inhaled microbes and toxicants. Diabetic hyperglycaemia has been associated with an increased susceptibility to acute lung infections. We hypothesised that diabetes does this by changing the state of the ASL proteome/peptidome. Therefore, we examined how hyperglycaemia changed the ASL peptide profile lung epithelial cell lines. Native peptides and their subsequent fragments underwent tandem mass spectrometry and analysed using the pNovo sequencing tool. Our preliminary results identified 4765 unique peptides (NHBE-BMI1: 646, Calu3: 3150, H441: 1197). Of these peptides, one belonging to Histone H1.4 had a proline/alanine composition similar to other antimicrobial peptides. Synthetic peptides were produced and the antimicrobial activity was tested against luminescent *Pseudomonas aurus*. Peptides were also exposed to Cyclophilin A to alter their cis/trans isomerisation of proline and examine the impact on antimicrobial activity.

14. Miss Farah Bocus

Audit to Review the Enhanced Recovery Programme following elective caesarean section in 2018

Bocus F

Background: The Enhanced Recovery Programme (ERP) is a set of principles applied to surgical patients to reduce mortality and morbidity risks of surgery through reducing hospital stay by focusing on eating, drinking and mobilisation, after surgery. Aim: To review the care and satisfaction of women undergoing the elective caesarean, in 2018, under the Enhanced Recovery principles Methods: A retrospective analysis was conducted, through a database, on 70 anonymised questionnaires that patients completed before they left hospital. The questionnaire included the following: time taken to first drink, eat and mobilise post-operatively, any reason for delay and length of admission. Results: The results from 2018 were compared to results from audits of previous years. 63% of women were discharged on day 1 compared to 56% on day 1 in 2017. Annually, the ERP is achieving its aim of reducing hospital stay. Yearly trends showed that 2018 had the biggest improvement in the percentage of women eating and drinking within the first few hours post-operatively. Conclusion: From the 2018 re-audit, the ERP continues to prove its worth in speeding the recovery process by reducing the morbidity risks of surgery through the methods investigated.

15. Ms Claire Broad

Development of bead-based enrichment methods targeting the *opcA* gene in *Neisseria gonorrhoeae* (NG)

Broad CE, Zhou L, Furegato M, Cooper P, Laing K, Sadiq ST

Background: Targeted DNA enrichment can facilitate whole genome sequencing directly from clinical samples, bypassing needs for culture, by isolating target from non-target DNA. We aimed to develop bead-based enrichment methods using a capture probe targeting *OpcA* gene in *Neisseria gonorrhoeae* (NG). Methods: Two methods were developed in parallel using whole NG spiked into PBS: direct (DC) and indirect capture (IC). For DC, the probe was immobilised directly onto magnetic Dynabeads™ (Thermo Fisher) prior to DNA capture; for IC, DNA was captured first on biotinylated probe and then removed using streptavidin beads (MyOne™ Thermo Fisher). A Wilcoxon semi-parametric test was used to assess differences between the methods. DNA recovery was calculated relative to initial PCR-estimated DNA load. Results: Total DNA recovery for DC enrichment was 6.11% (95%CI: 4.53-7.71) compared to 16.11% (95%CI: 2.20-29.86) for IC enrichment. ($p=0.019$). Conclusion: IC hybridisation shows promise for work with clinical samples, however, further evaluation and optimisation will be undertaken to determine minimum DNA recovery required for sequencing with sufficient whole genome coverage.

16. Dr Robert Brooks

Cell cycle heterogeneity and upregulation of the CDK inhibitor p27Kip1

Brooks RF and Barr AR

The cell cycle times of mammalian cells growing slowly in limiting concentrations of serum growth factors are highly heterogeneous within the same population. Some cells show extensive proliferation with multiple consecutive cell cycles while other adjacent cells withdraw into a reversible quiescent state. This heterogeneity arises at high frequency within a clone, with sister cells often showing divergent behaviour. When starved of growth factors, it is known that mammalian cells can upregulate the CDK inhibitor p27kip1, which is thought to contribute to cell cycle arrest. Using live-cell imaging of RPE1 cells expressing fluorescent derivatives of p27 and PCNA (a marker of DNA synthesis), we observed that upregulation of p27 is highly variable within a population growing in low serum. In some cells, p27 levels remain low and the cells continue to cycle with short G1 times. In others, p27 starts to rise in G1 but begins to disappear again shortly before the cell enters S phase. In other cells, p27 rises continuously to high levels and the cell remains arrested in G1. These preliminary data suggest that p27 upregulation may contribute to the cell cycle heterogeneity observed in low serum.

17. Ms Simonette Carlton-Carew

Alpha calcitonin gene-related peptide mediates calcium-sensing receptor-induced vasorelaxation in rat mesenteric arteries

Simonette Carlton-Carew, Iain Greenwood & Anthony Albert

Stimulation of Calcium-sensing receptors (CaSRs) expressed in arteries are reported to regulate vascular tone. However, its cellular pathway needs to be clearly defined and is therefore the focus of this work. Superior mesenteric artery branches were dissected from Wistar male rats. Immunohistochemistry showed CaSRs located on the endothelium, vascular smooth muscle (VSM) and perivascular neurones. Arterial segments, mounted on wire myographs, were pre-contracted with U46619 (thromboxane receptor agonist) then CaSRs were activated with increasing extracellular calcium (1mM-10mM) which induced relaxation. Calcium-mediated relaxations were significantly impaired in the presence of the CaSR negative allosteric modulator Calhex-231, functional endothelium removal and functional desensitisation of the perivascular neurones. Additionally, relaxations were hindered by blockers of nitric oxide, large-conductance calcium-activated potassium channels (BKCa) and the neuropeptide, alpha-calcitonin gene-related peptide (α CGRP). These data proposes that CaSR stimulation leads to α CGRP release from perivascular neurones which sequentially causes endothelial nitric oxide release to subjacent VSM to cause BKCa activation.

18. Dr Veronica Carroll

HIF-mediated suppression of DEPTOR confers resistance to mTOR kinase inhibition in renal cancer

Doan H, Parsons A, Devkumar S, Selvarajah J, Miralles F and Carroll VA

Mechanistic target of rapamycin (mTOR) is a fundamental regulator of cell growth, proliferation and metabolism. mTOR is activated in renal cancer and accelerates tumour progression. Here, we report that the mTOR inhibitor, DEP domain-containing mTOR-interacting protein (DEPTOR) is strikingly suppressed in clear cell renal cell carcinoma (ccRCC) tumours and cell lines. We demonstrate that DEPTOR is repressed by both hypoxia-inducible factors, HIF-1 and HIF-2, which occurs through activation of the HIF-target gene and transcriptional repressor, BHLHe40/DEC1/Stra13. Restoration of DEPTOR and CRISPR/Cas9 mediated knockout experiments demonstrate that DEPTOR is growth inhibitory in ccRCC. Furthermore, loss of DEPTOR confers resistance to second generation mTOR kinase inhibitors through deregulated mTORC1 feedback to IRS-2/PI3K/Akt. This work reveals a hitherto unknown mechanism of resistance to mTOR kinase targeted therapy that is mediated by HIF-dependent reprogramming of mTOR/DEPTOR networks and suggests that restoration of DEPTOR in ccRCC will confer sensitivity to mTOR kinase therapeutics.

19. Dr Florencia Cavodeassi

A zebrafish genetic model to search for novel genes involved in the aetiology of ocular malformations

Monfries C., Fourteia M., Ali I., Cavodeassi F.

Anophthalmia, microphthalmia and coloboma (MAC) arise from defects in eye morphogenesis and are amongst the most severe defects associated with blindness. Some of the genes affected in these conditions have been identified, but in most cases they are not known. Often mutations in genes relevant for eye formation may not display defective phenotypes by themselves and their potential relevance to understand eye malformations in humans is overlooked. A strategy to identify those genes is to perform searches in a genetic background sensitised to eye malformations. Here we present a genetic model that will be used for such purpose. *Fzd5* is a Wnt receptor expressed at several stages during eye morphogenesis. A mutation in *fzd5* that interferes in a dominant-negative way with Wnt signalling has been described in families with MAC. However, *fzd5* loss of function in animal models is phenotypically normal, probably due to functional compensation by other receptors. Our analysis indicates that despite their lack of eye defects, *fzd5* zebrafish mutants show compromised Wnt activity. We will present this analysis and our strategy to exploit the *fzd5* mutant as a sensitised condition to identify novel genes involved in eye malformations.

20. Mr Mohammed Chaudhry

Antihypertensive drug concordance in patients with apparent resistant hypertension: a tertiary hypertension referral centre experience

Chaudhry MMA, Antonios TF

Introduction: Non-adherence to antihypertensive medication is a major cause of resistant hypertension (RH), with rates reported as high as 66%. This study assessed the prevalence of non-adherence in individuals with apparent RH referred to the Blood Pressure Unit at St George's University Hospital NHS foundation Trust. **Methods:** After optimising drug regimens and excluding white coat and secondary hypertension, drug adherence was assessed using liquid chromatography–mass spectrometry analysis of urine samples in 124 individuals who met the criteria for RH. **Results:** Non-adherence was found in 57.3% of individuals. Of these, 63.4% had partial non-adherence and 36.6% had complete non-adherence. Non-adherent individuals were significantly younger, had a shorter history of hypertension, more likely to be a female and have depression, and less likely to have concomitant cardiovascular disease and/or target organ damage, type 2 diabetes mellitus, chronic kidney disease and retinopathy. Low levels of adherence were observed more in individuals on diuretics. **Conclusions:** The assessment of adherence at an early stage in individuals with apparent RH is essential for tailoring treatment strategies and saving vital healthcare resources.

21. Miss Amy Chiang

Is More Information Helpful? Intra and Inter-Observer Reliability of the Distal Radius and Ulna Classification for Assessing Skeletal Maturity in Patients with Adolescent Idiopathic Scoliosis

Chiang A., Houston J., Haleem S., Bishop T., Bernard J., Lupu C., Lui D.

Introduction: Accurate assessment of bone age enables correct management of idiopathic scoliosis. Current methods of assessment are limited in practicality and accuracy. This study aims to evaluate the inter and intra-rater reliability of the DRU classification and also to compare its application in a UK population to that in a Hong Kong population in the original study. **Methods:** Retrospective study of 50 randomly selected left-hand radiographs of patients with adolescent idiopathic scoliosis (AIS) was done. Bone maturity was assessed twice using the DRU by each of the four examiners. Intraclass correlation (ICC) method was used to assess reliabilities within and between the examiners. **Results:** The inter-rater ICC value was 0.918 and 0.939 for radius and ulna assessment respectively. The intra-rater ICC values for radius assessment are as follows: 0.897 (AC), 0.809 (DL), 0.769 (JH), 0.814 (SH); for ulna assessment: 0.948 (AC), 0.843 (DL), 0.786 (JH), 0.810 (SH). **Conclusion:** The DRU classification is a reliable way to assess skeletal maturity in AIS patients. The results of this study are consistent with that of the original Hong Kong-based study. Further studies would be needed to determine the validity of the DRU classification.

22. Dr Irina Chis Ster

Age-dependent prevalence of dengue and chikungunya in coastal Ecuador

Chis Ster I., Rodriguez A., Romero N., Lopez A., Montgomery J., Cooper J. P.

The frequency of dengue epidemics has increased in recent years accompanied by the recent emergence of chikungunya in the Caribbean and Latin America. There are few population-based estimates for the prevalence of these two arboviruses despite common epidemiological features. We developed a novel statistical approach and estimated age-dependent IgG seroprevalence for dengue, chikungunya, and co-infections and potential determinants in coastal Ecuador population. A bivariate binary response indicating presence/absence of dengue/chikungunya was analysed using a simultaneous logit model with shared random effects and Bayesian inferential framework. Dengue seroprevalence increased rapidly with age reaching 97% (95%CrI 93%-99%) by 60 years. Chikungunya seroprevalence peaked at 42% (95%CrI 18%-66%) around 10 years of age and averaged 27% (95%CrI 8.7%-51.6%) for all ages. Females living in urban settings were more likely to be chikungunya seropositive while rural men were more likely to be dengue seropositive. Our findings aim at informing the implementation of the 2018-WHO newly recommended dengue vaccination strategies in Ecuador.

23. Mr Regwaan Choudhury

Retrospective Analysis: Outcomes of Marginal Donor Kidneys in Marginal Recipients

Choudhury R

This study aims to investigate the effectiveness of transplanting marginal donor kidneys into marginal recipients as compared to non-marginal recipients, based on acute post-surgical outcomes.

Kidney transplantation has long been established as the first-line choice of treatment for Stage Five Chronic Kidney Disease. Expanded Criteria Donors (ECD) – otherwise known as marginal kidney donors for the purpose of this study – have however become a more prudent option in treatment as a result of the current high demand-low supply issue for a kidney transplant.

ECD is internationally defined as the kidney donor having had either Donated after Circulatory Death (DCD) or Donated after Brain Death (DBD) at age ≥ 60 years.

The exact prognosis of marginal donor kidney transplant recipients has not yet been established. Moreover, the impact of marginal donor kidneys in marginal recipients remains little investigated. Consequently, there is also a lack of publicly accessible information regarding the effectiveness of this form of transplant.

This study hypothesises that amongst those receiving a transplant from a marginal donor, acute post-operative complications are more common in marginal recipients compared to non-marginal recipients.

24. Dr. David Clark

Investigating a novel nucleic acid extraction technology

Clark DJ, Moore, CM, Krishna, S, Staines, HM

The aim of these studies was to assess nucleic acid extraction with a new spin column-based method (DNA-XT). DNA, or RNA from samples spiked with i. *Plasmodium falciparum* (whole blood), ii) *Leishmania donovani* amastigote culture or iii. HIV (serum) was extracted with DNA-XT and compared with that isolated with a commercial extraction kit. Eluates from large and small sample volumes were assessed by PCR (malaria and leishmania) and RT-qPCR (HIV). Using a small volume (5 μ l) of blood, the DNA-XT and DNeasy methods produced eluates with similar DNA concentrations, 0.63 versus 1.06 ng/ μ l, respectively. With blood, the DNA-XT method produced DNA with lower PCR inhibition than a commercial kit. When examining HIV (RNA) extraction (also with 5 μ l of sample), this result was similar, with approximately 2-fold difference between DNA XT and a commercial kit.

The new technique was twice as fast and required no hazardous reagents, fewer plastics and manipulations yet had reduced total recovered nucleic acid compared with current commercial kits. Depending on downstream requirements, this new spin method has potential for both point of care testing with finger prick sampling and laboratory nucleic acid purification.

25. Miss Natasha Clarke

Longitudinal change in linguistic markers of Alzheimer's disease

Clarke N., Barrick T., Garrard P.

Alzheimer's disease (AD) is a progressive neurological disorder that impacts cognitive function, including memory, executive function and language. Recent advances in Natural Language Processing (NLP) – a branch of computer science which aims to analyse human language at scale – has ensured robust, in-depth investigation of linguistic features in spoken discourse. Using these features, machine learning models are able to correctly classify groups of patients with and without AD with up to 94% accuracy. Yet few studies have followed patients longitudinally, which may be important given the impact of individual differences on language, and the heterogeneous spread of Alzheimer's pathology in the brain. In a previous study of 18 participants who described a picture, linear trends were found in syntactic complexity, semantic and lexical content from the Mild Cognitive Impairment (MCI) to moderate AD stage. We aim to explore longitudinal change in linguistic markers in a larger data-set, and using five different tasks to elicit speech, comparing their clinical utility. Longitudinal follow-up has recently been completed for 42 participants, and we will report results using NLP and machine learning methods.

26. Miss Ashleigh Clegg

Expression of Tuberculosis Vaccine Candidates in Tomato Fruits

Clegg A G, Reljic R, Paul M J, Drake P M W

This project aims to produce oral tuberculosis vaccine candidates in green unripe tomato fruits for delivery as an 'edible vaccine'. The vaccine candidates are polymeric structures comprising antibody and antigen sequences. Green tomatoes have been chosen as the pH of the apoplast where the molecules form should be particularly suitable for assembly of the vaccine candidates. In addition, green tomatoes contain an endogenous adjuvant, α -tomatine, which may contribute to the immunogenicity of the vaccines. To date, the growth conditions and establishment of plants both in vivo and in soil have been optimised, as measured by recording germination frequency, stem height and leaf size. Two vaccine candidates termed TB - Recombinant Immune Complexes and TB - Polymeric Immunoglobulin Scaffolds have successfully been expressed in tomato fruits using the plant vector *Agrobacterium tumefaciens*, as confirmed by ELISA and western blotting. The DNA sequence of a third vaccine candidate, which specifically targets M cells in the gut, has been synthesised and cloning into a plant expression vector is ongoing.

27. Mr Joel Coombs

An Assessment of Male Referrals to a DGH Breast Clinic

Coombs JC, Coombs NJ

Men referred to breast centres make-up a small yet vital part of the work load. This study identifies characteristics of men referred to a district general hospital breast centre, over a one-year period. The medical notes of all men referred to Great Western Hospital (GWH), Swindon, were reviewed for; cause of referral, risk factors (RFs), investigations, outcome and diagnosis. Association of Breast Surgeons (ABS) 2019 guidelines were used to assess suitability. Between June 2018 and May 2019, 196 (4.4%) men attended the breast clinic. The mean age was 51.5 years (range; 13-95). The most common referral symptom was a lump (unilateral; n=158, 81%, bilateral; n=15, 8). Symptoms were present for <2 months in 50% of men. Investigations were arranged in 172 (88%) patients. The most common diagnosis was gynaecomastia (72%, n=141), with the laterality related to age and RFs. Malignancy was diagnosed in three (1.5%) men. 48% of men did not meet guidelines for referral. The data suggests patterns between age and RFs in gynaecomastia development. Following the ABS guidelines and education of disease patterns may reduce men being over referred/investigated. This may aid in maintaining a high-quality service whilst meeting demands.

28. Ms. Susanna Cooper

Endocarditis and Sudden Cardiac Death

Cooper S, Griffin KJ, Westaby J, Sheppard MN

Endocarditis is growing in incidence due to increased interventions, valve replacements and immunosuppression. Difficult to diagnose clinically but if left untreated can present as sudden cardiac death (SCD). True incidence of endocarditis related to SCD is unknown. Retrospective analysis of our national database of 6000 cases of SCD showed 21 cases of endocarditis, 14(67%) were male and mean age was 32.6 ± 16.0 years. Post-mortem examination showed the aortic valve (AV) was affected solely in 12(57%), mitral solely in 3(14%), and tricuspid and pulmonary solely in 1(4.8%) each. Twelve (57%) had an identifiable valve abnormality or previous valve operation, the most common being bicuspid AV (6/50%). 12(57%) had prior symptoms but only seven (33%) had pre-mortem diagnosis. This study highlights that although rare, endocarditis is an important cause of SCD in those with valvular disease and/or previous valve surgery. Preceding symptoms can be vague, and most individuals are not diagnosed during life. Absence of a pre-mortem diagnosis additionally highlights the need for pathologists to be careful in their examination of the heart and cardiac valves. The gross appearance of vegetations can vary widely and can be missed at autopsy.

29. Dr Isabelle Crevel

Core Facilities Cell Sorter

Crevel I, Nolan J, Lympany P

Following a successful bid placed by Ingrid Dumitriu we acquired a new cell sorter: the BD Melody at the beginning of the year. This instrument has 3 lasers :Blue (488nm), Red (640nm) and Violet(405) and can analyse 9 colours on top of Forward Scatter & Side Scatter (11 parameters). We can perform a 2 way sort and also collection on 96 well plates. The instrument has been successfully used by several members of the university to select, for example, single cells after CRISPR-Cas genome editing or to collect cells in order to analyse RNA at a certain stage.

30. Miss Sohani Dassanayake

Analysis of healthcare professionals' role in identifying and supporting victims of human trafficking

Dassanayake SN.

Human trafficking is the illegal trade of individual for various types of exploitations and it involves the violation of many human rights. Healthcare professionals are in a privileged role to help victims they may encounter in clinical settings. Aims & Objectives: To explore what healthcare professionals could do to help victims of human trafficking. Methods: A short cross-sectional questionnaire survey was conducted. A total of 151 individuals participated in the survey, medical students from St George's University and doctors and nurses from St. George's Hospital Trust. Results: The 78% of participants were aware that human trafficking is increasing in the UK. 95% of participants felt they required formal training to identify and support these victims. Only 13% had confidence in identifying potential victims. 58% were not able to identify any red flags to identify a potential victim in a clinical setting. No one had completed the training made available by the Department of Health. Conclusion: It was evident from the survey that healthcare professionals require additional training to help them. By not being prepared to help victims, healthcare professionals are failing their ethical duty to protect an individual's rights.

31. Mr Benedict Davies

Characterisation of transition metal ion transport proteins from the malaria parasite *Plasmodium falciparum*

Davies B.M.O., Clark D.J., Krishna S., Staines H.M.

Background: Malaria is a major, worldwide public health problem. Due to the emergence of widespread drug resistance, the development of novel antimalarials is required. The regulation of transition metals such as copper and iron are essential to the parasite. Membrane transporters likely play a key role, thus making them attractive drug targets. We used the yeast heterologous expression system to characterise putative copper transporters PfCTR1 and 2. The ability of these proteins to confer functional rescue to a yeast line lacking endogenous copper transporters (MPY17) was determined by growth assays in liquid and solid media. Expression of full length and N-terminally truncated PfCTR1 and 2 variants did not confer functional rescue to MPY17 yeast when cultured in copper-limited media. However, MPY17 transformed with the PfCTR chimeras, made with regions from the human copper transporter (hCTR1) did provide some rescue compared to the negative control. Due to the apparent partial rescue of MPY17 yeast by the PfCTR chimeras, this suggests that these proteins could function as copper transporters, however further experiments will be required to determine if this partial rescue in the yeast system is biologically relevant.

32. Miss Anna Deal

Migration And Outbreaks Of Vaccine-Preventable Disease In Europe: A Systematic Review

Deal A, Rustage K, Hayward S, Ramsay M, Edelstein M, Mounier-Jack S, Knights F, Carter J, Friedland J, Hargreaves S

Migrants are suspected to be an under-immunised population in Europe and are increasingly being associated with outbreaks of vaccine-preventable diseases. We performed a systematic review (PROSPERO ID: CRD42019157473) to compile all existing research on VPD outbreaks in migrants in the EU/EEA. 52 studies met our criteria and were included, reporting on 55 VPD outbreaks across 13 countries. Measles had the highest number of reports of outbreaks involving migrants (n=21; involving 5508 cases), followed by varicella (n=10; 595 cases), hepatitis A (n=8; 1082 cases), diphtheria (n=5; 35 cases), rubella (n=4; 512 cases), mumps, N. Meningitidis, sabin-like polio (all n=2; 147, 7 and 15 cases, respectively) and pertussis (n=1; 10 cases). 21 of Outbreaks (40%; 911 cases) were reported from camps or shelters for asylum seekers and refugees. 64 outbreak reports had to be excluded from our systematic review due to unclear migrant status. In conclusion, migrants, especially camp-based refugees, represent a group involved in VPD outbreaks in Europe. Strategies to improve data collection and reporting on migrant status across Europe are crucial to understanding the complex relationship between migration and occurrence of VPD outbreaks.

33. Dr Paraskevi (Vivian) Dimou

Exploring the involvement of T lymphocytes in patients with atrial fibrillation

P. Dimou, S. Dover, S. Kaur, V. Mengoni, J.A. Camm, I.E. Dumitriu

Molecular & Clinical Sciences Research Institute, Cardiology Clinical Academic Group

Atrial fibrillation (AF) is the most common type of arrhythmia, with an increasing incidence worldwide. AF impairs the heart's blood pumping efficiency, leading to higher risk of blood clots and stroke. Inflammation has been implicated in AF, but the precise roles of T lymphocytes have not been elucidated yet. Previous work from our laboratory in patients with long-standing/persistent AF revealed a significant decrease in regulatory T cells (Tregs, a subset specialized in preventing excessive inflammation) and an increase in pro-inflammatory CD4+CD28null T cells. We are currently performing a follow-up study to assess changes in the frequency and function of these two T cell subsets in different forms of AF (short-term/paroxysmal vs. persistent AF) as well as over time. Preliminary findings suggest that the frequency of Treg is similar in paroxysmal and persistent AF in the patients studied. Interestingly, CD4+CD28null T cell expansion occurs more commonly in persistent compared to paroxysmal AF patients. Collectively, the results of our study indicate a role for T cell mediated inflammation in AF.

34. Dr Cameron Dowling

First-in-human experience with patient-specific computer simulation of transcatheter aortic valve implantation in bicuspid aortic valve morphology

Dowling C, Firoozi S, Brecker SJ

Background: In this study we wished to prospectively evaluate the clinical utility of patient-specific computer simulation of transcatheter aortic valve implantation (TAVI) in bicuspid aortic valve (BAV) morphology.

Methods: Nine patients, who were referred for TAVI and found to have BAV on workup cardiac computed tomography, prospectively underwent patient-specific computer simulation. Results: Sievers Classification was Type 0 (n=2) and Type 1 (n=7). The simulations suggested moderate-to-severe paravalvular regurgitation in 3 patients (33%) and they were referred for considering of surgery. The remaining 6 patients underwent TAVI. In 5 of these patients (83%) the transcatheter heart valve (THV) size and/or implant depth was altered to minimise paravalvular regurgitation and/or conduction disturbance. Following treatment, all 9 patients had none-to-mild paravalvular regurgitation and no patient required a permanent pacemaker.

Conclusion: Patient-specific computer simulation of TAVI in BAV can be used to identify patients in whom TAVI may be associated with an unfavourable clinical outcome. Patient-specific computer simulation may be useful to guide THV sizing and positioning for potential favourable clinical outcomes.

35. Prof Vari Drennan

Physician Associates providing emergency medicine consultations in England: mixed methods study of the processes and outcomes of care

Drennan VM, Halter M, Chao W and the PA-SCER research team

Background. Growing numbers of physician associates (PAs) are employed in emergency departments (EDs). PAs are trained in the medical model to work at an advanced clinical practice level. There is little research evidence of PAs in the ED. In a National Institute of Health Research funded study, we investigated the clinical effectiveness of PAs' emergency medicine consultations compared to FY2 doctors. Methods.

Retrospective chart and clinical review. Primary outcome measure: rate of re-consultation within seven days at the same ED, assessed for difference between PA and FY2 doctors using logistic regression, adjusting for confounders (age, sex and acuity). Results. 613 records sampled: 305 attended by six PAs; 308 by 22 FY2 doctors. Re-attendance within seven days of the index ED visit was eight percent (n=48), with no statistically significant difference between PAs and FY2 doctors after adjustment (p=0.399). PA patients were statistically significantly more likely to receive an X-ray and be within the ED for a shorter period (26 minutes less) than FY2 doctors' patients. Clinical review suggested no errors or omissions with a probability of patient harm.

Conclusions. PAs safely treat patients with a range of conditions in EDs.

36. Mr Felix Effah

The ontogenic characterisation of the cerebral oxytocin receptor system in germ-free rats

Effah F., Rabot S., Bombail V., Bailey A.

Early neurodevelopment is a critical and sensitive period to shape the emotional wellbeing of an individual in later life. It is known to be influenced by environmental factors such as bacterial colonisation, nutrition and stress, which could affect brain neurochemistry and hence lead to behavioural impairment. In recent years, emerging evidence suggests that gut microbiota play pivotal roles in modulating brain development and functional behaviours. Interestingly, the composition of the gut microbiota is altered in autistic and depression patients compared to healthy volunteers. In addition, impairment in central oxytocin (OT) and its receptor (OTR) system have been associated with neurological disorders such as autism. However, the influence of the gut microbiota on the ontogeny of OTR expression that may lead to alterations in brain development still remains elusive. Furthermore, it has been demonstrated that prolonged milk casein exposure after the normal age of weaning in rats (PND21) induces brain region-specific alterations in OTR density and leads to a depressive-like phenotype. Nevertheless, the mechanism via which this occurs remains unclear. Therefore, we the influence of gut microbiota on OTR ontogeny in germ-free rats

37. Mr Felix Effah

Effect of Prolonged Milk-Casein Exposure During Early Development on Mood and μ - Opioid Receptor Density (MOPr) of Conventional and Germ-Free Rats: An Investigation of Diet x Gut Microbiota-Brain Axis Interaction

Effah F., Joly F., Rabot S., Simreekhea I., Sohal A., Wong E., Poupon CL., Raynaud A., Kitchen I., Osman A, Bombail V., Bailey A.

Prolonged exposure to milk caseins during early development could have detrimental effects on brain and behaviour. We previously demonstrated that prolonged exposure to casein-rich (CR) but not casein-free (CF) milk in rats at early post-weaning age induces a depression-like phenotype and region-specific alterations in MOPr density in the brain. There is evidence suggesting that gut microbiota may be involved in mediating this effect via the gut-brain axis. To assess the involvement of gut microbiota on the effect of milk casein on mood, we analysed depressive-like behaviour and quantitative receptor autoradiography of conventional (CON) and germ-free (GF) rats exposed to CR or casein-free CF milk from PND 21-26, with the FST. No change in depressive-like behaviour was detected between CON and GF rats exposed to CR milk, a marked reduction of depressive-like behaviour was observed in GF rats exposed to CF milk. An overall upregulation of MOPr was detected in the olfactory orbital cortex of GF animal irrespective of their casein exposure. Conversely, casein-rich milk exposure induced upregulation of MOPr in the motor cortex but downregulation in the nucleus accumbens, irrespective of microbiota presence.

38. Miss Lucy Fang

Investigating texture analysis of MRI to aid diagnosis and treatment of knee osteoarthritis patients

Fang L, Sofat N, Howe FA

Background: Osteoarthritis (OA) is one of the most common causes of disability and pain in adults and its prevalence is increasing exponentially because of an ageing population. There is a need for a better understanding of disease processes and accurate biomarkers of disease severity. Objectives: We are investigating whether image texture scores from knee MRI may indicate OA in areas where there is no damage visible by eye. Texture analysis may provide more objective information relating to the OA knee condition than radiological assessment. Methodology: Regions of interest (ROI) were drawn on the neck of the femur and head of the tibia on T1-weighted sagittal knee scans in 8 mild and 10 advanced OA patients. Results and discussion: ROI image variance correlated with BMI in the advanced group ($p=0.043$ $R=-0.457$) but not in the mild OA group. More statistical tests are required to see if variance is significantly different between ROIs in the femur and the tibia. Further exploration will be to compare radiological damage scores and pain scores with image texture parameters to better understand if image texture from visibly normal bone provides a useful clinical marker.

39. Miss Vittoria Ferlisi Vianelli

Comparison of patient reported outcomes of primary total knee replacement based on the Oxford Knee Score (OKS) in different constituencies with different levels of socioeconomic deprivation

Ferlisi Vianelli V.

I was inspired to undertake this project after I read a research paper reporting that post-operative outcomes of primary knee replacements were worse for patients living in poorer socioeconomic areas (1). Studies also suggest that greater pain and lower preoperative physical function results in worst postoperative function. This may occur in patients who present at a later stage of the disease or because of lower educational status or multiple comorbidities (4). A large multicenter, multinational study confirmed that worse preoperative functional status and greater preoperative pain results in a lower postoperative physical functioning score (5). These findings are particularly relevant in the UK; where patients can wait up to twelve months for a referral to a secondary care centre and an increasing proportion of these patients are no longer being treated within 18 weeks of this referral. Thus, socioeconomic factors are correlated to preoperative pain and functional status. My aim has been to investigate whether there is a correlation between lower socioeconomic group and postoperative functional outcome in knee replacement patients treated at a south-west London regional orthopaedic centre (5).

40. Miss Navindi Fernandopulle

Development of an acute general paediatrics service specification at a major London teaching hospital

Fernandopulle NH, Avery J, Etheridge L

Background and aims: 28,000 patients between the ages of 0-18 present acutely to St George's Hospital. To ensure the delivery of a safe, patient centred, high quality service, we created a service specification.

Methods: Relevant guidance was identified through a variety of search methods: direct search of national bodies' websites, expert opinion and liaison with Trust managers to identify standards reported to regulators. Results: 62 key standards were identified from six different guidelines. Thematic analysis of these standards identified nine overarching themes and within each, a number of sub-themes. A Red Amber Green (RAG) rating system was used to identify the performance of the service against each theme. An action plan has been created linked to the service governance strategy to ensure the standards can be achieved in the future. Conclusion: The new service specification will be used by clinical staff to reflect on practice and outcomes. It enables clinicians to identify standards, rather than accessing them from various sources. It will aid planning, commissioning and provision of acute paediatric services and provide a framework against which to audit provision and demonstrate improvement.

41. Miss Anca Frinculescu

Good Golly, Miss 'Molly': Quantification and Dissolution of Ecstasy Tablets Seized 2001 - 2018

Frinculescu A., Hecht M., Sobreira CC., Kipper K., Shine T., Ramsey J., Johnston A., Holt DW., Couchman L.

MDMA ('ecstasy') tablets are recreationally used and known to vary in their appearance and MDMA content. This project studied the variation in dose and dissolution profiles for samples collected 2001- 2018.

For quantification, approximately 10 mg of crushed tablet was accurately weighed and dissolved in a methanol/water solution. For dissolution, 247 whole tablets were dissolved in an HCl solution (37 °C) with samples collected at 11 time points over a 3 h period. All measurements were conducted using LC-MS/MS. The median MDMA content (N=412) decreased from 2001 to 2009 and increased after 2010.

The proportion of slow-releasing tablets decreased over the period studied, but there was still significant between-tablet variability in dissolution. Our data supports the concerns on the prevalence of high-content MDMA tablets in circulation. Drug identification is useful in non-laboratory settings, but cannot fully-assess the risk to users due to fast- or slow-releasing MDMA tablets in circulation.

42. Mrs Martina Furegato

Macrolide resistance in mycoplasma genitalium is strongly associated with sti coinfection

Furegato M, Broad CE, Phillips LT, Harrison M, Fuller SS, Harding-Esch EM, Sadiq ST

Background: Azithromycin treatment of Chlamydia trachomatis (CT) may be inadequate for Mycoplasma genitalium (MG) coinfection, particularly with MG macrolide resistance associated mutations (MR-MG).

Methods: Samples collected from symptomatic sexual health clinic patients in England aged ≥ 16 years and tested for CT/Neisseria gonorrhoeae (NG) /MG. MR-MG derived using Sanger sequencing. Odds Ratios (ORs) for MR-MG calculated using logistic regressions. Results: MG prevalence was 6.5%(95%CI:4.6-8.9) in women, 12.8%(9.1-17.3) in men who have sex with women and 12.3%(8.5-17.1) in men who have sex with men (MSM). Coinfection of CT and/or NG with MG was 18.7%(8.9-32.6), 9.5%(3.6-19.6) and 4.9%(1.4-12.2), respectively. MR-MG was 62.1%(42.3-79.3), 77.4%(58.9-90.4) and 90.9%(70.8-98.9), respectively. In multivariable analysis, being MSM (aOR:3.31[1.44-7.61]), of black ethnicity (3.31[1.58-6.94]), having more than one regular partner (3.32[1.21-9.08]) and having a coinfection (10.35[4.32-25.30]) were associated with MR-MG. Discussion: Having a coinfection and being in particular risk groups were strong factors for MR-MG, suggesting macrolide resistance may be maintained in sexual networks exposed to antibiotic selection pressures.

43. Dr Anne Geniets

Visualising and mapping the meningeal lymphatic system of the human brain: a pilot study

Geniets A, Fowler T, Richardson D, Rees S, Addis P.

After the visualisation in 2017 of meningeal lymphatic vessels in in-vivo human and non-human primates, our project aimed to locate and identify meningeal lymphatic vessels, and their potentially systemic nature, in human cadaveric brains, using histo- and immunohistochemistry. We identified both lymphatic vessels and blood vessels on serial sections in the superior sagittal sinus, suggesting that a slight adjustment of our immunohistochemistry protocol might yield more promising results in our next research phase. These findings hold promise for the development of a protocol for future anatomy curricula, to teach new generations of students on the normal physiology of lymphatic brain drainage, as well as potential lymphatic pathologies contributing to neurological diseases.

44. Miss Jessica Gilchrist

Investigating the von Willebrand Factor glycome in situ using fluorescent lectins

Gilchrist J., Sagayanathan S., Carter T.

Von Willebrand Factor (VWF) is a large, heavily glycosylated plasma protein essential in both primary and secondary haemostasis. VWF mutations cause bleeding disorders collectively termed Von Willebrand's disease (VWD) affecting 1% of the population. The pattern of VWF glycosylation varies between individuals e.g. in the N-linked glycan's encoding ABH blood group antigens. Individuals with blood group O have low circulating VWF levels due to enhanced clearance of the protein. VWF mutations perturbing glycosylation are now known to affect the intracellular synthesis, storage and release of the proteins or its function or degradation in the blood. While modern Mass spectrometry methods have been developed to study the glycosylation profile of secreted VWF there are few tools available for the direct detection and analysis of the VWF glycome in situ within intact cells. In this study we have assessed the use of fluorescent-labelled plant lectins as cheap and simple tools to detect and study the VWF glycome within intact endothelial cells. We show that selected lectins can be used to detect with high specificity VWF within the biosynthetic and storage compartments of endothelial cells from a variety of different sources.

45. Miss Nicole Gill

A data analysis of self-harm, suicide ideation and suicidality in a bdd case note review in a specialist bdd service

Gill N, Pampaloni I

Many healthcare professions are unfamiliar with Body Dysmorphic Disorder (BDD) and its disturbing characteristics including the risk to life. There is limited literature, particularly in London NHS settings, on self-harm and suicidality in BDD.

The main aim of this retrospective case note review was to analyse and interpret data on self-harm, suicide ideation, and suicidality in patients referred to the South West London and St. George's Mental Health NHS Trust BDD service. We also aimed to analyse data on the psychiatric co-morbidities that may occur alongside body dysmorphic disorder. Sociodemographic and clinical data were collected from the electronic medical record system. After removal of non-BDD cases, and the application of the exclusion criteria, there was a total of 32 patients. 71.9% of patients had a history of suicide ideation, and 34.4% had attempted suicide. 87.5% of patients have psychiatric co-morbidities. Common psychiatric co-morbidities included depression, anxiety and OCD, which were distributed at 28%, 21%, and 21% respectively. BDD is a complex disorder that triggers harmful thoughts and behaviours. This review reveals that BDD will often present alongside other psychiatric co-morbidities.

46. Mr Philip Goff

Enhanced mc1r signalling increases pigmentation in hermansky-pudlak syndrome models via pH neutralisation of lysosomes

Goff, PS., Patel, S., Obeng-Adjei, N., Marks, MS. and Sviderskaya, EV.

Pigmented melanosomes mature from acidic, non-pigmented precursors by the delivery of melanogenic components primarily from early endosomes. The onset of pigmentation requires pH neutralisation, mediated through the delivery of transporters such as OCA2, to activate tyrosinase. Melanocortin-1 receptor (MC1R) signalling enhances eumelanin synthesis by upregulating expression of melanogenic enzymes and transporters (including OCA2). Hermansky-Pudlak syndrome (HPS) comprises 10 known disorders characterised by hypopigmentation and other variable symptoms due to defects in the biogenesis of lysosome-related organelles, such as melanosomes. HPS7-9 result from loss of biogenesis of lysosome-related organelle complex 1 (BLOC-1), which is required to deliver many melanogenic enzymes and transporters to melanosomes. We tested whether MC1R signalling and pH modulation enhance pigmentation in BLOC-1-deficient melanocytes by compensating for trafficking defects through cargo overexpression and subsequent tyrosinase activation. Our data suggest that alkalisation of endolysosomal organelles by MC1R signalling and pH modulation may lead to a loss of organelle identity and subsequent enhancement of pigmentation in BLOC-1-deficient melanocytes.

47. Dr Lucy Goldsmith

Coproducing a Randomised Controlled Trial

Goldsmith LP, Stepanian K, Morshead R, McWilliam C, Forbes G, Ussher M, Simpson A, Lucock M, Gillard S.

Objectives: To explore the challenges and solutions adopted to design and deliver a coproduced randomised controlled trial in mental health. **Background:** ENRICH is the world's first coproduced randomised controlled trial. In coproduction, the knowledge of people with lived experience of mental health problems is used throughout to inform key decisions and power is shared. **Methods:** Two methods were used. Data from minutes of meetings of the groups that collectively manage the trial were used to identify how, when and why the decisions which shaped the scope and focus of the research were reached and the potential impact of those decisions on the research process and outputs. Second, members of the team contributed reflections about implementing those decisions. **Results and Conclusions:** Establishing and communicating clearly which methodological and practical decisions and processes can be coproduced, when, by whom, and how, has been vital. RCTs can be conducted in a way which incorporates and values service user perspectives, delivering research with greater quality, social accountability and relevance to service users and their journeys through mental health.

48. Dr Lucy Goldsmith

Interrupted Time Series and Synthetic Control Study to Evaluate Mental Health Decision Units in Acute Care Pathways: Design and Protocol

Goldsmith LP, Anderson K, Smith JA, Thompson J, Turner K, Gillard S.

Objectives: Rigorous, comprehensive assessment of Mental Health Decision Units (MDHUs) using non-trial methods assess their effectiveness, value for money and optimum configuration. **Background:** MDHUs provide dedicated 24-hour facilities for enhanced mental health assessment, offering short-term, alternative treatment targeting people for whom inpatient admission is being considered. MHDUs have been developed in response to the pressure on acute mental health care internationally. Acute crisis care is a difficult area in which to run a randomised controlled trial, giving rise to interest in alternative research methods. **Methods:** Two complimentary research methods are presented: an interrupted time series (ITS) and an ITS with synthetic control. **Results and Conclusions:** We present a methodologically sophisticated approach to research in an area in randomised controlled trials are difficult to run. This will be the first formal evaluation of MHDU services in England and the only project to date that includes comparison of different MHDUs, enabling us to identify and model optimum configuration and scale up of MDHUs.

49. Dr Lucy Goldsmith

Results from the Development and Testing of the World's First Principles-Based Fidelity Index for Peer Support in Mental Health Services

Goldsmith LP, Stepanian K, White S, Banach N, Barlow E, Marks J, McWilliam C, Morshead R, Verey A, Gillard S.

Background: Measuring whether a complex healthcare intervention is delivered as designed (fidelity) is essential for research in complex interventions. There is no measure of peer support fidelity in the literature. Methods: Principles underpinning one-to-one peer support in mental health services were identified and semi-structured interviews with guidelines for conducting and scoring these were developed. They were piloted at independent peer support organisations, U.K. NHS peer support services and at the sites of the ENRICH trial of peer support. Blind double-rating was used to verify inter-rater reliability and the psychometric properties of the scale were verified. Experts with lived experience were involved throughout the research (coproduction). Results: Across the entire index, the total score had an acceptable internal consistency, Cronbach's alpha = 0.81. The intra-class correlation coefficients were all 0.67 or above, indicating good inter-rater reliability. Conclusions: The index is a valid measure of fidelity to peer support. It is acceptable and feasible to develop robust measures of values-based fidelity for complex healthcare interventions where psycho-social and relational mechanisms are core change processes.

50. Mr Dionysios Grigoriadis

Genotyping in a population-based study identifies a genetic association with Lipoedema

Ozkan E., Grigoriadis D., Pittman A., van Zanten M., Brice G., Martin-Almedina S., Ogmen K., Gordon K., Ostergaard P.

Lipoedema is a relatively rare condition almost exclusively found in females and results in excessive, abnormal subcutaneous fat deposition, affecting the legs. It seems to affect women, who report painful legs and discomfort. The prevalence of the disease is still elusive, and liposuction is yet the only relief from symptoms. There is often a family history of lipoedema, suggesting that a genetic association is likely. To investigate this hypothesis, we recruited a total number of 312 individuals including families and sporadic cases. The lipoedema patients were selected using the following main criteria: BMI < 35 (kg/m²) and a Waist:Hip Ratio (WHR) < 0.80. Array genotyping was performed in 212 white British patients, while whole genome sequencing (WGS) was carried out in 94 recruits through the "100,000 Genomes Project". Genotyping data from patients and 5,400 sex and age-matched controls (UK Understanding Society) were used to perform a Genome-Wide Association Study (GWAS). The preliminary findings of the GWAS, supported by a meta-analysis using the WGS data, revealed a suggestive association of four loci, including a region on chromosome 15. This study is supported by the lipoedema Foundation.

51. Dr Arya Gupta

Antimicrobial resistance (AMR) genes transfer at high-level via endogenous bacteriophage between clinical MRSA from different European countries

Gupta A, Rasigade JP, Schouls L, Lina G, Vos MC, Lindsay J

Horizontal gene transfer (HGT) of AMR, virulence and host adaptation factors is crucial for the evolution and adaptation of methicillin-resistant *S. aureus* (MRSA), including the dominant MRSA clones. Studies in piglets and humans have suggested high level transfer of AMR markers between colonising MRSA populations. We sought to develop in vitro models of AMR gene transfer and investigate factors that control transfer and gene stability. Pairs (n = 80) of clinical MRSA (of the same lineage/CC) isolated from the UK, Netherlands and France, each with naturally occurring unique AMR profiles, were co-cultured and sampled for double resistant progeny. Pair-wise competition of progeny with parental strains determined relative fitness of obtained progeny. The impact of sub-inhibitory concentrations of antimicrobials on transfer was assessed. Gene transfer was detected in 51/80 pairs. Sodium citrate inhibited transfer, indicating transfer occurred via endogenous bacteriophage. Double resistant progeny did not exhibit a fitness cost. Sub-inhibitory concentrations of certain antibiotics decreased transfer. High frequency AMR gene transfer occurs between a wide range of naturally occurring clinical MRSA isolates, indicating few barriers.

52. Ms. Junika Gurung

Identifying new causative mutant genes for Noonan syndrome

Gurung J and Enson Z

Primary lymphoedema is an associated feature of Noonan's syndrome (NS). The pathogenesis of NS tends to be severe, it can involve congenital heart disease, facial dysmorphia, short stature and learning difficulties. NS follows an autosomal dominant inheritance with 15 known causative mutations. Examples include heterogeneous germline mutations in PTPN11 and SOS1. Both play a role in the Ras/MAPK pathway. Our investigation involves two families affected by NS, known causative genotypes have been ruled out. Through whole exome sequencing, candidate novel variants have been selected for each family. We will design primers for these candidate genes, followed by temperature gradient PCR with control DNA to find optimum annealing temperatures. PCR products undergo gel electrophoresis. If successful, the process is repeated with patient DNA. Successful PCR products undergo Sanger sequencing and these traces will be presented via FinchTV. DNA of family members will also be sequenced to find any co-segregation. Analysis of the data is expected to reveal novel mutant genes for NS. A clear molecular diagnosis can provide psychological relief for families. We also hope our results can help develop therapeutic interventions for NS.

53. Miss Zoe Haines

Identifying the role of cardiac endothelial NOX1 in heart failure with persevered ejection fraction (HFpEF)

Haines ZHR

HFpEF is a debilitating disease that is the largest unmet clinical complication in the vascular field. Having a 5-year mortality rate >75%, HFpEF is defined as the inability for the heart to relax sufficiently to fill with blood, but a normal ejection fraction. Dysfunctional cardiac endothelial cells (ECs) are identified as an underlying cause in HFpEF. Mechanisms include increased apoptosis, senescence and perturbed angiogenesis. We hypothesize that increased reactive oxygen species (ROS) is the mediator of the change in EC functionality and the ROS-generating NADPH oxidase 1 (NOX1) and primary culprit. Assessing human heart failure samples, we identify upregulation of NOX1 protein by western blotting, which is accompanied by an increase in ROS production. Extending to an in vivo murine model of hypertension-induced HFpEF using angiotensin-II (AngII), we show increased cardiac NOX1 expression. We next investigated the mechanism of increased NOX1 using an in vitro approach employing an EC cell line. Stimulating cells with AngII or 7N3, we identified activation of MAPK signalling that appears to regulate NOX1 expression. This project advances our understanding of HFpEF aetiology and suggests NOX1 as a novel therapeutic strategy.

54. Miss Nadine Hall

Phytocannabinoids can reduce tumour cell growth and enhance the actions of different chemotherapeutics

Hall NK, Dalgleish AG, Liu WM

Cannabigerol (CBG) is one of the over 120 different phytocannabinoids identified in the cannabis sativa plant. CBG is the precursor of tetrahydrocannabinol (THC) and cannabidiol (CBD). Studies have shown certain phytocannabinoids to possess anticancer activity. We have investigated the potential anticancer properties of CBG and CBD in vitro, and focused particularly on their ability to potentiate the activity of other treatment modalities. Results show both can inhibit tumour cell growth when used alone and in combination. Furthermore, combining them with conventional chemotherapy can reduce the dose of chemotherapy required, thus potentially reducing toxicity. Interestingly, the order of the combination seems to play a crucial role in the result. Western blotting analyses revealed alterations to a number of intracellular proteins, including p21 and cyclin B1. Taken together, our results suggest that both CBG and CBD can disrupt the way that certain cancer cells grow. Our work continues to attempt to understand the complex nature of phytocannabinoids, an area of research which has gathered so much interest recently.

55. Miss Mawiyah Haq

T Year Clinical SSC: Analysing Vaccination Uptake in Patients with Sickle Cell Disease registered at St. George's Hospital

Haq M, Isitt C, Calvert A, Rhodes E, Sirkorska J, Thomas A, Heath P, Cosgrove C

According to the Sickle Cell Society UK and Public Health England, a number of additional vaccinations, such as MenACWY and the PPV vaccine, are needed to ensure adequate vaccination coverage in sickle cell disease (SCD) patients. The reason for this is because SCD is an autosomal recessive condition in which, the spleen becomes non-functioning and the body is not able to mount an appropriate immune response. These patients are at an increased risk of infection, which can easily be lowered if given the additional vaccinations. We have analysed the vaccine uptake in a range of SCD patients registered at St. Georges Hospital that have been reviewed by the hematology clinic within the last two years, by analysing hospital and GP records and recording this in Excel. It was found that both groups had low rates of vaccine uptake, and that more awareness needs to be given to doctors and HCPs about additional vaccinations for these specific patients. It is crucial for these patients to be vaccinated, and by ensuring that not only doctors know about these specific vaccinations, but also that patients are well aware could potentially help vaccination uptake rates, and ultimately improve patient quality of care.

56. Dr Deborah Harding

Practitioner Permeability: Insights from conversations with allied health professionals about navigating practice uncertainties in supervision

Harding DJ

In a Grounded Theory PhD study of allied health professions' (AHPs) supervision, practitioners spoke about career-long practice uncertainties. Long recognised as an everyday feature of healthcare, it has been suggested that preparing health professionals for practice uncertainties is an important part of training. The PhD study found that AHPs who recognise uncertainties are self-aware, aware of and for others, are feedback-seeking and open to alternatives while also critically aware. They have a learning disposition and are willing to make changes in practice. We can think about practitioners who display these behaviours and characteristics as permeable practitioners. A permeable practitioner not only recognises but also seeks to resolve uncertainties through a range of recalibrating practices; checking, assuring and adjusting. Participants in this research have indicated a willingness to use supervision as a place to check, assure and adjust when they perceive certain favourable conditions are met. The research suggests there are training and development opportunities to encourage permeable behaviours and characteristics and to better equip health professionals to recognise and address inevitable practice uncertainties.

57. Mr Muhammad Yousuf Hayat

A retrospective analysis on the outcome of Expanded Criteria Donor Kidneys in Marginal Recipients

Hayat MY

Background: Expanded Criteria Donor (ECD) kidneys are defined as coming from patients who are 60 or more years old, or aged 50-59 with two or more significant co-morbidities or suffering from cardiac death. A marginal recipient is someone above 60, or less than 60 with significant co-morbidities.

Aim: To look at the outcome of ECD Kidneys in marginal Renal transplant recipients as compared to non-marginal recipients, by monitoring graft survival and patient survival at 1, 2 and 3 years post-transplant.

Methods: This was a retrospective analysis of 120 patients. 60 were renal transplant recipients and 60 were the corresponding donors. Follow up data was obtained using electronic records such as yearly blood creatinine to calculate eGFR using the MDRD equation. **Results:** Kaplan Meier analysis showed a 4.8% reduction in survival in marginal transplant recipients as compared to non-marginal recipients after 2 years ($P = 0.42$), however graft survival was 9.0% greater in marginal recipients after 2 years ($P = 0.52$). **Conclusion:** The results were contrary to the hypothesis that ECD kidney transplants in Marginal recipients results in poorer graft survival, however marginal recipients were shown to have greater follow up mortality.

58. Miss Sally Hayward

Is Poor Mental Health a Risk Factor for Tuberculosis? A Systematic Review.

Hayward SE, Rustage K, Deal A, Nellums LB, Boccia D, Friedland JS, Hargreaves S

Background: There are known to be high rates of co-morbidity between tuberculosis (TB) and mental illnesses; however, whether mental health plays a causal role in TB incidence is unknown. This systematic review examines evidence on whether poor mental health may be a risk factor for TB disease.

Methods: Following PRISMA guidelines, we identified relevant original research published 1970-2019. Key databases (MEDLINE, PsycINFO and PsycEXTRA) were searched, alongside reference list and citation searching. Data was extracted, and studies were critically appraised using CASP and AXIS checklists. The findings were synthesised narratively. Results: Data were synthesised from over 600,000 individuals reported in nine studies, investigating various mood and psychotic disorders. Despite variable study quality, all included studies found an association between mental health and TB, including robust evidence from cohort studies in Asia that depression and schizophrenia can increase TB risk. Conclusions: Evidence that poor mental health may be associated with increased TB incidence identifies an at-risk population that could be targeted for TB screening and treatment, and supports interventions that tackle mental illnesses to fight TB.

59. Dr Louise Hill

Colonisation with resistant micro-organisms in septic neonates treated with vancomycin

Hill LF, Planche T, Heath PT, Sharland M, Lindsay JA

Background: Antibiotic exposure interferes with colonising flora in neonates and may lead to colonisation with resistant organisms, e.g. vancomycin resistant enterococci (VRE), coagulase negative staphylococci with reduced vancomycin susceptibility (CoNSRVS), as well as candida. Colonisation with these organisms is a risk factor for invasive infection which has associated morbidity. Methods: Rectal, nasal and axilla swabs from 3 timepoints were screened from neonates treated with vancomycin. Samples were plated onto selective agars to detect the organisms of interest. Agars were incubated at 37°C for up to 5 days. MALDI was used to confirm species and vancomycin susceptibility testing undertaken. Results: 15/16 babies were colonised with CoNSRVS at ≥ 1 site at at least one timepoint; axilla was the commonest colonisation site. Colonisation with CoNSRVS reduced after vancomycin therapy in the gut and nose. 5/16 babies were colonised with candida. No babies were colonised with VRE. Discussion: 15/16 babies were colonised with CoNSRVS, which is of concern as colonisation is a potential source for invasive disease, with significant associated morbidity. A further 14 babies will be screened to explore this further.

60. Miss Dhrisha Hirani

Sickle cell disease (SCD) is a global health problem affecting an estimated 310,000 new-borns each year. The disease is caused by a mutation in the HBB gene, which codes for the beta chain of haemoglobin and leads to the production of sickle haemoglobin (

Roumia A., Hirani D., Okeoma J., Rhodes E., Nirmalanathan N., and Bax B.E

Sickle cell disease (SCD) is a global health problem affecting an estimated 310,000 new-borns each year. The disease is caused by a mutation in the HBB gene, which codes for β chain of haemoglobin and leads to the production of sickle haemoglobin (HbS) and subsequently erythrocyte sickling. The disease can affect every body system. Therapies for SCD are limited, vary in their effectiveness and are associated with risks and tolerability issues. This project investigates the ex vivo introduction of HbA (the healthy counterpart of HbS) into the erythrocytes of patients with SCD with the aim of inhibiting the sickling process.

61. Prof Franklyn Howe

Multimodal MRI to aid prediction of low-grade glioma growth characteristics

Howe FA, Jones T, Rich P, Colman J, Yang G, Raschke F, Liang V, Denley A, and Barrick TR

INTRODUCTION: Low-grade gliomas (LGG) present as slow-growing tumours and a conservative “watch and wait” strategy frequently used until they undergo malignant transformation. We investigated how multimodal MRI could aid earlier prediction of transformation. **METHODS:** MRI was acquired every 6 months from 27 LGG patients. Tumour metabolite and diffusion MRI parameters were used in a Cox proportional hazards analysis to derive predictors of transformation or increased growth rate. **RESULTS:** Above a critical tumour size (25mm radius) higher growth rates and more likely a clinical intervention occurred. Tumour core NAA and mean diffusivity (MD), combined with tumour volume, provided a predictor (PC1) of clinical treatment needs that was better than volumetric measures alone. A ROC analysis gave an AUC of 0.86 to predict tumours likely to undergo malignant progression, and AUC of 0.98 when including those undergoing early debulking. **DISCUSSION:** PC1 aids detection of a high fraction of tumour cells within the lesion core, and combined with a volume measure, indicates the capacity for greater tumour growth, hence transformation or need for debulking. PC1 has the advantage over monitoring growth rates of being derived from a single timepoint.

62. Miss Holly Hughes

Glutamate transport visualised by novel FRET sensors

Hughes HJ, Mohammed A, Török K

Glutamate is the main excitatory neurotransmitter in the brain. Excitatory amino acid transporters (EAATs) remove glutamate from the synaptic cleft after a post-synaptic response, preventing excitotoxicity associated with neurological disorders such as Huntington’s disease (HD). Using a fast optical glutamate sensor, our group recently demonstrated that the rate of glutamate removal from synaptic clefts in the striatum is reduced in HD mice, indicating that EAAT function is impaired (Dvorzhak et al. 2018; Helassa et al. 2018). Our aim is to develop optical sensors to monitor EAAT function in cells and in vivo. EAATs undergo significant conformational changes and so are strong candidates for Fluorescence Resonance Energy Transfer (FRET) studies. Mammalian EAAT kinetics will be characterised using fluorophore-labelled hEAAT1 protein reconstituted into liposomes. We have already created EAAT1 variants with suitable chemical labelling sites. Variant EAAT1 sensors, with missense mutations identified in diseases such as episodic ataxia type 6 and are hypothesised to undergo less frequent FRET state transitions, will be generated. For in vivo imaging, we designed genetically-encoded EAAT2 sensors based on fluorescent protein FRET pairs.

63. Mr Samsul Islam

Review of the management of children with mastoiditis: A single centre experience

Islam S, Chowdhury T, Alexander V, Drysdale SB

Aims: To review the diagnostic features, management and outcome of children with acute mastoiditis. To review the Trust’s antibiotic policy on management of mastoiditis. **Methods:** We identified 25 children admitted between 01/01/17 and 10/05/19 with an initial diagnosis of mastoiditis from the Trust’s antimicrobial database. We retrospectively analysed presenting symptoms, investigations, medical and surgical management. **Results:** Diagnosis of mastoiditis was confirmed in 16 of 25 patients (64%). These patients had a mean (range) age of 4.5 (0.1-12) years. On admission mean CRP was 113.9 (SD 103.4) mg/L and mean WCC $15.5 \times 10^9/L$ (SD $4.4 \times 10^9/L$). No patients had confirmed intracranial infection. 69% (n=11) received IV co-amoxiclav, the remaining 31% (n=5) ceftriaxone and metronidazole. Mean (SD) duration of total antibiotics was 16.5 (11.1) days. 31% (n=5) had surgical intervention; one (6%) child had positive microbiology in a pus sample. **Conclusion:** All patients received a first line antibiotic in line with Trust guidance, although no patients had confirmed intracranial infection. As pus samples did not alter antibiotic choices, this suggests, in our population, most patients can be safely managed with co-amoxiclav as first line therapy.

64. Miss Greta Jata

An unmet need to improve awareness of conditions associated with Endometriosis amongst primary care clinicians

Jata G., Chowdhury T., Hussein F., Vijayakumar C.

Aim; Reviewing the association of anxiety depression, PMS, migraine, IBS and bladder problems in endometriosis patients. Background: Women are symptomatic for years before confirmed diagnosis; greater awareness of associated diseases could ensure earlier diagnosis, improving long-term outcomes. Method: Adopting a novel perspective of endometriosis as a chronic pain syndrome, retrospective analysis of clinic records between 1/6/17-1/12/18 identified 106 patients. Chronic pain was defined as dysmenorrhoea, dyspareunia, pelvic pain and lower back pain. Endometriosis severity was graded as mild peritoneal, moderate or severe. Patients aged 21-60 were assessed for the aforementioned co-morbidities. Results: Preliminary results show 29.2% of our cohort suffered from anxiety depression (95% CI 8.92-11.75). There is also a high incidence of PMS (39.6%) [95% CI 30.8-49.1], migraines (12.3%) [95% CI 7.3-19.9], IBS (21.7%) [95% CI 14.9-30.5] and bladder problems (16%) [95% CI 10.3-24.2]. Conclusion: Our results relate endometriosis with associated symptoms however limited data is available for comparison. Establishing statistical significance is of diagnostic value as raising awareness of co-morbidities may reduce pre-diagnostic periods.

65. Dr Kameljit Kalsi

Effect of exogenous ceramide on barrier function of human airway epithelial cells

Kalsi KK, Jackson S, Baines DL.

Maintaining the integrity of the airway epithelial barrier is essential in preventing increased permeability to harmful molecules and pathogens, which may lead to increased risk of developing respiratory infection and disease. We have previously shown that metformin increases tight junction (TJ) assembly via an AMPK-PKC ζ pathway. During bacterial infection alpha toxin activates the acid sphingomyelinase/ceramide system leading to cleavage of membrane proteins releasing ceramide that can activate protein kinase C isoforms such as PKC ζ . This study aimed to investigate the effect of ceramide on epithelial integrity. TJ assembly was measured after calcium switch assay by measuring the transepithelial electrical resistance (TEER) and paracellular transport of sodium-fluorescein in the presence of 0.1 μ M or 1 μ M ceramide. We found that after 24h there was 11% increase in TEER and 10% decrease in Papp with 0.1 μ M ceramide but no change with 1 μ M ceramide. Immunofluorescence staining for occludin, claudin-1 or claudin-3 did not show differences in localisation with ceramide. These results indicate so far that in airway epithelial cells activation of PKC ζ by ceramide only evokes a minor effect on tight junction reassembly or permeability.

66. Mr Mohammed Athif Khan

A Systematic Review of the use of intravenous vitamin C in the treatment of sepsis and septic shock

Khan MA, Leaver S, Rhodes A

Recent evidence proposes the use of intravenous vitamin C as adjunctive therapy in the treatment of sepsis and septic shock. However, vitamin C's ability to reduce mortality in the critically ill remains unclear. We performed a systematic review of the literature using PubMed, MEDLINE and Cochrane Library up to 10/06/2019. Studies were screened based on inclusion and exclusion criteria and PRISMA guidelines adhered to. The primary outcome measured was mortality at final follow-up. Secondary outcomes included duration of vasopressor support and length of stay (LOS) in ICU. A total of 7 studies were eligible. 4 studies showed no statistically significant difference in mortality when compared to controls, whilst 2 studies showed reduction in mortality. 3 studies reported statistically significant reduction in vasopressor support in favour of vitamin C, whilst 2 studies did not. 3 studies directly measured ICU LOS, and all showed no significant difference. Conclusion(s): IV vitamin C may produce vasopressor sparing effects, though it's effect on overall mortality is debatable. There is no association between vitamin C and LOS in ICU. Presently, there is insufficient evidence to recommend use of vitamin C in the treatment of sepsis.

67. Mr Inayat Khan

Is there a role for Metformin in the management of Colorectal Cancer?

Khan IH

Colorectal cancer is a common cancer in Western society, currently being the third most common type of cancer. Most colorectal cancers are due to old age and lifestyle factors such as obesity, smoking and lack of physical activity. The symptoms of bowel cancer include blood in stool, change in bowel habit, weight loss and feeling tired of the time. Current treatments for colorectal cancer include surgery, radiation therapy, chemotherapy and targeted therapy. Recently, aspirin and other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have received attention is being able to reduce the risk of bowel cancer, however due to their side effect profile they are not routinely recommended for patients. Non-cancer medications are an unexplored bank of novel cancer therapies. Repurposing existing drugs is a cost-effective strategy for developing novel treatment strategies. This study evaluated the use of metformin, a drug commonly used in the treatment of diabetes for the prevention or treatment of colorectal cancer. Metformin showed promising results in the treatment of colorectal cancer in many studies. Further study is required to evaluate the effectiveness of metformin in the management of Colorectal Cancer.

68. Dr Soo Hyun Kim

WDR11 links Kallmann syndrome with ciliopathy

Kim YJ, Lee JY, Ataliotis P, Bennett D, Brown N, Wylie C, Kim SH

Several ciliopathies are associated with infertility, which has been mostly attributed to defective movement of the motile cilia in the sperm flagellum or oviduct. However, our own studies indicate that primary (non-motile) cilia also play a role. Congenital hypogonadotropic hypogonadism (CHH) and Kallmann syndrome (KS) are human developmental genetic disorders defined by delayed puberty and infertility. We previously identified that WDR11 was mutated in CHH/KS patients. Our recent studies have demonstrated that WDR11 is required for ciliogenesis, and animal models with defective WDR11 exhibit disruptions in both primary cilia and motile cilia formation and function. This places KS/CHH in the human ciliopathy spectrum. We report that the reduced fertility of WDR11-deficient individuals may be due to the delayed migration of the pluripotent primordial germ cells (PGCs) resulting in a reduced number of germ cells present in the gonads at birth. By live-imaging of mouse embryo slice cultures, we confirmed Wdr11 KO reduced the migration capacity of PGCs. Hedgehog signalling could alter PGC motility without affecting their directionality.

69. Miss Soraya Koushesh

Early damage in knee osteoarthritis can be detected using type II collagen degradation products and may be used as a biomarker in OA

Soraya KO, Nidhi SO, Vivian EJ, Christine HE, Olakunbi HA, Lena AS, Anasuya KU, Tom BA, Guy WH, Franklyn HO

The relationship of pain and structural damage in the synovium, bone and wet biomarkers in Osteoarthritis are not well understood. We assessed the relationship of the molecular biomarker urinary C-terminal telopeptide of type II collagen (uCTX-II) in knee OA in relation to structural damage by MRI. We recruited 130 participants with advanced OA (80), mild OA (n=42) and non-OA controls (n=8). The MRI Knee Osteoarthritis Score (MOAKS) was used to assess knee MRI in 90 subjects. MOAKS scores were created for osteophytes number and effusion/Hoffa synovitis. Pain was evaluated by using WOMAC and uCTX-II levels were measured. The advanced OA group had higher levels of pain, with a mean WOMAC Pain of 58 +/- 22 compared with the mild OA group, mean WOMAC_P of 41 +/- 26. Greater levels of MOAKS' derived synovitis was also associated with higher levels of pain. Levels of uCTX2 correlated with total synovitis (R=0.313, p=0.03) and number of osteophytes (R=0.33, p=0.002). CTX-II and WOMAC pain scores represent independent variables for severity of knee OA. Their combined use with detailed MRI provides promise as biomarkers to enable stratification of subjects with different stages of OA and improve future diagnosis and earlier intervention.

70. Dr Agnieszka Lewko

Test-retest reliability of respiratory muscle testing in stroke

Lewko A., Kulnik ST., Sidaway M., Krawczyk M.

Introduction: Although respiratory muscle strength tests are used in assessment post stroke, the reliability has not been tested. The aim was to evaluate test-retest reliability of Maximal Inspiratory (MIP), Expiratory (MEP) and Sniff Nasal Inspiratory Pressure (SNIP) in stroke patients. Methods: MIP, MEP and SNIP were assessed in 3 sessions (S1-3) within 24-hour period. Baseline spirometry was taken. Mean Differences (MD) between sessions were analysed with SPSS using paired t-tests and intraclass correlation coefficient (ICC). The Bland-Altman method was used to describe 95% limits of agreement. Results: Eighteen patients (11 male), mean (SD) age 59.1(14.5) years and with FEV1 2.81(0.78)L (88.2(12.2) % pred.) and FVC 3.46(1.02)L (87.6(14.6) % pred.) were assessed at median(range) 50(21-128) days post stroke. There was good reliability for all 3 measures (ICC 0.98-0.99), but there were significant differences between sessions for SNIP only ($p < 0.05$). Limits of agreement for MIP S1-S2 were 22.2 to -23.0 and S2-S3 17.0 to -12.7; for MEP S1-S2 19.9 to -29.0 and S2-S3 24.9 to -24.3; for SNIP S1-S2 17.37 to -38.5 and S2-S3 15.2 to -27.3. Conclusion: There was good test-retest reliability of all measures, but SNIP shows more variation.

71. Dr Clare Logan

Candi-Sol: A multi-site retrospective audit and analysis of Candidaemia across three South London Teaching Hospitals

Logan C, Goodman A, Ward C, Fife A, Bicanic T.

Candidaemia is associated with high mortality, particularly in critical care and immunocompromised patients. Emergence of multi-resistant candida species, notably *C. glabrata* and *C. auris*, pose further challenges in treatment. This retrospective surveillance and audit study reviews both adult and paediatric candidaemia cases between January 2012- December 2018. 509 candidaemia episodes were identified. Data on species and susceptibility will be presented alongside clinical data regarding the candidaemia foci, the ECHO and ophthalmology findings, antifungal therapy and duration, B-D-glucan result if available, length of stay and mortality.

72. Dr Jackie McRae

Feasibility study of a screening tool to identify dysphagia risk in people following acute cervical spinal cord injury in two trauma units

McRae J, Smith C, Beeke S, Emmanuel A

Dysphagia is recognised as a complication of cervical spinal cord injury (SCI) with a reported incidence of 40-55%, impacting on pulmonary function, nutrition and length of stay in intensive care (Brady et al., 2004; Shem, Castillo, Wong, & Chang, 2011). Signs are subtle and poorly recognised but early screening can prevent symptom development. This study used a dysphagia risk screening tool and evaluated its utility in two major trauma centres. A 12-item screening tool developed from a previous Delphi study, was used in a two-phase pragmatic prospective observational feasibility study set up in two matched intensive care units (ICU). In phase one, staff recorded standard decisions on commencement of oral intake for each acute SCI patient. Staff were then trained to use the new tool and used this in phase two for their clinical decisions. Data was collected on timing and number of decisions per patient, staff group and feedback on utility. With the tool, staff made more frequent and timely decisions about commencement of oral intake with greater awareness of dysphagia risk factors and referral for further interventions. Further multi-site studies are required to capture clinical outcomes and impact on complication rates.

73. Dr Alamin Mohammed

Developing glutamate and glutamine sensors

Mohammed AM, Török KT.

The aim of this project is to develop novel chemically labelled and genetically encoded Indicators for glutamate (Glu) and glutamine (Gln) to further understand and resolve their cellular dynamics during neurotransmission. Upon stimulation of a glutamatergic neuron, Glu, stored in synaptic vesicles, is released into the synaptic cleft and binds receptors on the postsynaptic neuron. The majority of released Glu is taken up by surrounding astrocytes, where it is converted into Gln, exported from the astrocyte and taken up by the presynaptic neuron. Here it is converted back into Glu and packed into synaptic vesicles. Inability to clear Glu from the synaptic cleft results in excitotoxicity which is implicated in disease models.

We are generating novel variants of the Glu and Gln binding proteins by site directed mutagenesis to allow the addition of various reactive fluorescent dyes. Several mutation and dye combinations are tested and their fluorescence dynamic ranges quantitated in the presence or absence of its ligand. Genetically encoded Gln sensors are developed by insertion of circularly-permuted EGFP at various sites within the Gln-binding protein; these constructs are currently being optimised for increased dynamic range.

74. Dr Síle Molloy

One year mortality outcomes from the ACTA trial of cryptococcal meningitis treatment in Malawi

Molloy SF, Kanyama C, Chan AK, Lupiya D, Chawinga C, Adams J, Bright P, Lalloo DG, Heyderman RS, Lortholary O, Jaffar S, Loyse A, van Oosterhout JJ, Hosseinipour MC, Harrison TS.

Mortality from cryptococcal meningitis (CM) remains unacceptably high in Sub-Saharan Africa. The most widely used treatment, fluconazole (FLU) monotherapy is associated with mortality of 50-60% at 10 weeks and >70% at 1 year. The Advancing Cryptococcal meningitis Treatment for Africa (ACTA) trial recently tested new induction treatment strategies against the recommended standard of 2 weeks amphotericin (AmB)-based induction treatment. The aim was to improve outcomes with regimens that could be sustained in resource-limited settings. In Malawi, 236 participants from the ACTA cryptococcal meningitis treatment trial were followed-up for 12 months. The overall trial outcomes reported at 10 weeks were sustained to 1 year. One-week AmB plus flucytosine (5FC) was associated with the lowest 1 year mortality (27.5% [95%CI: 16.3 to 44.1]). The long term benefit seen with 1 week AmB+5FC supports updated WHO guidelines recommending this regimen as first-line induction therapy, and underlines the need for rapid wide access to 5FC.

75. Dr Cathy Moore

Expression and characterisation of a highly potent and near pan-neutralising anti-HIV antibody

Catherine M. Moore, Melanie Grandits, Audrey Teh, Julian Ma

HIV remains one of the most important health issues worldwide, with 40 million people living with HIV. Although patients develop antibodies against the virus, its high mutation rate causes immune evasion. Some patients, however, produce 'broadly neutralising' antibodies such as 'N6'. Identified in 2016, N6 can neutralise 98% of HIV-1 isolates. This neutralisation breadth makes N6 a very promising therapeutic candidate. N6 was expressed in *ΔXF N. benthamiana* plants (pN6) and compared to the mammalian cell-expressed equivalent (mN6). Expression optimisation techniques have yielded 12.3 mg/kg, so far. Glycosylation pattern assessments demonstrated that pN6 had only trace amounts of plant-associated glycans. Surface plasmon resonance revealed that pN6 bound with a similar affinity as mN6 to gp120, the HIV epitope. In the antibody-dependent cell-mediated cytotoxicity assay, pN6 induced a 10-fold higher response than that seen with mN6. In neutralisation assays with a panel of HIV strains, pN6 neutralised as effectively as mN6. The successful expression of N6 in tobacco supports the prospect of developing a low-cost, low-tech production platform for a monoclonal antibody cocktail to control HIV in low- to middle-income countries.

76. Dr Francesca Morgante

Exploring the relationship between motor and non-motor fluctuations in Parkinson's disease: patient's perspective, clinician's assessment and objective measures from a wearable device

De Angelis A, Leake A, Horne M, Paviour D, Coebergh J, Pereira E, Edwards MJ, Ricciardi L, Morgante F

We aimed to evaluate the relationship between motor (MF) and non-motor (NMF) fluctuations in Parkinson's disease (PD). We enrolled consecutive PD patients who presented at least motor fluctuations. The Parkinson's KinetiGraph™ (PKG), an accelerometry-based system for automated assessment of dyskinesia and bradykinesia was employed. Fifty-six patients were included. Multivariable regression analyses showed that D-Ag LEDD, UPDRS-III-OFF, UPDRS-IV and 'percent time with fluctuation' as per PKG were significantly associated with MF. NMF were associated to UPDRS-III-OFF and Non-motor symptoms scale. Patients without fluctuations had lower D-Ag LEDD, lower score at dyskinesia rating scale and Wearing OFF Questionnaire (WOQ-19) motor sub-scale. Only WOQ-19 psychiatric fluctuation score was significantly associated to quality of life as per PDQ-39. Our findings suggest that MF and NMF are related to each other but independently associated to specific clinical variables. NMF and specifically, psychiatric fluctuations, impact patient's quality of life.

77. Dr Francesca Morgante

Novel DBS targeting for Cervical Dystonia: 1 year follow-up study

Morgante F, Ricciardi L, Sarchioto M, Sadnicka A, Leake A, Mostofi A, Edwards MJ, Pereira E

Deep Brain Stimulation (DBS) may be ineffective in 30% of subjects with Cervical Dystonia (CD). We believe that phenotypic heterogeneity of CD may underline lack of response and specific phenotypes require different brain targets. In this study we have employed a novel targeting approach, based on phenomenology stratification, and tested its efficacy and safety. We have enrolled 5 patients with tremor dominant or painful tonic CD. They all had impaired quality of life by CD-24 and severe disability by TWSTRS. Each subject underwent DBS with an octopolar linear electrode which allowed to target the ventralis intermedius nucleus (VIM) of the thalamus and the subthalamic (STN) nucleus. Assessments were done and videotaped before DBS (T0) and at 1 year follow (T1) in OFF and ON stimulation condition. Rating was done by 2 raters blinded to stimulation condition. TWSTRS and Tsui scale at T1 were significantly lower compared to T0 and at T1 in ON stim compared to OFF stim. Quality of life by CD-24 was significantly improved by STN/VIM DBS. Our data support the efficacy of DBS with dual targeting of STN and VIM in subjects with tremor dominant and tonic painful CD.

78. Mr Mostafa Nagi

Outcome analysis of ECD Kidney Transplantation into marginal recipients. A retrospective analysis.

Nagi M

Introduction: Due to growing demands for kidney transplants, ECD kidneys have become a desirable method of treatment. Although ECD kidneys increase risk of delayed graft function and rejection, recipients have improved survival outcomes in comparison to dialysis patients, making ECD kidneys an important resource.

Aim: To study outcomes of ECD transplants in marginal patients in comparison to standard patients.

Methods: This study was a retrospective analysis of 200 patients. Data identified 91 SCD and 84 ECD donors. Of these 84 ECD kidneys, 38 were transplanted into marginal recipients and 46 to standard. Outcomes were measured by looking at length of hospital stay, PGF, DGF and Rejection. **Results:** Data shows that ECDs have more detrimental outcomes in Marginal recipients. Delayed graft function occurred in 21.74% of Standard recipients, in comparison to 55.26% of Marginal recipients. UTIs were also significantly more common in marginal recipients. **Discussion:** ECDs have detrimental outcomes in both category of recipients, however this is more observable in the Marginal recipients. T-test showed a significant relationship between marginal recipients and increase risk of DGF and UTIs in comparison to standard recipients.

79. Mr. Giyoon Nam

Combination of rifampicin and colistin against antibiotic resistant Enterobacteriaceae

Nam G., Coates A. and Hu Y.

Today, patients who admitted to the intensive care unit have been exposed to higher risk of healthcare associated infections mostly caused by antibiotic resistance since the imprudent use of antibiotics over the years. The discovery of new antibiotics is facing difficulties with the continuous evolution of bacteria and the reduced investment in R&D for antibiotics. In this study, however, we observed the antibiotic combinatory effect of rifampicin and colistin against Extended Spectrum Beta Lactamase (ESBL) or carbapenemase producing and colistin resistant Enterobacteriaceae through the checkerboard method and time kill curve assay to determine the Minimum Inhibitory Concentration values and Fractional Inhibitory Concentration index, and the efficacy. Interestingly, we found that the combination of the two drugs indicated synergistic activities against the tested bacteria, showing FIC index ≤ 0.5 . The time kill curve also showed 99% of bacteria were eradicated, whilst the single antibiotic had no activities. Thus, the combination of rifampicin and colistin demonstrated synergistic effect with reduced MIC and the increased rate of killing against ESBL and colistin and carbapenem resistant Enterobacteriaceae.

80. Mr Ahmed Nazari

The classification and characterisation of human corpus luteum development and demise

Ahmed Shah Nazari and Suman Rice

The corpus luteum (CL) plays an integral role in hormonally dictated menstrual cycle in women. Formed from the remnants of the Graafian follicle it undergoes luteinisation of its constituent granulosa (GC) and theca cells (TC), in preparation for steroidogenesis. The life cycle of CL in a non-pregnant woman is 14 days beyond which point luteolysis occurs unless rescue occurs due pregnancy by human chorionic gonadotrophin (hCG). This study aimed to establish a classification system for the life cycle of the CL into early, mid and late luteal phases using trichrome and H&E staining; whilst exploring the expression of oestrogen receptors ER α , ER β , progesterone receptors (PR) and Luteinising Hormone receptor (LHR) and their correlation with luteolysis using immunohistochemistry. We successfully established a classification system for various stages of the CL life cycle that correlated with established trends in expression of LHR and PR2. All receptors showed high intensity staining at the mid luteal phase with a decreasing trend towards the late luteal phase, with the exception of LHR which maintained expression throughout. ER α was not detected in the early luteal phase and also had the lowest expression level throughout.

81. Miss Dorette Ngemoh

'Why are we waiting?' - a quality improvement project of outpatient waiting times and issues with clinic templates

Ngemoh D and Fleming C

Waiting times in clinic are a concern both in times of clinician stress and patient experience. The aims of this project are to look at current psoriasis clinic waiting times in a tertiary referral centre for psoriasis, explore reasons for the delay in appointment times and suggest possible ways to improve waiting times and overall patient satisfaction. Data on waiting and appointment times were collected over a period of 5 weeks for the consultant, clinical nurse specialist and registrar patient lists in a single tertiary centre. Data recorded were the original scheduled appointment time, the time the patient arrived, the time the patient was seen and the time they left their appointment. The average time waited (in minutes) for the consultant, CNS and registrar lists were 27.8, 24.1 and 25.1 respectively. The results reflect the long wait many patients are subject to on arrival for their appointments. The project also sheds light on the challenges in adhering to the template of scheduled appointment times and how many patients are left waiting more than 25 minutes to be seen. This project highlights the need to look into the cause of long waiting times in clinic and ways to reduce them.

82. Dr Anh Nguyen

Does anticoagulant thromboprophylaxis increase bleeding complications in spinal surgery and spinal cord injury? A systematic review and meta-analysis

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This systematic review and meta-analysis aims to collate the evidence and quantify the risk of bleeding associated with anticoagulant thromboprophylaxis in the spinal patient. MEDLINE, EMBASE, Cochrane Trial Register databases and the grey literature were searched. Data were pooled via a meta-analysis from randomized trials and cohort studies comparing the rates of spinal epidural haemorrhage and wound haemorrhagic complications in spinal surgery patients receiving low molecular weight and low dose unfractionated heparin (LMWH/UFH) thromboprophylaxis and those not anticoagulated. The meta-analysis included 11 studies of 92,406 patients with 1,007 relevant haemorrhagic complications. A significant increase in the risk of extra-spinal wound haemorrhage was found in patients receiving peri-operative LMWH/UFH thromboprophylaxis compared to controls (OR 1.62, 95%CI 1.24 - 2.11, $p = 0.0004$, $I^2 = 6\%$) (Figure 1). The same comparison revealed no significant increase in the risk of spinal epidural haemorrhage (OR 1.20, 95%CI 0.65 - 2.22, $p = 0.56$, $I^2 = 0\%$). The quality of current evidence is low. Our findings support current recommendations that mechanical thromboprophylaxis alone is the optimal option in patients undergoing spinal surgery.

83. Dr Glenn Nielsen

A randomised controlled trial of specialist physiotherapy for functional motor disorder (Physio4FMD): a multicentre randomised controlled trial protocol

Nielsen G, Stone J, Buszewicz M, Carson A, Goldstein L, Holt K, Hunter R, Marsden J, Marston L, Noble H, Reuber M and Edwards MJ

Background: Patients with functional motor disorder (FMD) experience persistent and disabling neurological symptoms such as weakness, tremor, dystonia and disordered gait. Physiotherapy is usually considered an important part of treatment, however evidence for effectiveness is lacking. Here we present the protocol of a NIHR funded randomised controlled trial (RCT) that aims to evaluate the clinical and cost effectiveness of a specialist physiotherapy programme for FMD. Methods/Design: The trial is a pragmatic, UK-wide multicentre, single blind RCT with parallel groups. 264 Adults with a clinically definite diagnosis of FMD will be randomised to receive either the trial intervention (a specialist physiotherapy protocol) or treatment as usual. Participants will be followed up at 6 and 12 months, the primary outcome is the Physical Function domain of the Short Form 36 questionnaire. Discussion: This trial will be the first adequately powered RCT of physical-based rehabilitation for FMD. International Standard Randomised Controlled Trials Number ISRCTN56136713.

84. Dr. Kazim Ogmen

Predicting pathogenicity by functional classification of EPHB4 non-synonymous variants in Hydrops Fetalis and Hereditary Hemorrhagic Telangiectasia.

Ogmen K., Martin-Almedina S., Sackey E., Karapouliou C., Gordon K., Josephs K., Mortimer P., Mansour S. and Ostergaard P.

EPHB4 kinase-inactivating mutations have been associated with primary lymphoedema and autosomal dominant susceptibility to nonimmune hydrops fetalis. Additionally, mutations in the EPHB4-RASA1 axis have been identified to be associated with distinct capillary vascular malformation disorders. The discovery of multiple and divergent lympho-vascular phenotypes caused by mutations in the same gene requires better understanding of the impact of identified mutations in downstream cellular signalling, particularly to elucidate the specific roles of EPHB4 in both lymphatic and vascular systems. Functional analysis of the different variants was performed in lymphatic endothelial cells (LECs) by overexpressing EPHB4 variants. Subsequently, protein amount, phosphorylation dependent-activity and localisation of EphB4 variants were determined. Finally, the role of EPHB4 function in VEGF-C-driven in vitro lymphangiogenesis was investigated. As a result, seven novel variants of EPHB4 demonstrates heterogeneity of dysfunctional mechanisms, highlighting the presence of additional molecular mechanisms involvement in EPHB4-related pathogenesis.

85. Dr Agata Pacho

How is the value of point-of-care tests for STIs negotiated in the context of a nationalised health system?

Pacho A., Heming De-Allie EG., Furegato M., Harding-Esch E., Sadiq ST, Fuller SS.

BACKGROUND: Affordability, ease-of-use and laboratory-equivalent accuracy of point-of-care tests (POCTs) for STIs do not guarantee their adoption into sexual health services (SHSs). Qualitative research can provide contextual understanding for how POCT characteristics are valued in relation to structural and political processes within the NHS. **METHODS:** We conducted in-depth interviews with key stakeholders self-identified as integral to adoption of POCTs into their services. Interviews were thematically analysed in NVIVO. **RESULTS:** 31 healthcare professionals from 6 SHSs were interviewed in 2018. Cost-effectiveness and ease-of-use were identified as important in assessing POCTs attractiveness to SHSs. POCTs were seen as cost saving if they affected costs directly incurred by the service. Potential effectiveness of POCTs was assessed in the context of their ability to improve appropriate and timely treatment. The potential for POCTs to increase the competitiveness of their service by meeting new policy targets encouraged adoption.

CONCLUSION: The need for POCTs and their desirable characteristics are negotiated within complex processes of funding constraints, service restructuring and commitments to increasing inclusivity of care.

86. Dr Agata Pacho

Identifying key stakeholders and their roles in the integration of POCTs for STIs into clinical services

Pacho A., Heming De-Allie EG., Furegato M., Harding-Esch E., Sadiq ST., Fuller SS

BACKGROUND: Despite potential to positively impact patient management, sequelae, and patient experience, few point-of-care tests (POCTs) for STIs have been implemented into sexual health services (SHSs). Qualitative research can identify the decision-makers and their roles in the adoption of STI-POCTs in UK SHSs. **METHODS:** Sexual healthcare professionals (HCPs) were invited to in-depth interviews and workshops where participant observation notes were taken. We defined key stakeholders and, using a thematic approach in NVIVO 11, we explored the process of POCT integration. **RESULTS:** 8 SHS workshops took place in 2017 and 37 interviews in 11 UK SHS took place between 2015 and 2018. Participants included HCPs, managers, laboratory staff and commissioners. Although many participants considered senior clinical staff most likely to introduce and drive change, they stressed the importance of engagement of all clinical staff, particularly when tackling resistance to change. **CONCLUSION:** Supportive interpersonal relationships, such as between clinical leads and commissioners when considering adoption, and between all levels of clinical staff during implementation, are vital to the successful integration of POCTs in SHSs.

87. Dr Xiaosu Pan

Molecular basis of DNA capture and gating by type II topoisomerase

Pan XS, Laponogov I, Veselkov DA, Crevel IMT, Skamrova GB, Umrekar T, Sanderson MR, Fisher LM

Type II topoisomerases act as ATP-operated clamps that function to capture and present DNA for transport via the sequential operation of ATPase, DNA and C-gates. In 2013 we solved the first structure of a three-gate 'open clamp' topo IV-DNA complex, the seminal complex engaged in DNA recognition and capture. Here, we present the first structure of a closed ATPase gate complete with bound DNA by co-crystallising the 44-kDa ATPase domain (ParE44) of *S. pneumoniae* topo IV with a nonhydrolyzable ATP analogue and a 14-mer palindromic T-segment DNA. The X-ray crystal structure solved at 2.8Å revealed a closed ATPase dimer whose central 22Å hole is occupied by the kinked DNA duplex and stabilised by positively-charged amino acid residues lining the hole. Mutation of these residues inhibits DNA decatenation and DNA relaxation by topo IV suggesting the complex is involved in DNA strand passage. These results give new insight on how the closed ATPase gate captures a DNA segment as a prelude to strand transfer and provides a new interface for drug targeting.

88. Miss Radhika Patel

Identifying Correlation Between Metabolic and Structural Characteristics in Gliomas

Patel R, Jones T, Rich P, Barrick TR, Raschke F, Howe FA

MRI aids diagnosis of brain tumours, high-grade tumours require surgical resection, chemo- and radio-therapy. Exact margins between tumour and oedema allow reduction of radiological overtreatment. We are investigating whether metabolic characteristics obtained by ¹H magnetic resonance spectroscopy (MRS) can better distinguish oedema from tumour infiltration than MRI. Multivoxel ¹H MRS from a dataset of N=10 metastatic and meningioma brain tumours, which are non-infiltrative with sharp boundaries, were analysed. Selection of concentric rings of voxels around the tumour and lines of voxels allowed assessment of metabolic changes with distance from tumour core. Normal tissue voxels contralateral to the tumour were used for comparison. Data quality was assessed prior to statistical comparison. The glutamate+glutamine ratio to creatine (Glx/Cr) was higher in oedema compared to normal tissue (p = 0.00). N-acetyl aspartate to creatine ratio (NAA/Cr) was lower in oedema compared to normal (p = 0.00). Initial analysis suggest Glx/Cr has no spatial dependency within oedema but NAA/Cr reduces closer to the tumour. Glx/Cr may indicate excitotoxic effects that cause neuronal dysfunction. The next analysis will assess changes in glial tumors.

89. Dr Nikil Patel

The Mini Linguistic State Examination (MLSE) – A Standardised Tool to Classify and Monitor Primary Progressive Aphasia

Patel N, Peterson K, Barrick T, Lambon-Ralph M, Paterson K, Rowe J, Garrard P.

Background: Language assessment is critical in the diagnosis of patients with neurodegenerative diseases, in particular those presenting with progressive speech and language impairment such as the primary progressive aphasia (PPA). Current diagnostic criteria identify three main variants of PPA based on clinical and neuroimaging features: semantic variant PPA - characterised by dramatically reduced ability to understand the meaning of words and objects; nonfluent variant PPA – featuring problems with the grammatical and prosodic aspects of language production; and logopenic variant PPA – characterised by a striking inability to repeat spoken sentences. Most currently utilised assessments of the heterogeneous language profiles of PPA are time-consuming and not readily comparable across languages. Improved tools to screen, diagnose, and monitor these conditions will be essential to progress in the characterisation and treatments for brain diseases underlying PPAs. The MLSE will provide a much-needed short clinical tool to classify and monitor PPA. Additionally, the MLSE will be a template for further language-specific versions.

90. Mrs Laura Phillips

Rapid whole genome sequencing for antimicrobial resistance surveillance in *Neisseria gonorrhoeae*

Phillips LT, Witney AA, Furegato M, Izquierdo-Carrasco F, Zhou L, Mayes S, Laing K, Sadiq ST

Background: Whole genome sequencing (WGS) of *Neisseria gonorrhoeae* (NG) may help to detect transmission networks. ONT MinION provides rapid “run-until” sequencing to a target coverage. We assessed MinION capacity to rapidly predict NG WGS type in sexual health patients. Methods: DNA library preparations from 45 prospectively collected NG isolates were run on MinION flow cells and Illumina MiSeq. Comparison of MiSeq and MinION of variant calling at key antimicrobial resistance (AMR) associated markers (RAM) and phylogenetic tree topology at different MinION coverages were derived. Results: Maximum WGS and RAM accuracy was achievable within 10x coverage or approximately 30 minutes of sequencing. Placement of MinION sequences on a MiSeq tree was more accurate for closely related isolates and most isolate pairs with a molecular distance of less than two years were placed correctly. Conclusion: MinION sequencing enabled the placement of the majority of NG sequences onto the correct location on a MiSeq tree after 30 minutes of sequencing, suggesting that this method, particularly with newer iterations of the technology, might support early identification of sexual networks, as well NG AMR surveillance.

91. Mr Gideon Pomeranz

Diabetic kidney disease: using zebrafish as a model

Pomeranz G., Osborn D., Long D.

An early sign of diabetic nephropathy (DN) is proteinuria, which is characterised by changes in the glomerular filtration barrier of the kidney. As there is no cure, DN will often lead to end stage renal failure, followed by lifelong dialysis and the wait for a kidney transplant. This project aims to create a model of diabetic kidney disease that mimics the complications seen in patients, using zebrafish.

The ideal fish will express two transgenes. The first is a Vitamin D binding protein and enhanced Green fluorescence protein (VDBP–GFP) fusion that allows me to assess glomerular filtration by fluorescence microscopy. Normally, VDBP is kept in the overall vasculature. However, a leaky glomerulus will allow VDBP through the filter, causing accumulation of GFP in the proximal tubules. The second, is a podocyte specific expression of a bacterial protein called nitroreductase (NTR). In combination with metronidazole the presence of NTR leads to cell death in podocytes, which in turn causes proteinuria. The goal is the creation of a model which can be used for drug testing.

92. Miss Grace Poole

To Scan Or Not To Scan: Magnetic Resonance Imaging for Paediatric Cerebellar Astrocytomas

Poole, G. Hettige, S.

MRI is used as a surveillance tool to detect asymptomatic recurrence of paediatric cerebellar pilocytic astrocytomas (CPAs). There is no guidance outlining the frequency or duration of MRI when gross-total (GTR) or sub-total (STR) resection is achieved. Our study analyses the recurrence pattern of CPAs to propose an appropriate surveillance MRI schedule. A retrospective review was performed of 25 paediatric patients, with a histopathological diagnosis of CPA, that underwent surgical resection at St. George's Hospital between 2005 and 2015. Early post-operative imaging divided individuals into two groups depending on whether GTR or STR of the primary tumour was achieved. 13 patients had no residual tumour on post-operative imaging. Surveillance MRI in these patients was uniformly negative for recurrent disease at an average of 5 years follow-up. The first craniotomy provided sub-total resection for 12 patients. Tumour recurrence was detected on surveillance MRI in 10 of these patients, on average 31 months following. Children who have undergone total resection of CPAs may not benefit from routine post-operative surveillance MRI. Patients in which sub-total resection is achieved may benefit from MRI in the first 5 years.

93. Ms Laxmee Ramkhelawon

Using a Multiplex Suspension Bead Assay to Establish a Serocorrelate of Protection for Group B Streptococcus Disease

Ramkhelawon Laxmee, Hall Tom, Le Doare Kirsty

Group B Streptococcus (GBS) is a Gram-positive coccus which is part of the normal microbiota of the GI and GU tracts. However, GBS is also a major cause of neonatal and infant disease, including septicaemia and meningitis, globally. Although intrapartum antibiotic prophylaxis has greatly reduced incidence of early onset disease there are concerns over emerging antibiotic resistance. Therefore, the most promising strategy to prevent neonatal and infant GBS disease is the implementation of a vaccine. Maternal IgG antibodies targeting capsular polysaccharides have been observed to provide protection against disease. Establishing a serocorrelate of protection could assist in the pathway to licensure of a GBS vaccine. A consortium led by Kirsty Le Doare and funded by Bill and Melinda Gates Foundation is in place in order to establish a standardized multiplex immunoassay (MIA) based on Luminex Xmap technology, along with an opsonophagocytic killing assay (OPkA). This will be followed by an inter laboratory study between multiple partners to establish assay parameters and reproducibility. Standardized reagents (CPS-PLL and IgG standards) are being developed and characterized. There are also plans being put in place for the inter laboratory study.

94. Miss Khadijah Rashid

Improving the documentation of regional anaesthesia catheter procedures at St George's Hospital, London

Rashid K

Background: Regional anaesthetic techniques provide analgesia in patients. Documentation of the regional anaesthesia (RA) procedures is an issue due to the recent transition from paper to iCLIP computerised system to document electronically and also documentation of pain scores. An 'Anaesthetic catheter procedure template' suited for iCLIP can improve documentation which will include pre and post-block pain scores. Methods: This was a retrospective review of the available data from hospital paper notes and iCLIP from 13/05/19-24/05/19. 21 patients were included in this study. The following were analysed: documentation of catheter procedure and where it was documented, documentation of pain scores pre and post-catheter. Results: Differences were found in the location of documentation varying from electronic to paper. 12 procedures were documented under documentation section within iCLIP. 11 procedures were documented in paper. About 76% of the patients did not have pain scores documented prior to the nerve block. 14 patients had their pain scores documented on day 0 post-block. Conclusion: A template enables to document the procedure with consistency as well as pain scores before and after to measure effectiveness of the nerve block.

95. Miss Gabriela Rezende

Rehabilitation and oncological palliative care: a literature review

Rezende G., Bacon I., De Carlo MMRP

Aims: To identify and evaluate the evidence found in the international scientific literature regarding rehabilitation in the context of oncologic palliative care. Methods: Integrative literature review, performed in electronic databases: LILACS, CINAHL e PubMed, WEB OF SCIENCE, OTseeker e PEDro, looking for studies published until July 2019. Search terms included the descriptors "palliative care", "supportive care", "terminal care", "hospice care", "end of life care", "life care end", "rehabilitation", "reabilitação", "habilitation", "neoplasm", "neoplasia", "cancer", "cancro", "onco", "tumor". The identified articles were inserted into the RAYYAN software and they were blindly evaluated by two collaborators and one final reviewer. Results: A total of 1,341 articles were identified and 21 papers were selected. The articles were classified into 2 thematic units: 1- Conceptualization of Palliative Rehabilitation (N=11), 2- The importance of rehabilitation in the context of oncologic PC (N=10). The results show the importance of the inclusion of rehabilitation in PC, but the little recognition of this modality. They emphasize the need for conceptual definitions, approaches and protocols.

96. Mr Daniel Richardson

Magnetic Resonance Spectroscopy in Delirium

Richardson D. Howe F. Davis D. Rich P. Binnie L. Khan U. Truscott S. Hainsworth A. Isaacs J.

Delirium is a short-term confusional state accompanied by fluctuations in conscious level. Typically delirium is seen in unwell older people. Unfortunately, delirium is not a benign disorder of cognition, it is associated with significant mortality and morbidity. There is a growing body of evidence suggesting delirium occurs as a response to systemic inflammation and is a form of brain injury. Glutamate levels are raised in a number of other brain injuries, including hepatic encephalopathy, a specific form of delirium associated with liver failure. We sought to quantify glutamate levels in the brain during delirium in medically unwell older people using 1-H (proton) Magnetic Resonance Spectroscopy (MRS). Inpatients over 65 years old were recruited alongside age-matched controls. Clinical assessments of delirium were undertaken prior to MRS of four brain regions. Twenty-six patients were recruited, ten delirium patients and five controls. Significant differences were seen between clinical scores. Glutamate levels were significantly raised in parietal white matter ($p < 0.05$) in delirium patients. These findings provide a potential explanation of how delirium may cause brain injury.

97. Dr Catherine Roberts

The essential role of retinoic acid degrading enzyme CYP26B1 in cardiac development and disease

Ahmed M., Lasoye S., Schmidt K., Thesia D., Ahmed T., Abdallah A., Vernay B., Moulding D., Cook A., Anderson R.H., Ivins S., Scambler P.J. and Roberts C.

Retinoic acid (RA) is a small lipophilic Vitamin A derivative essential for development. RA synthesising (retinaldehyde dehydrogenases-RALDH) and degrading enzymes (cytochrome P450 subfamily 26-CYP26) control availability of RA for signalling and establishing patterning gradients. Loss of Cyp26b1 phenocopies craniofacial, thymus and heart defects of human 22q11 Deletion Syndrome (22q11DS). Mouse mutants for Tbx1, the major 22q11DS candidate gene, exhibit similar phenotypes. Synergistic increases in postnatal mortality in Tbx1+;/;Cyp26b1+/- mice and the number of embryos displaying the most severe aortic arch phenotype in Tbx1+;/; Cyp26b1-/- embryos. This implies a genetic interaction/modifying effect between Tbx1 and Cyp26b1 during cardiac development. Cyp26b1 also has major role regulating RA during epicardial and coronary vascular development. Cyp26b1-/- embryos die at mid-gestation due to lack of coronary vessels. This can be traced to earlier epicardial abnormalities including reduced epicardial epithelial-mesenchymal transition. Known epicardial genes and ECM are affected and RNA-Seq has identified new down-stream targets to explore as possible therapeutic targets.

98. Mr Ahmad Roumia

The application of a reversible hypo-osmotic dialysis process in preventing the sickling of erythrocytes from patients homozygous for sickle cell disease

Roumia A., Hirani D., Okeoma J., Rhodes E., Nirmalanathan N., and Bax B.E.

Sickle cell disease (SCD) is a global health problem affecting an estimated 310,000 new-borns each year. The disease is caused by a mutation in the HBB gene, which codes for β chain of haemoglobin and leads to the production of sickle haemoglobin (HbS) and subsequently erythrocyte sickling. The disease can affect every body system. Therapies for SCD are limited, vary in their effectiveness and are associated with risks and tolerability issues. This project investigates the ex vivo introduction of HbA (the healthy counterpart of HbS) into the erythrocytes of patients with SCD with the aim of inhibiting the sickling process.

99. Mr Kieran Rustage

Multidrug-resistant tuberculosis treatment adherence in migrants: a systematic review and meta-analysis

Nellums LB, Rustage K, Hargreaves S, Friedland J.

We conducted a systematic review and meta-analysis to identify and synthesise data on MDR-TB treatment adherence in migrant patients to inform evidence-based strategies to improve care pathways and health outcomes in this group. This systematic review and meta-analysis was conducted in line with PRISMA guidelines (PROSPERO 42017070756). Fifteen studies were included. The estimated adherence to MDR-TB treatment across migrant patients was 71% [95% confidence interval (CI) = 58-84%], with non-adherence reported among 20% (95% CI = 4-37%) of migrant patients. There were no differences in estimated rates of adherence [risk ratio (RR) = 1.05; 95% CI = 0.82-1.34] or non-adherence (RR = 0.97; 95% CI = 0.79-1.36) between migrants and non-migrants. Treatment adherence is approaching global targets for treatment success (75%), and are comparable to rates in non-migrants. The findings highlight that just over 70% of migrant and non-migrant patients adhere to MDR-TB treatment. The results point to the importance of increasing adherence in all patient groups, including migrants, with an emphasis on tailoring care based on social risk factors for poor adherence.

100. Anna Sadnicka

Reduced drift rate: a biomarker of impaired information processing in functional movement disorders

*Sadnicka A1,2 *shared first authorship Corinna Daum2,3 *shared first authorship Anne-Marthe Meppelink2,4 Sanjay Manohar5 Mark Edwards1*

Functional neurological disorder is a common and diverse condition. Resultant disability is caused by both the dominant clinical presentation, e.g. paralysis or tremor and additional symptomatology such as cognitive symptoms. Recently the similarity of neuropsychiatric profiles across a range of functional syndromes has been highlighted. This is suggestive of a common underlying mechanism with a theoretical deficit of information processing proposed. In this study, we took the temporal discrimination threshold, as a paradigm that can be used to model sensory processing in functional movement disorders. We used a well-established model for decision-making (the drift diffusion model) that uses both response accuracy and reaction time data to estimate mechanistic physiological dimensions of decision-making and sensory processing. This revealed pathologically reduced drift rate in the patient group, a parameter that quantifies the quality and rate of information accumulation within this sensory task ($p=0.002$). Reduced drift rate is a potential experimental marker for a generalised deficit in information processing across functional disorders that allows diverse symptomatology to be quantified under a common disease framework.

101. Eleftherios Samaras

iASiS: Big Data to Support Precision Medicine and Public Health Policy

Krithara A., Paliouras G., Rentoumi V., Tzortzis G., Triantafyllou A., Vidal M-E., Auer S., Menasalvas, E., Gonzalo-Martin C., Rodriguez-Gonzalez A., Provencio Pulla M., Torrente M., Garrard P., Samaras E., Kassiss M., Evans A., Guigo R., Raschid L.

The vision of iASiS is to turn the wave of data heading our way into actionable knowledge for decision makers. This will be achieved by integrating data from disparate sources, including genomics, electronic health records and bibliography, and applying advanced analytics methods to discover useful patterns. Big Data in healthcare is in its early days, and most of the potential for value creation is being unclaimed. One of the main challenges is the analysis of acquired data. While information is becoming ever easier to obtain, the infrastructure to collect, integrate, share, and mine the data remains lacking. These data are an invaluable resource for deriving insights to improve decision and policy making. The goal is to turn these large amounts of data into actionable information to authorities for planning public health activities and policies. The integration and analysis of these heterogeneous sources of information will enable the best decisions to be made, allowing for diagnosis and treatment to be personalised to each individual. Data resources for two different disease categories will be explored, dementia and lung cancer.

102. Dr Marianna Sarchioto

Immunesystem involment in Tourette's syndrome: a study of brain metabolites and antigen-presentingcells

Sarchioto M, Howe F, Morgante F, Dumitriu I, Edwards M, Sterne J, Martino D.

Pathophysiology of Tourette's syndrome (TS) is still incompletely understood. Data suggests that a neural-immunecrosstalk dysfunction might lead to altered maturation of brain and stress responses. We aim to study in vivo aspects of neuro-inflammation in TS patients exploring relationships between peripheral and central markers of immune dysregulation. We studied 18 patients and 18 healthy volunteers. Subjects affected by inflammatory or auto-immune disease were excluded. We collected patients' demographic and clinical data as well as measures of disease severity. Flow cytometry of venous blood was used to study myeloid (mDC1, mDC2) and plasmacytoid (pDC) dendritic cells. MR spectroscopy (1H-MRS) was acquired in frontal white matter (FWM) and putamen (PUT) to enable metabolite quantitation. There were no significant differences between brain metabolites and dendritic cells in patients and controls. mDC1 inversely correlated with total creatines (tCr) in FWM but not in PUT. GLM across both regions show a significant relation of tCr with MDC1. pDC are a significant predictor of disease severity. Data suggests a possible interaction between altered energy metabolism in patients' brain and peripheral immune system.

103. Miss Sajedah Shah

The future of antenatal care: self-monitoring for proteinuria in pregnancy.

Shah S

Introduction: Hypertensive disorders of pregnancy (HDP), particularly pre-eclampsia, are the leading causes for maternal complications. Proteinuria is a symptom for pre-eclampsia when present alongside hypertension and other systemic symptoms. Urinalysis is often carried out by a healthcare professional (HCP) using a semi-quantitative method by visually identifying a colour change on a urine dipstick. Self-testing for proteinuria in pregnancy could be more efficient and more convenient. Aim: To investigate the ability of pregnant women to self-test for proteinuria and HCPs' perspectives on self-testing for proteinuria during pregnancy. Methods: A pilot study comprised of 2 parts: 1) pregnant women's (n=31) urine self-testing abilities using a dipstick compared with readings by a HCP and an automated reader; 2) staff questionnaire asking for views on self-testing urine for proteinuria. Results: There was no statistically significant difference between the accuracy of HCP readings and pregnant women's readings ($p = 0.856$) when compared to the automated reader. Conclusion: Pregnant women are able to self-test their urine for proteinuria as accurately as a HCP and self-testing for proteinuria is considered safe to HCPs.

104. Mr Vafie Sheriff

The current most essential determinants to infant, child and maternal health in Sierra Leone

Sheriff V

Background: Sierra Leone is one of the poorest countries in the world, suffering from some of the worst maternal and child health outcomes. The purpose of this study is to determine the current most essential determinants to infant, child and maternal health. Methods: The study included a review of relevant policies and analysis of relevant maternal health data to inform questions for Key Informant Interviews (KII). 11 KIIs were conducted with stakeholders from UN Organisations, iNGOs and the Ministry of Health and Sanitation (MoHS). The Interviews were transcribed verbatim, and then coded and analysed using NVIVO. Findings: Main themes impacting maternal and child health were: the current landscape; the socio-economic and cultural determinants; and lastly the opposing perspectives of the MoHS and partners on what the most essential determinants were. Conclusion: Lack of effective coordination between the MoHS and partners, systematic problems with the attitude of the healthcare workforce towards women and socio-cultural restriction on women limiting their ability to make choices about their own health were key issues. Interventions focused on women's empowerment will address most of the determinants highlighted.

105. Miss Tawakalitu Shittu

Investigating the role of KIF11 in cell-cell junctions in lymphatic endothelial cells (LECs)

Shittu T., Martin-Almedina S., Ogmen K. and Ostergaard P.

Lymphoedema is the chronic swelling of tissue, which normally affects the extremities of the body, as a result of impaired lymphatic drainage. Previous studies have shown that mutations in the gene KIF11, which codes for the protein EG5, causes microcephaly with or without chorioretinopathy, lymphoedema or intellectual disability. EG5 is necessary in mitotic division but its additional roles outside mitosis, and the link between KIF11 mutations and lymphoedema, are still to be investigated. For the lymphatic system to function properly, its structure, integrity and cell-cell communications must remain intact. We hypothesised that EG5 is involved in the formation and/or maintenance of cell-cell junctions between lymphatic endothelial cells (LECs). Therefore, any dysregulation in KIF11 expression will cause defects of these cell-cell junctions in LECs. This investigation aims to determine whether downregulation of KIF11 affects the expression of the cell-cell junction molecules: VE-Cadherin, Cingulin, ZO-1 and Claudin-5, at mRNA level, using qPCR and at protein level, using western blot and immunocytochemistry.

106. Mr Amar Sidhu

Time to theatre: an audit assessing best practice in Neck of Femur (NOF) fractures at St George's Hospital

Sidhu A, Hing C

In 2017, there were 63,845 cases of neck of femur (NOF) fracture in England and Wales with 1 in 45 hospital beds occupied by recovering patients at any one time. With this incidence, morbidity and a mortality of 10% within the first month, NOF fracture is of great importance to healthcare professionals.

Prompt surgery has shown to significantly reduce mortality in NOF fracture patients, NICE currently recommends surgery should occur within 36 hours. We performed a retrospective audit investigating time to theatre over a 5-month period from 01.01.18 at St George's Hospital, London.

Of 74 patients undergoing surgery for NOF fracture, 68 (92%) underwent surgery within 36hrs. The mean time to theatre was 27hrs 7mins with a standard deviation of 24hrs 37mins. Of those who did not undergo surgery within 36hrs, 67% were awaiting review by doctors and 17% were awaiting space on the theatre list. Future improvements should focus on reducing administrative/logistic reasons for delayed surgery (>36hrs) as it was found there was no significant difference between patients who had surgery within 36hrs and those who had delayed surgery for medical reasons.

107. Miss Pirruntha Sivaharan

Functional validation of ANO7 mutations in epithelial prostate cell lines

Sivaharan P, Aung JT, Visoka AJ, Raupelyte E, Shoroye T, Mahmud AA, Larken I, Perry, Patel H, Valderrama F, Cieza-Borrella C

ANO7 gene (NGEP-L/TMEM16G) encodes for a transmembrane protein expressed in prostate epithelial cells. Low expression levels are associated with worse clinical outcome in prostate cancer (PCa). Studies suggest a role for ANO7 as a calcium activated chloride channel and scramblase protein involved in cell structure, adhesion and motility processes. Next Generation Sequencing (NGS) studies have identified several ANO7 variants, including six stop-gained mutations. Our project aims to characterise these six mutations and determine the molecular mechanisms underlying their association with PCa.

We have transfected two human prostate cell lines: WPE1-NA22 (low tumorigenicity) and WPE1-NB26 (high tumorigenicity) with either a GFP-tagged ANO7 wildtype (WT) plasmid or one of the six mutants. We are performing rt-qPCR to assess differences in ANO7 transcription levels between the mutant- and WT-expressing cells. Using confocal fluorescent microscopy, we want to identify changes in ANO7 protein expression and localization. Co-staining with Alexa 546-Phalloidin and DAPI will also allow us to identify alterations in cell and nuclear morphology that correlate with the acquisition of the mesenchymal phenotype observed in PCa cells.

108. Dr Peter Smith

Effect of SCFA on T-cell immune responses

Smith PL, Padel K, Dalgleish AG

The intestinal microbiome influences host immune response through a number of mechanisms. These mechanisms include the generation of metabolites capable of modulating adaptive immune responses. Of particular interest are metabolites called short chain fatty acids (SCFA). A number of chemotherapeutic agents have been shown to have immune modulatory properties but how these interact with SCFA in the activation of immune responses is unknown. In this project the ability of SCFA such as acetate and propionate and chemotherapeutic agents including Lenalidomide were studied for their ability to activate T-cell immune responses.

109. Dr Peter Smith

In vitro analysis of immunogenic chemotherapy

Smith PL, Dalgleish AG

Immunotherapy has revolutionised cancer treatment however its only effective in a minority of patients and ineffective against many cancer types. Chemotherapy is typically used to treat cancer based upon its ability to block cell division and/or kill tumour cells but some chemotherapies also have immune modulatory properties. The research presented here details the immune modulatory properties of common chemotherapies used as single agents or combinations and demonstrates that different chemotherapies have distinct effects of different aspects of the immune system. Chemotherapeutic combinations including Pomalidomide are particularly notable for their ability to enhance T-cell responses. These data support the development of chemotherapy-immunotherapy combinations to treat cancers that are currently refractive to immunotherapy.

110. Ms Jennifer Smith

Open Research Demystified

Smith, J

Ever wondered what DOI stands for?

Curious about how you can be more open but not sure about how?

And who or what is DORA?

Come and have a look at our jargon busting poster and find out what these and other terms mean, and how they help make research more open.

111. Dr Catherine Spilling

Clinical risk factors for smoking-related neurobiological damage

Spilling CA, Bajaj MPK, Burrage DR, Ruickbie S, Baker EH, Barrick TR, Jones PW

Elderly cigarette smokers have an elevated risk of cognitive decline and dementia, however, the neuropathological mechanisms are unclear. This study investigated which biological factors are responsible. 100 participants (age: 68 ± 8 years, 69% male) with significant smoking history and range of respiratory and cardiovascular disease were recruited. Demographic, clinical and biochemical markers assessing respiratory function, oxygen saturations, breathlessness, COPD disease status, psychological status, cognitive impairment, systemic inflammation, cardiac damage, retinal microcirculation and brain magnetic resonance (MR) markers of cerebral blood flow, cerebral atrophy, cerebral small-vessel disease and white matter microstructure were acquired. Principal component analysis was used to reduce brain, retinal, cardiovascular and respiratory variables into components. Multiple linear regression showed that higher blood pressure, low respiratory function, hypoperfusion, cardiac damage (troponin T) and systemic inflammation (C-reactive protein) were associated with MR markers of neurobiological damage and there may be complex interactions between them. Results support a vascular aetiology with contributions from systemic inflammation.

112. Dr Catherine Spilling

Quasi-diffusion Magnetic Resonance imaging (QDI): optimisation of acquisition protocol

Spilling CA, Howe FA, Barrick TR

Quasi-diffusion image (QDI) is a new ultra-high b-value diffusion magnetic resonance imaging (dMRI) technique based on a special case of the Continuous Time Random Walk model of diffusion dynamics which assumes the presence of non-Gaussian diffusion within tissue microstructure. QDI parameterises the diffusion signal attenuation according to the rate of decay $D_{1,2}$ and the shape of the power law tail, α . QDI provides conventional dMRI contrast, plus α maps, which provide additional insight into microstructural complexity in healthy and diseased tissue. A minimal QDI tensor (QDTI) acquisition requires a $b=0$ s mm⁻² image followed by 2 non-zero b-value images in 6 diffusion gradient directions. Here we use permutation analysis to optimise a clinical QDTI acquisition from a gold standard multi b-value protocol (28 non-zero b-values) by comparing different b-value combinations (2 non-zero b-values) to the gold standard using X2 difference in parameterised signal decay curves. We obtain an optimal acquisition protocol of $b=0, 1080, 5000$ s mm⁻² which has excellent tissue contrast and can be acquired in a clinically acceptable time (2 mins). Possible applications include aiding in diagnosis of lesions such as brain tumours and stroke.

113. Pooja Sunildath

The Effect of TRAIL in Combination with Chloroquine on Pancreatic Cancer Cell Survival

Sunildath P and Androulla Elia

Pancreatic cancer (PC) currently has the lowest survival rate of all cancers with less than 10% of those diagnosed surviving for five years (Ecpc.org, 2019). This is due to a combination of poor prognosis and limited treatment options. A treatment currently undergoing clinical trials is TRAIL (TNF-related apoptosis-inducing ligand) which induces apoptosis in pancreatic cancer cells specifically by interacting with death receptors DR4 and DR5; (Yang et al., 2011; Elia et al., 2017). PC cells can also be targeted with chloroquine which inhibits the cells' protective mechanism known as autophagy (Yang et al., 2011). Some pre-clinical studies also suggest that chloroquine inhibits tumour growth through additional mechanisms (Verbaanderd et al., 2017). This includes pathways such as inhibiting the TLR9/nuclear factor kappa B signalling pathway; stabilising the tumour suppressor gene p53; normalisation of tissue vasculature amongst many other methods (Verbaanderd et al., 2017). This research poster will summarise the results of a range of experiments conducted to explore the effects of TRAIL and chloroquine (both individually and in combination) on the survival and viability of pancreatic cancer cells.

114. Ms Francesca Taylor

Introducing physician associates to hospital patients: development and evaluation of an intervention to inform patients about the new role

Taylor F, Ogidi J, Chauhan R, Ladva Z, Brearley S, Drennan VM

Aim: To identify and evaluate how best to inform hospital patients about the new physician associate (PA) role given low awareness and understanding. Method: A two-stage qualitative study among patients and participant PAs who attended them. Stage one elicited patient expectations and preferences on being informed about the PA role. At stage two, the intervention was tried out and evaluated in terms of its feasibility and acceptability. A co-design group including patient representatives, PAs and study researchers collaboratively developed intervention ideas shown to patients at stage one, and the intervention trialled at stage two. Results: 33 patients and three PAs participated in interviews. Based on patient preferences elicited at stage one, the intervention developed was a two-sided, hand-size information card. PA participants personally introduced the intervention to patients. The intervention was thought to clearly communicate the PA role. While there was some hesitancy among PAs about introducing the intervention unprompted, patients accepted this approach. PAs adapted how they introduced the intervention to suit personal style. Conclusions: The intervention can feasibly be used to introduce PAs to hospital patients.

115. Tiago Teodoro

Is Functional Cognitive Disorder characterised by disproportionate effort and exhausted attentional reserve?

Teodoro T., Koreki A., Chen J., Ferreira JF., Edwards MJ., Isaacs JD.

Introduction: Functional Cognitive Disorder (FCD) is an emerging functional neurological disorder of increasing prevalence in cognitive clinics. Following a recent review, we hypothesised that FCD is characterised by high symptom burden, high subjective effort, impaired sustained and divided attention but normal performance on other cognitive tests. Methods: We have developed an experimental paradigm to test effort, objective performance and physiological parameters during cognitive tasks that involve varying attentional demand. Results: Pilot data suggest that individuals with FCD report large increases in subjective effort during cognitive tasks as demands on working memory and attention are increased. Further work will determine the extent to which test performance correlates with effort and is affected by increased attentional demand. Conclusion: Our experiments will help determine whether FCD is a state of heightened effort, disordered attention or both. This will guide treatment paradigms towards reinterpreting "effort" and/or resetting basal levels of attention.

116. Dr Malou van Zanten

Multimodality imaging of the lymphatic system to assist phenotyping in people with primary lymphoedema.

van Zanten M, Mills M

Intro: The lymphatic system is vital for fluid homeostasis and immunity. Lymphoedema, the accumulation of lymph in tissues, may be congenital (primary lymphoedema, PL) or externally caused (secondary). Defective lymph vessels underly lymphoedema. The clinical standard for imaging the lymphatics is lymphoscintigraphy, however two novel techniques which overcome its poor spatial resolution, 2D nature and use of ionizing radiation are gaining popularity: Magnetic Resonance Lymphangiography (MRL) and Indocyanine Green (ICG) near infrared imaging. Aim: Optimize and combine MRL and ICG imaging to elucidate functional differences in lymph vessels in a cohort of people with PL compared to healthy controls (HC). Methods: NIR imaging, post injection of ICG (Verdye), has been performed for both HC and PL. HC lower limb MRL has been performed using high resolution T2 weighted MRI, while PL subjects had additional dynamic contrast enhanced T1 imaging (prior work). Post processing performed with VirtualDub 1.10.4 and ImageJ. Results/Conclusions: ICG and MRI demonstrate functional defects, torturous vessels, and retrograde flow in PL recruits with known gene mutations while HC show vessels demonstrating normal anatomy.

117. Mr Stanislavs Vasiljevs

Investigation of lung pathogens growth patterns using Artificial Sputum Medium (ASM)

Stanislavs Vasiljevs, Arya Gupta, Deborah Baines

High blood glucose has been linked with increased glucose concentration in the lungs. In order to investigate the effects of hyperglycaemia on the pathogens residing in the lungs, we used Artificial Sputum Medium (ASM). *S. aureus* and *P. aeruginosa* were used for the study as they are some of the most abundant lung pathogens. *S. aureus* and *P. aeruginosa* were grown in the ASM at varying glucose concentrations. Bacteria were then grown at 37°C with constant shaking. Growth curves were constructed by quantifying CFUs. Interestingly when performing colony counts for the CFU calculations, it was impossible to count individual colonies of *P. aeruginosa*. Instead, bioluminescent *P. aeruginosa* (H174) were used to construct the growth curve. Both strains demonstrated increased growth rate in the presence of 4mM glucose. Peak bacterial population in 4mM glucose medium was higher in *P. aeruginosa* when compared to no glucose, while *S. aureus* reached the same peak population in both cultures. Both *S. aureus* and *P. aeruginosa* growth were directly correlated to the glucose depletion in the media. In conclusion, ASM mimics lungs environment and allows the study of lung pathogen growth patterns in the presence of glucose.

118. Mr Ronald Patrick Vergara

Investigating the changes in linguistic features of written discourse in Alzheimer's Disease and Mild Cognitive Impairment: A Natural Language Processing Approach

Vergara R.P, Clarker N, Garrard P

Alzheimer's disease (AD) is characterised by a gradual decline in cognitive functions such as memory and language abilities. Developments in Natural Language Processing (NLP) have enabled a fast and objective approach to investigating linguistic markers that could serve useful in clinical practice.

281 samples of written discourse (obtained from 22 cognitively normal individuals, 10 patients with AD and 10 with Mild Cognitive Impairment (MCI) were transcribed. The Computerised Propositional Idea Density Rater and Linguistic Inquiry and Word Count were applied to extract and analyse language markers. Individuals with a clinical diagnosis of MCI or probable AD were found to differ in their use of written language over time when compared to controls. The most significant markers identified were those associated with analytical thinking, lexical processing and grammatical complexity. Variation in data may have been due to the lack of inter-rater reliability in transcribing or as an artefact of education. Studies of larger numbers, as well as robust statistical analysis is necessary to confirm the applicability of these markers to the detection of neuropathological changes in AD.

119. Ms Charlotte Wahlich

Effectiveness of adult community-based physical activity interventions with objective physical activity measurements and long-term follow-up: a systematic review and meta-analysis

Wahlich C, Chaudhry U, Fortescue R, Cook D, Hirani S, Knightly R & Harris T

Physical inactivity is a global public health concern. Interventions can increase short-term physical activity (PA) levels, but health benefits require sustained increases. We aimed to identify randomised controlled trials (RCTs) with objective PA outcomes in adults and evaluate whether intervention effects were sustained beyond 12-months. For this systematic review and meta-analysis seven databases were searched from January 2000 until April 2018. RCTs reporting objective PA outcomes beyond 12-months with community-based participants aged ≥ 18 years were included. Outcomes were daily steps and weekly minutes of moderate-to-vigorous PA (MVPA). Of 26,041 records identified, nine studies (at generally low risk of bias) were included, 5 in meta-analyses with 12-months to 4-yr follow-up. We observed 12-month increases for intervention versus control participants in steps/day (mean difference (MD) =554 [95% CI: 384, 724] $p < 0.0001$; 2446 participants; four studies,) and weekly MVPA minutes (MD=35 [95% CI: 27, 43] $p < 0.0001$; 2647 participants; four studies). Effects were sustained up to 4-yrs. This review provided evidence of PA intervention effects sustained up to 4yrs with important implications for long-term health benefits.

120. Nathan Walker

Do not attempt resuscitation (DNAR) discussions in surgery - are we following the guidance? An educational quality improvement project

Walker N, Beynon V, Karim A

Introduction: Resus council guidelines around DNAR discussions are not surgery specific and may be open to interpretation. This audit aimed to evaluate concordance with DNAR guidance in surgery and implement intervention to improve practice. Method: Initial case-note audit was conducted for general surgical inpatients at a large teaching hospital. Standards were taken from Resus Council guidance. DNAR status/documentation of discussion was recorded for each patient. Data including presentation, age, comorbidities & performance status was collected and used to assign patients into high, moderate & low chance of surviving cardiac arrest. Intervention included delivery of educational sessions. Re-audit followed. Results: Initial audit comprised 32 patients; 12(37.5%) high, 12(37.5%) moderate & 8(25%) low chance of cardiac arrest survival. DNAR was discussed/documentated in 0 cases. Re-audit included 30 patients; 15(50%) high, 10(33%) moderate & 5(16.7%) low chance of surviving cardiac arrest. 3(10%) DNARs were discussed/documentated ($p=0.012$). 100% of patients with a DNAR had low chance of survival. Conclusion: Re-audit demonstrated a significant improvement in appropriate peri-operative DNAR discussions held following intervention.

121. Dr Joseph Westaby

Cardiac innervation in the normal heart

Westaby, JD and Sheppard, MN

Sudden and unexpected cardiac death, mediated by ventricular arrhythmia, is the most common cause of death worldwide. Recent studies have highlighted the importance of the autonomic nervous system (ANS) as a trigger and predisposing factor for VA.

The aim of this study is to describe the topography of cardiac innervation observed microscopically in the normal heart. Cases were panel reviewed. Two sections of right ventricular outflow tract were stained with PGP9.5. Within the epicardial fat there are large nerve fibres and ganglia. These nerves are seen prominently around the coronary arteries at the atrioventricular junction. Thick nerves extend into the myocardium from the epicardium associated with blood vessels. These nerves become smaller as they progress into the myocardium becoming fascicles and fibrils extending between and parallel to myocytes. Small nerve endings lie in close contact to myocytes. Only very thin fibrils are seen in the subendocardium which surround the myocytes. Clarification of the mechanisms and alterations which occur in the ANS within sudden cardiac death victims would allow the development of specific targeted neuromodulatory techniques and therapeutic strategies.

122. Miss Ella Whittle

Pharmacological chaperone therapy for protein misfolding diseases.

Whittle E, Broda K, Mohamed A, Torok K and Carroll C.

Pharmacological chaperones (PC) are molecules that function to stabilize misfolded proteins which they bind to causing a shift in the equilibrium toward the folded state. PC have been of interest in recent years as therapeutic compounds in genetic diseases caused by protein misfolding and loss of protein function resulting in pathological dysfunctions of the cell. Stabilizing a mutated protein and reinstating normal levels of protein production is an extremely promising approach to treating protein misfolding diseases. We are developing pharmacological chaperones for protein destabilizing mutations in mitochondrial proteins associated with mitochondrial oxidative phosphorylation deficiencies, a group of diseases for which there is a large unmet need for therapy. This will be achieved by structure-based in-silico screening of small compound libraries to identify compounds that are predicted to bind the mitochondrial ribosomal protein MRPL44 followed by functionally testing compounds with a differential screening fluorimetry assay for their effect on the MRPL44 L156R missense mutation. A knock-in transgenic mouse model harbouring the MRPL44 L156R mutation has been generated to test promising compounds in vivo.