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Undergraduate Prizes

Best undergraduate oral presentation

Comparing Outcomes of Stent Retriever Thrombectomy versus Direct Aspiration for the Endovascular Treatment of Acute Anterior Circulation Stroke

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Introduction Endovascular therapy with a stent retriever has been shown to be superior to standard medical therapy in the treatment of acute ischaemic stroke and is recommended by the American Stroke Association. Direct aspiration thrombectomy is another commonly used method increasing in popularity with advances in catheter technology. Few studies have directly compared the efficacy of the two methods, with current evidence equivocal. This study compares the stent retriever and direct aspiration methods.

Patients and methods 101 patients presenting to the Queen Elizabeth Hospital Birmingham between January 2013-November 2017 with anterior circulation ischaemic stroke, fulfilling the criteria for endovascular therapy, were retrospectively analysed. 45 patients underwent first-line stent retriever thrombectomy and in 56 patients, direct aspiration was the primary method. The primary outcome was successful revascularization (TICI 2b/3) and secondary outcomes included procedural and clinical measures.

Results Successful revascularization was achieved more frequently when direct aspiration was the primary chosen method (91.1% vs. 57.8%, p=0.000) and was significantly more likely to be successful with a single pass (p=0.005). Direct aspiration procedure time was shorter (51 minutes, IQR 34-75) than stent retriever thrombectomy (72 minutes, IQR 58-99), despite more frequently needing rescue therapy (p=0.019). A favourable early neurological outcome was more frequently achieved in those undergoing direct aspiration (75.5% vs. 53.8%, p=0.033), although there were no significant differences in mortality (p=0.633).

Conclusions First-line treatment with direct aspiration may be superior to stent retriever thrombectomy, offering potential clinical, procedural and cost benefits. To our knowledge, this is the first study at a UK centre of its kind.

Best undergraduate poster

Investigation of the microbial community associated with Mycobacterium abscessus infection – An emerging pathogen in Cystic Fibrosis.

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Introduction Cystic fibrosis (CF) is a multi-systemic genetic disorder characterised by frequent pulmonary exacerbations. Exacerbations are typically associated with pathogens such as Pseudomonas aeruginosa, a known accelerator of lung function decline. Previous sequencing studies

investigating the community structure of P. aeruginosa have demonstrated that it is a dominant community member and is highly resilient to antibiotics.1 In comparison, limited knowledge exists for pathogens such as Mycobacterium abscessus which has also been linked to accelerated lung function decline.2

The aim of this study was therefore to describe the community composition of M. abscessus, and retrospectively analyse the impacts of M. abscessus on lung function over a three-year study period.

Patients and methods Sputum samples were collected from 44 people with CF – 23 chronic M. abscessus cases and 21 chronic P. aeruginosa controls. Clinical and demographic data was collated, and lung function analysis was conducted comparing lung function decline between the groups. Lung function decline was also analysed by sub-dividing cases based on the presence of nontuberculous mycobacterium pulmonary disease (NTM-PD).

16S rRNA sampling was utilised on the Illumina MiSeq platform, to sequence 60 DNA extracts (phenol/chloroform extraction), and an Operational Taxonomic Unit (OTU) table was generated allowing for compositional analysis.

Results The presence of M. abscessus led to a significant decline in lung function in the cases (-7.88%) compared to controls (+1.00%), (p=0.002) and a significant decrease was noted with the presence of NTM-PD (p=0.006). Significant compositional differences were seen between the two groups (p=0.0113, R=0.08015) with no significant difference seen in taxa diversity or richness.

Conclusions The presence of M. abscessus leads to a unique bacterial community structure in the CF lung compared to P. aeruginosa colonised controls. Accelerated lung function shown in this study further highlights the clinical significance of this bacteria. This is the first study to find a significant association with NTM-PD, and the presence of compositional differences may indicate a need to re-evaluate current treatments.

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Commended undergraduate poster

The positional variation of the median nerve: An ultrasound study

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Introduction Near-nerve steroid injection is a common conservative treatment for carpal tunnel syndrome with varying rates of success. This is frequently performed using a ‘blind’ technique, referencing surface anatomical landmarks to estimate the position of the median nerve. The morphological variants of the median nerve have been described, however little study has been carried out investigating the positional variation of the nerve relative to the landmark tendons. This

study aims to establish an accurate estimate of the positional variation of the median nerve relative to palmaris longus (PL) and flexor carpi radialis (FCR) within the general population, with variation in wrist width between individuals considered.

Patients and methods Sixty wrists of thirty normal subjects were studied. Ultrasonography was performed at sites 0, 1 and 2cm proximal to the distal wrist crease. Measurements were taken of the position of the medial border of the median nerve relative to the medial borders of the PL and FCR musculotendinous units.

Results There were statistically significant differences in the average distances from the median nerve to palmaris longus and flexor carpi radialis at each scanning site. Also, when patient's wrist width was considered the significant differences persisted. The prevalence of PL agenesis in the sample was 21.7%. Mean measurements (in mm) of PL-MN at each scanning site were as follows: DWC +2= -5.09. DWC +1=-1.39. DWC=2.45. And the mean measurements for FCR-MN at each site were: DWC+2=2.24. DWC+1=6.40. DWC=10.82.

Conclusions There is significant positional variation of the median nerve in the distal forearm which should be considered by clinicians when utilising blind techniques used for injection into the carpal tunnel. Without this, there may be an increased risk of nerve damage and reduction in efficacy. Despite this, using ultrasound guidance may further reduce the potential risks associated with blind techniques.

Commended undergraduate poster

Assessment of Retina and Choroid Using Optical Coherence Tomography in Health, Hypertension and Chronic Kidney Disease.

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Introduction Using optical coherence tomography (OCT) we have previously demonstrated strong associations between chorioretinal thinning and degree of renal dysfunction and systemic inflammation, in patients at high cardiovascular disease risk. The progression of chorioretinal structural changes over time and in different patient subgroups remain unexplored.

Patients and methods We used the SPECTRALIS-OCT machine to re-examine the retinal and retinal nerve fibre layer (RNFL) thickness, macular volume, and choroidal thickness of 28 subjects, a median of 43 months after their index scans. We recruited 11 patients with hypertension (clinic blood pressure ≥140/90 mmHg prior to treatment); 10 with pre-dialysis CKD (estimated glomerular filtration rate (eGFR) 8-125 ml/min/1.73m^2); and 7 matched healthy controls. The same, masked investigator carried out each study.

Results On follow-up, outer-temporal retinal thickness and macular volume were reduced in CKD ($P < 0.05$), temporal-inferior RNFL thickness was reduced in CKD and hypertension ($P < 0.05$), and choroidal thickness at location I was reduced in hypertension ($P < 0.01$).

Conclusions Increasing age is associated with chorioretinal thinning, which may be accelerated in CKD and hypertension. Larger studies evaluating these changes over longer periods of time are necessary to fully assess the extent of this impact.

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Postgraduate Prizes

Best postgraduate oral presentation

Prevalence of hereditary alpha-tryptasemia in an unselected UK population

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Introduction In 2016, in collaboration with colleagues at the National Institutes of Health, USA, our group identified a new, dominantly inherited genetic disease, termed alpha-tryptasemia. Allele duplication (or higher copy number multiples) of the TPSAB1 gene resulted in elevated serum mast cell tryptase and a constellation of symptoms, including troublesome allergies, diarrhoea and abdominal pain, flushing and angioedema, chronic pain and dizzy spells. Symptom burden is variable, but is generally increased with higher gene copy number, as is serum tryptase level. In a group of American blood donors, the prevalence of this disease was estimated to be 4-6%. In this study we sought to investigate the prevalence of this disease in an unselected UK population.

Patients and methods Using droplet PCR, we developed a robust assay to screen for TPSAB1 duplications. We tested 52 samples from either patients with high serum mast cell tryptase and clinical suspicion of alpha-tryptasaemia, or their relatives with normal phenotypes. We then obtained 432 DNA samples (216 male and 216 female) from the 1958 Birth Cohort, an unselected population sample representative of the British population, and screened these for prevalence of TPSAB1 duplications.

Results In an initial run of 24 patients and relatives, TPSAB1 duplications were identified in 12 individuals with high serum mast cell tryptase and clinical symptoms, and normal genotypes were confirmed in individuals with normal phenotypes. In an initial run of 184 donors from the 1958 Birth Cohort, 10 were found to have TPSAB1 duplications (5.4%). Full results are pending as the work is ongoing, but will be available by November 2018.

Conclusions Hereditary alpha-tryptasemia causes a constellation of troubling symptoms that have been traditionally labelled as ‘medically unexplained’. In many cases, this is likely to have led to extensive, often invasive, investigations with little diagnostic yield, to the vexation of both patients and physicians. Ascertaining the prevalence of this disease in the UK population will help to increase our understanding of this disease, and to highlight the importance of making clinicians aware of its existence. It is an essential first step towards establishing a routine testing facility.

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Best postgraduate poster

The use of rapid evaporative ionization mass spectrometry in the identification and classification of cervical cytology samples

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Hull-York Medical School

Introduction Cervical cancer is the fourth most common cancer affecting women worldwide. Invasive cervical cancers are preceded by a long phase of precancerous disease better known as cervical intraepithelial neoplasia (CIN). The National Health Service (NHS) offers a Cervical Screening Programme (CSP) to women between the ages of 25 and 64 in order to detect CIN using cytology-based assessment. Cytological assessment presents with a number of limitations which result in a substantially high number of false-positives and false-negative results. This leads to an increased burden on the NHS and can have a negative psychological impact on the patient's quality of life. These factors combined reflect the need for a better primary screening test.

Patients and methods Rapid evaporative ionization mass spectrometry (REIMS) is an evolving technique that allows prompt identification of biological tissue. Previous studies utilizing REIMS have shown that the technology can identify cancerous tissue with an accuracy of higher than 97%. Based on these findings, this study aimed to show that REIMS is superior to cytology-based assessment by investigating if it can correctly classify 1) cancerous vs healthy, 2) HPV status, 3) clinical status, and 4) CIN grade of the liquid-based cytology (LBC) cervical samples acquired from 106 patients at the Imperial College Healthcare NHS Trust, in line with the histological diagnosis. Spectral profiles of the samples were obtained with REIMS and further subjected to multivariate analysis.

Results The REIMS approach proved to be superior to cytology as it differentiated between cancerous and normal samples with 100% accuracy. This differentiation was attributed to the increased levels of phosphatidylcholine found in the cancer samples. REIMS also identified the HPV status and CIN grade of the samples with higher accuracy than cytology-based assessment.

Conclusions Our findings demonstrate that REIMS offers an alternative to cytology-based assessment for the accurate identification of cervical samples in the CSP. Future studies will involve the use of REIMS to construct an accurate classification database against which unknown samples can be tested and correctly identified. Moreover, the REIMS spectral profiles could be further analysed to recognise novel metabolites that can aid in the development of bespoke treatments.

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Commended postgraduate poster

Identification of a novel autoantibody directed against the sarcoglycan complex in patients with idiopathic inflammatory myopathies

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Introduction The idiopathic inflammatory myopathies (IIM) are a group of rare heterogeneous disorders characterised by muscle weakness and are associated with the development of different autoantibodies. Each autoantibody may be associated with a distinct clinical phenotype. A novel autoantibody targeted against the sarcoglycan complex has recently been identified that has been associated with the missense mutation c.799C>T located in beta-sarcoglycan gene (SGCB). The aim of this study was to validate these findings by re-testing the patients previously identified and screening a new patient cohort with a similar clinical phenotype.

Patients and methods Plasma and DNA of 30 patients was recruited and prioritised based on clinical and serological data from UK Myositis Network (UKMYONET) and Euromyositis registry. Plasma and DNA was also recruited from four patients previously identified to possess an antisarcoglycan antibody and the SGCB c.799C>T missense mutation. Antibody testing was conducted by Western blotting using patient plasma as the primary antibody. PCR was used to amplify exon 6 of the SGCB gene. Sanger sequencing was used to identify the presence of the missense mutation.

Results None of the prioritised patients demonstrated an anti-sarcoglycan antibody or carried the missense mutation c.799C>T. None of the four previously identified patients demonstrated an antisarcoglycan antibody or carried the mutation as expected.

Conclusions This study has not been able to validate the presence of an anti-sarcoglycan antibody in patients exhibiting the clinical phenotype of interest. This study also questions any association previously considered between the anti-sarcoglycan antibody and the missense mutation c.799C>T. However, identifying an antibody specifically targeted against a muscle tissue component rather than a ubiquitously expressed antigen could be associated with a distinct clinical phenotype that would potentially be amenable to treatment.

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Undergraduate abstracts

Cohort study measuring cost-benefit analysis of the Otago Exercise Programme in Community Dwelling Adults with Rheumatoid Arthritis

Siyar Abdulrazaq, Jackie 5 Oldham, Dawn A Skelton, Terence O'Neill, Luke Munford, Brenda Gannon, Mark Pilling, Chris Todd, Emma K Stanmore

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Introduction The aims of this study were to determine the healthcare cost of falls in adults with RA, and estimate whether it may be cost efficient to roll out the an exercise programme (called OEP-Otago Exercise Programme) to improve function and prevent falls in adults living with RA.

Patients and methods 535 patients with Rheumatoid Arthritis aged ≥18 years were recruited from four rheumatology clinics across the Northwest of England. Participants were followed up for 1 year with monthly fall calendars, telephone calls and self report questionnaires.

Results Cumulative medical costs resulting from all injury leading to hospital services is £374,354 (US$540,485). Average estimated cost per fall is £1120 49 (US$1617). Estimated cost of implementing the OEP for 535 people is £116,479 50 (US$168,504) or £217.72 (US$314.34) per-person. Based on effectiveness of the OEP it can be estimated that out of the 598 falls, 209 falls would be prevented. This suggests that £234,583 (US$338,116) savings could be made, a net benefit of £118,104 (US$170,623).

Conclusions Implementation of the OEP programme for patients with RA has potentially significant economic benefits and should be considered for patients with the condition.

Service Improvement Project (SIP): ASSESSING THE OUTCOMES OF THE ERAS2 PATHWAY IN TOTAL HIP AND KNEE REPLACEMENTS

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Introduction ERAS stands for Enhanced Recovery after Surgery. This pathway was designed to achieve early recovery after surgical procedures by maintaining pre-operative organ function and reducing the profound stress response following surgery (Melnyk et al).

The main goals of ERAS are to accelerate recovery, reduce post-operative pain and allow multimodal rehabilitation.

ERAS2 was an audit carried out at Castle Hill Hospital (Hull) from 14/02/18 to 11/04/18 to build on and further improve the original ERAS pathway. The objective was to assess whether the ERAS2 pathway was more effective at improving post-operative outcomes for patients having total hip (THR) and knee replacements (TKR) than the standard ERAS pathway.

Patients and methods Changes ERAS2 pathway made (compared to standard ERAS):

- Injection of tranexamic acid into joint whilst in surgery – aim was to reduce bleeding (which would be indicated by a lower post-op haemoglobin (Hb) measurement)

- Quicker physiotherapy pathway – ERAS2 focused on discharging patients when medically fit and functionally safe (with a focus on early mobilisation after surgery), compared to ERAS, where there are rigid criteria needed to be fulfilled by patients for them to be discharged.
- Introduction of pre-operative joint class – focus on patient education.

Two orthopaedic surgeons were on the ERAS2 pathway with the remaining surgeons continuing the standard ERAS. Data on 29 surgical patients (9 ERAS2 and 20 ERAS) was collected – the small sample size can be explained by winter pressures, which causes several surgeries to be cancelled. Both groups were compared based on length of stay of patient, post-op Hb and post-op blood pressure.

Results Results showed that ERAS2 had a lower length of stay in comparison to ERAS (2.4 days compared to 2.89) and a lower average drop in Hb pre-and post-surgery (25.27 to 29.11). ERAS2 patients did however have a slightly higher average systolic blood pressure after surgery (130.63 to 129.33). Overall, ERAS2 pathway was shown to reduce hospital stay and bleeding after surgery.

Conclusions ERAS2 was shown to reduce hospital stay by promoting early mobility and removing discharge criteria and reducing bleeding from surgery. Quicker discharge means more beds are freed up for new patients. If expanded on a larger scale, ERAS2 can reduce surgical waiting times (a current problem in the NHS) which in turn alleviates the pressure on NHS resources.

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Association of Exercise and Physical Activity with Disease Activity and Disability in Rheumatoid Arthritis

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Introduction Rheumatoid arthritis (RA) is an incurable and progressive disease, primarily resulting in inflammation and swelling in the joints and often first manifesting in the smaller joints of the hands and feet (1, 2). Studies on the positive impact of exercise in patients with RA have found gains in muscle strength and growth and along with that promotion of psychological well-being with improvements being shown in fatigue, depression and anxiety (3). However, there is limited research into the association between daily physical activity in relation to lifestyle or occupation in RA patients. Previous studies have focussed on exercise interventions and comprised relatively small sample sizes in selected populations. Therefore, this study aimed to identify if physical activity as part of patients general lifestyle and occupation was associated with disease activity and disability in a large contemporary cohort of patients with RA.

Patients and methods This study used data originally collected as part of the TRACE-RA clinical trial. TRACE-RA involved 3,002 RA patients who completed a lifestyle questionnaire at baseline assessment. Disease activity and disability were measured at baseline using the 28 joint Disease Activity Score (DAS28) and the Health Assessment Questionnaire Standardised Disability Index (HAQ-SDI). Cross-sectional associations between exercise, level of physical activity and employment status with DAS28 and HAQ-SDI were investigated using univariate and multivariate linear and logistic regression models.

Results Participants who exercised more frequently had lower DAS28 and probability of HAQ-SDI scores of ≥1. Physical compared to sedentary lifestyles/occupations were associated with a lower probability of high disability. Compared to those working full-time, students had the highest DAS28 and those not working as sick/disabled were the most likely to have a HAQ-SDI score of ≥1. Full-time and part-time workers had little difference in disease activity. However, part-time workers had a higher probability of having high disability.

Conclusions Our results show that there is an association between exercise/physical activity and disease activity and disability in RA. We can also see the relationship between employment status and its association with measures of level of disease activity and disability. However, there is a need for longitudinal studies to determine the direction of these associations.

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Assessing the impact of digital storytelling in medical ethics education

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Introduction Stepping into the shoes of the storyteller and seeing things from their perspective - digital storytelling provides a novel insight into the patient experience. Research into the effectiveness of digital storytelling was carried out using 12 third year medical students at the University of Manchester. With a specific focus on end of life care, the aim was to measure the extent to which digital stories affect the students' understanding of ethics and law. A questionnaire was devised to determine if these videos would add to the undergraduate curriculum and complement the learning outcomes proposed by the Institute of medical ethics (IME).

Patients and methods I started my study by selecting 3 digital stories from the patient voices database. Using a structured questionnaire, I then planned to collect data from a group of 12 third year medical students regarding their perceptions and understanding of each video.

It was necessary that each video illicit a number of different ethical themes and questions, whilst remaining relevant and appropriate for third year students.

Results Whilst students appreciate the importance of ethics and law in practice, they have a tendency to prioritise other aspects of their learning during personal study. Despite this, the digital stories proved to be an engaging method of encouraging reflection and patient- centred thinking. The videos conveyed a strong emotional message and the students deemed them to be a helpful learning resource.

Conclusions By grounding important ethical themes in a real life context, the stories promoted reflection and empathy, and encouraged students to think about patient care holistically. They allowed viewers to step into the shoes of the storyteller, see things from their perspective and gain an invaluable insight into the patient experience.

The research also provided an interesting insight into student study habits. It became clear from the data that respondents dedicated the majority of their study time to learning science and clinical knowledge. The wider aspects of medicine, such as ethics and law, were focused on during ward time.

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Exploring the early management of neuropathology in the Emergency Department

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Introduction Head injuries are the largest cause of morbidity and mortality in the 1-40 years age group (1) The National Institute for Health and Care Excellence (NICE) have clear guidelines for CT head scans being carried out in a timely manner. (3) These guidelines also have a target time for the provisional reporting of CT head scans by a consultant radiologist. (3) This is topical at the moment as the use of out-of-hours teleradiology rises, amid concerns over its effectiveness. (4) Direct oral

anticoagulants (DOACs) are also bringing new challenges to EDs when dealing with head injuries, as no reversal agent is currently available.

Patients and methods A retrospective, single-centre study of patients in the ED who had a CT head scan. Three months of weekend data was collected from January to March 2018 - with 146 patients in total. Data was anonymised, with only age and gender recorded, alongside key data from the ED including times and discharge locations. Cause of presentation and anticoagulation status were also recorded. Data was compared against existing guidelines.

Results Time taken from arrival in the ED to head CT scan was statistically significantly greater (mean of 162 minutes) than the 60-minute target ($p < 0.001$). Time taken to CT report was statistically significantly below (mean of 41 minutes) the target of 60 minutes ($p < 0.001$). 65% of patients admitted due to their head injury were admitted purely for observation, despite 80% having no pathology on their CT scan. Results for anticoagulated patients were inconclusive due to the small sample size.

Conclusions Time taken from arrival in the department to CT head scan exceeds NICE guidelines by a statistically significant time. The length of time taken for a provisional CT report by a consultant radiologist is below the suggested time specified in the NICE guidelines, by a statistically significant time. Patients with head injuries admitted to hospital, despite having no pathology on CT head scans, are mostly admitted for observation purposes. More research is needed to investigate why clinicians choose to admit these patients. There is no significant difference between the management of patients taking anticoagulant medication versus those who are not anticoagulated. Further studies with larger patient cohorts would be useful, especially with regard to patients taking DOACs.

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The role of the HDU in the perioperative care of gynaecological oncology patients

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Introduction Surgery for gynaecological malignancies can be extensive. The women who undergo such procedures often also have significant comorbidities, making them a high-risk group. Postoperative admission to the HDU has been considered beneficial in some cases but is not without its disadvantages 1. The aim of this study was to determine the role of the HDU in the perioperative care of women undergoing surgery for gynaecological cancers and to identify the factors that influence their need for HDU support.

Patients and methods A retrospective case note review of the gynaecological oncology patients admitted to the HDU following surgery between 1/1/2018 and 25/5/2018 was conducted to obtain information on the pre-operative factors and post-operative outcomes of each patient. Attempts were then made to identify any relationships between the variables examined.

Results The results were unable to demonstrate any clear associations between the preoperative elements studied and the length of HDU stay or the need for interventions.

Conclusions In conclusion, as an objective and reliable predictive model that would indicate a patient's postoperative risk in the pre-operative setting has not yet been designed, sound clinical judgement on the part of the clinician is still the most important in deciding a patient's care needs.

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An Evidence Review to determine the efficacy of Novel Oral Anticoagulants (NOACS) compared to Warfarin at reducing Venous Thromboembolism recurrence in adult patients.

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Introduction Venous thromboembolism (VTE) is responsible for 25,000 deaths a year in the UK. Treatment of patients with previous VTE is vital to prevent recurrence. Anticoagulants form the basis of therapy, with warfarin the mainstay of secondary prevention. However, newly developed drugs not requiring regular monitoring exist. These Novel Oral Anticoagulants (NOACs) are beginning to see use as a substitute for warfarin.

Patients and methods This review aims to determine the difference in VTE recurrence in adult patients, without chronic coagulopathies, receiving a single NOAC (dabigatran, rivaroxaban, apixaban, edoxaban) versus those receiving standard warfarin therapy as a preventative measure, following initial anticoagulation for the acute VTE.

The NICE Evidence portal was used to look for guidelines and evidence summaries. Search strategies combined free-text and index terms to search bibliographic databases (MEDLINE, EMBASE, CENTRAL and Web of Science) for systematic reviews (SR) and randomised control trials (RCTs). A strict eligibility criteria was applied, following the population in question, intervention, comparator and outcomes to include recurrent VTE.

Results 1184 records were screened for suitability and of these 17 were appraised. Records were appraised using either the AGREE II or CASP checklist. Guidelines and evidence summaries were reviewed but did not contain sufficient detail regarding NOACs. The remaining records comprised of 1 SR and 6 RCTs reported NOACs as non-inferior to conventional therapy (low molecular-weight heparin followed by warfarin) in reducing VTE recurrence.

Conclusions This review has found that all NOACs are non-inferior to warfarin in preventing VTE recurrence. Despite limitations with cost and the limited reversibility of their anti-coagulant effect,

the comparative convenience of NOACs versus warfarin and safety in the reduction of major bleeding events may provide a more clinically acceptable alternative for patients. A review of evidence directly comparing NOACs to one another is an important subsequent step for the management of VTE recurrence.

An exploration of factors behind DNA (did not attend) rates in a deprived area

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Introduction In 2017 7.8 million (6.6%) outpatient appointments were not attended in England. In 2012 the total cost of outpatient appointment non-attendance was estimated as £12.52 billion. Despite this obvious financial burden minimal research has been conducted to analyse potential factors for non-attendance and the health implications of this behaviour. First-hand experience in Oldham revealed significant socio-economic barriers to patients engaging with healthcare services and generated serious concerns that attendance may be disproportionately high in deprived communities.

The aim of this research was:

- To explore DNA (did not attend) rates at hospital outpatient appointments within a deprived population and to identify patterns of non-attendance and sub-groups within this population which can then be:
  - Highlighted and targeted for further research
  - Facilitate the development of interventions to improve engagement with healthcare services
  - Ultimately help improve health outcomes
- To add to the body of literature around deprivation medicine and highlight inequitable access to secondary care: an important contributor to the difference in health outcomes between the least and most deprived populations.

Patients and methods

- The list of patients who DNA'd and attended hospital outpatient appointments was attained from Hill Top Medical Surgery (Oldham) for April 2017 (the most recent month allowing for one-year follow-up) via EMIS (Egton Medical Information Systems) using the population reporting aspect.
- 48 adult patients were studied in both groups (DNA and non-DNA) and scrutinised using EMIS and Docman.
- Patients were followed-up for 1 year from April 2017-March 2018 for investigated factors e.g. hospital appointments attended and not.
- Excel and SPSS statistical software was used to collate, process and present the data collected.
- No comparator data set was collected due to the introduction of the EU General Data Protection Regulation (GDPR).

Results

- The % of DNAs at Hill Top is exceptionally high.
- At the practice, 54/262 of all the outpatient appointments booked in April 2017 were DNAs. This amounts to 20.6%, which is roughly 1 in 5 not attended. The national average of England is reported as 6.4%, which is less than a third of the rate at Hill Top.
- First DNA is strongly suggestive of not being seen subsequently.

- Just 1 in 4 patients were followed-up by the hospital specialty for which they missed their appointment.
- Only 52% of the DNAs reported in April 2017 were one-off DNAs the other patients had serial DNAs.
- 36.4% of patients with <3 outpatient DNAs had multiple comorbidity (≥4 significant active medical problems) compared to 53.3% of those with ≥3 outpatient DNAs and 15.2% compared to 26.7% respectively had complex co-morbidity (≥4 significant active medical problems and a significant active (and/or past) mental health problem.
- This research suggests a relationship between the increased complexity (comorbidity) of a patient and the increased likelihood to DNA.

Conclusions

- Results support practitioners' concerns that those in most need may be those least likely to engage with healthcare services.
- Further statistical analysis is required with a larger patient group to check for statistical significance and correlations between factors.
- A comparative data set from a more privileged background is required for comparison to confirm hypotheses that:
- DNA rates are indeed higher in deprived populations
- Follow-up rates in deprived populations for missed outpatient appointments are significantly lower
- There is a relationship between increasing complexity and increased likelihood to DNA, and
- Because of this, health outcomes are ultimately worse in deprived populations and therefore
- Poor secondary care attendance should be addressed as a significant contributing factor to health inequality in England.

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What is the incidence of late detected developmental dysplasia of the hip (DDH) in England?

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Introduction Developmental dysplasia of the hip (DDH) diagnosed after the neonatal period is considered a ‘late’ diagnosis, and carries significant health and socioeconomic implications. This is the first UK based study to investigate the incidence of late diagnosed DDH; including age-, sex-, year- and region-specific incidence rates.

Patients and methods A descriptive observational study was performed by linking primary and secondary care information from two independent national databases of routinely collected data: the UK Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES). All children

aged between one and eight years old were identified, with a new first diagnostic code for DDH after 1-year-old, from 01/01/1990 to 01/01/2016.

Results The incidence of late-diagnosed DDH was 1.28 cases per 1000 live births. Within the study population, 754 children were identified with a diagnosis of DDH after one year of age. Of all late diagnoses, 536 (71.1%) were detected between 1-2 years of age. The ratio of females to males was 4.2:1. Distribution was evenly spread throughout England.

Conclusions The incidence of late diagnosed DDH is unchanged from that reported forty years ago, prior to the introduction of the national selective screening programme for DDH. This national study contributes to the debate concerning the efficacy of selective screening implementation.

Women's health needs in rural Nepal

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Introduction Twelve international and nine Nepalese health sciences students participated in the second Universitas 21 Global Learning Partnership programme in March 2018 focusing on the United Nations Sustainable Development Goals which aims to banish poverty to create inclusive societies around the world1. The project began with one week of workshops on leadership, advocacy and research, followed by three weeks of community-led work involving women's health in Dhungkharka, a rural municipality within the Central Developmental Region of Nepal.

Patients and methods This was a cross-sectional, community-based study among women aged 15-80 years. A community needs assessment was carried out to establish the health needs in distinct areas differing in altitude, ethnicities and proximities from the health centre. Self-designed questionnaires, a Pelvic Organ Prolapse Screening Score2 (POP-SS) and the International Consultation on Incontinence Modular Questionnaire for Urinary Incontinence3 (ICIQ-UI) were administered. Healthcare staff took part in semi-structured interviews while female health volunteers participated in a focus group.

Results A total of 84 women were surveyed, 44.5% of which were not formally educated. Most women married young, left school early and had multiple children before reaching 20. The average fertility rate was high at 3.23. The questionnaire and POP-SS revealed symptoms of pelvic organ prolapse (POP) and urinary incontinence (UI) which were proportional to parity. However, these formed only 2% of presentations to clinics. The ICIQ questionnaire found that 25% of women suffered from urinary leakage with 15.5% having stress incontinence.

Conclusions Women had minimal health awareness, possibly resulting from the lack of formal education. A healthcare programme was implemented to educate women and staff. Colourful posters helped to teach symptoms of POP and UI and a Styrofoam pelvis model allowed visualisation of anatomical structures. We used a traditional Nepalese piece to create a song and dance about POP to disseminate our message.

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Are INVOcell and simplified culture system cheap, effective and safe alternatives to conventional ivf for young women under-35 in developing countries?

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Introduction There are more than 70 million infertile couples worldwide and most are found in low-resource countries. In these countries, bilateral tubal blockage is the leading cause of infertility. While in vitro fertilisation (IVF) is the most effective intervention for tubal blockage, access to IVF is limited and expensive with only half of all infertile couples having access to infertility services. In recent years, two new low-cost techniques have been introduced as possible alternatives to IVF. They are INVOcell (2008) and the Simplified Culture System (2013), which are estimated to reduced the cost of one IVF cycle by 30% and 50% respectively. As there is no single paper which directly compares conventional IVF against INVOcell and Simplified Culture System (SCS), this literature review aims to compare the three techniques on the basis of clinical effectiveness, cost effectiveness and safety.

Patients and methods PubMed, Medline, EMBASE and Google databases were searched for relevant studies on costs, clinical effectiveness and safety profiles of IVF, Simplified Culture System (SCS) and INVOcell. Further unpublished data were obtained through email exchanges with lead authors.

Results The 3 techniques have comparable clinical effectiveness, IVF (32.8%), INVOcell (35.2%) and SCS (30.4%). In terms of cost per live birth, SCS (£7,552) is the most cost effective, followed by INVOcell (£8,935) and IVF (£13,547). More importantly, INVOcell and SCS cycle would make up 73% and 54% of annual household expenditure respectively, down from an unrealistic 106% (IVF), making a cycle significantly more affordable. No adverse complications for mother and newborn has been reported, although existing data is limited.

Conclusions Future studies are required to produce more robust data on clinical effectiveness and safety profiles, however the author is encouraged by the potential of INVOcell and SCS in widening access to infertile couples, making low-cost IVF a viable and equitable option.

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What are the important factors that promote uptake and sustainable use of mobile health applications (mHealth apps) in the general adult population?

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Introduction In 2012, the World Bank reported more than 6 billion mobile subscribers worldwide, connecting almost 75% of the global population. This has led to an explosion of mobile applications (apps), which are increasingly seen as a potentially viable tool in delivering cheap and flexible medical interventions. There are approximately 1.6 million mHealth apps available but a 2013 report by IMS Institute of Healthcare Informatics noted that most mHealth apps, regardless of popularity, had limited functionality and lacked a solid scientific basis.

Therefore, this dissertation aims to investigate important factors that promotes app uptake and sustainable use of mHealth apps in the general adult population, thus guiding creation of a more effective and competitive scientifically-grounded health app.

Patients and methods Target patient group : General adult population

Method: A literature search across 3 databases using the search term “mobile applications” identified 11 studies on mobile app users’ opinions and preferences of apps and their features. Only apps intended for health promotion were included while samples with long-term conditions were excluded, except obesity which is reflective of the general population.

Results 5 recurring factors were identified, namely: i) effectiveness; ii) novel features; iii) privacy; iv) cost; and v) user interface (UI). High user uptake poorly correlated with app effectiveness, whereas novel features like gamification and achievable goal-settings increased patient satisfaction and self-efficacy. This motivated continuous use of the app, thus improving overall intended health app intervention outcome.

Although data privacy is an important concern for users, current evidence suggests that users are becoming increasingly desensitized to prevalent data collection.

While users tended to value low cost or free apps higher in initial adoption, paying for apps does not reduce reported users’ satisfaction as this is compensated by an ad-free, smooth user experience. Hidden costs are common reasons for app discontinuance.

Conclusions These findings are aimed to guide future creation of evidence-based health apps, which are able to attract initial users as well as maintain their interest in order to maximize the potential benefits of mHealth apps interventions.

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Do lifestyle factors modify the risk of Breast Cancer in post-menopausal BRCA mutation carriers? A systematic review

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Introduction Breast Cancer (BC)1 is the most common cancer in women. In the UK, it is estimated that 38% of post-menopausal breast cancer cases are preventable with lifestyle modifications (body fatness, weight gain, inactivity and alcohol consumption). Modifiable factors, such as smoking and diet, have also been implicated in increased risk. Inherited mutations in BRCA1/2 genes are strongly associated with the development of BC by increasing the risk of dramatically with age. Aim: To assess if lifestyle factors modify BC risk in post-menopausal BRCA1 and BRCA2 mutation carriers.

Patients and methods Following the PRISMA guidelines, a systematic review was undertaken. Primary studies, investigating the effect of these modifiable factors in post-menopausal BRCA1/2 mutation carriers were retrieved from extensive database and manual searching. The lifestyle factors examined were: smoking, weight, weight gain, physical activity, diet and alcohol drinking. Studies which included both pre- and post-menopausal women were eligible for inclusion if the mean age of participants > 45 years.

Results Eleven primary articles were generated from the study selection process. Articles assessing smoking reported conflicting results. Narrative synthesis of weight, weight gain, physical activity and alcohol provided some, yet inconclusive evidence of modifying BC risk. It seems likely that diet diversity has a greater impact than isolated dietary components.

Conclusions Results provide limited evidence in terms of how lifestyle modifies risk in BRCA mutation carriers. Nevertheless, lifestyle should not be overlooked in the presence of a strong genetic risk as it can still influence prognosis and outcome after diagnosis.

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The Role of Infectious Agents in Idiopathic Inflammatory Myopathies

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Introduction The aim of this literature review was to investigate the association between infectious agents (virus, bacteria, parasite and fungi) and the development of idiopathic inflammatory myopathies (IIM). IIM is a group of heterogenous autoimmune conditions with three main clinical subgroups; dermatomyositis (DM), polymyositis (PM) and inclusion body myositis (IBM). IIM presents with muscular weakness and fatigue along with the infiltration of inflammatory cells.

Patients and methods A systematic PubMed search was conducted using the PRISMA statement. From the search results, 585 studies were initially found. Through analysis and exclusion, a final number of 23 studies were deemed acceptable for use.

Results Results show that from the 23 studies, 244 patients were identified and 354 infectious agents were detected. Organ based infections accounted for the bulk of infections causing IIM with respiratory infections amounting to 65/354 (18.4%), gastroenteritis 24/354 (6.8%), otitis media 19/354 (5.4%), urinary tract infections 15/354 (4.2%) and skin infections 12/354 (3.4%). Specific infections such as Streptococcus pharyngitis accounted for 40/354 cases (11.3%), Flu-like virus 35/354 (9.9%) and HIV virus 30/354 (8.5%).

Furthermore, viral infections were shown to be the most prominent genus to cause IIM with 74/88 (84%) cases reported. Bacterial infection accounted for 12/88 (13.6%), parasites for 2/88 (2.3%) and no fungal infection were reported. Geographical mapping of infectious agents causing IIM showed a large volume of DM patients in North America.

Conclusions Infectious agents are associated with the increased development of IIM through various mechanisms such as dysregulation of immune response, molecular mimicry and epitope spreading.

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Under pressure - Anti-Embolism Stockings Fail to Measure Up: An audit of size, fit and efficacy in the maternal and bariatric population

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Introduction Deep vein thrombosis (DVT) and pulmonary embolism (PE) are highly preventable conditions common in hospitalised patients. DVT and PE are one of the leading causes of maternal mortality in developed countries[1]. Risk of venous thromboembolism increases 2-3 fold in obesity[2], 4-6-fold during pregnancy[3] and 20-fold post-partum[4]. Anti-embolism stockings (AES), fitted according

to leg size, exert pressure in accordance with the Sigel profile[5] to maintain blood flow and prevent thrombus formation. There is uncertainty surrounding the efficacy of AES, particularly in Class III obesity (body mass index (BMI) ≥40kg/m^2). This study audited the sizing and fitting of AES in pregnant and postnatal women and evaluated staff and patient opinions on AES.

Patients and methods A convenience sample of pregnant and postnatal women was recruited. Six measurements were taken on legs and feet and compared with AES manufacturers sizing charts and against British Standards. Pressures exerted by AES were measured using a PicoPress pressure sensor and compared with the Sigel profile, NICE guidelines and British Standards, and correct fitting of AES was assessed against manufacturers sizing. Questionnaires were completed by women and staff.

Results A total of 4,944 measurements were taken. Obese class III women had larger measurements than BMI <40kg/m^2 at key measurement points. Obese class III women's' calves were 41.6% larger than normal BMI women. Fewer than 16% of obese class III patients fitted AES with 2 or more sizing points. All patients had the wrong size of stocking, and all recorded stocking pressures failed to match recommended pressure profiles. All patients had a positive gradient pressure profile, increasing the risk of DVT. Staff highlighted difficulty with fitting and sizing AES, especially larger women (68.8%).

Conclusions This audit casts doubts on the effectiveness of AES for the obese bariatric population, and highlights difficulties in correct sizing and fitting of AES. The failure of AES to exert the correct pressure profiles suggests that AES fail to reduce the risk of DVT in the obese bariatric population. This audit hopes to inform future design of AES, with particular emphasis on achieving optimum pressure profiles and sizing and leg shape for the obese bariatric population.

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Using quality improvement methodology to implement a Short Stay Admission policy for children in a Quaternary Scottish Paediatric Hospital

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Introduction Rising service demand, increased staffing pressure and a planned move to a new site prompted a trial of a new discharge process in the Royal Hospital for Sick Children, Edinburgh. Our

aim was to use quality improvement methodology with process mapping of systems, delineating good and bad variation and multiple PDSA cycles to measure the effectiveness of a Short Stay Policy (SSP) for acute general paediatric admissions. This policy streamlined patient discharge processes by empowering the middle grade team, who assessed the children overnight, to discharge patients prior to the medical consultant ward round the next day. The Standard Policy (StP) only enabled consultants to discharge children. As low acuity stable children would be seen on the later aspect of the ward round, some patients waited an additional 4 to 8 hours for the decision to discharge.

We aimed to calculate the potential time, personnel and financial savings made by this new policy, and to ensure we maintained a high quality, safe service without diminishing child and family.

Patients and methods Our study grouped patients into those seen through the SSP, and those through StP. Patient journeys were mapped out and our online patient record (TRAK) was used to assess timings along the pathway and total length of stay. A Delphi group established which diagnoses and types of patients could be included in the SSP and readmissions rates were considered with qualitative surveys gathered to understand child and family experience.

Results An inpatient admission costs £400 per child in a 24 hour period. The SSP saved an average of 12.1 hours per patient saving £200 per patient[1]. Detailed patient notes reviewed demonstrated the same level and quality of care was experienced by the patient.

100% of parents contacted indicated feeling happy and comfortable at discharge. Spending less time in hospital meant patients and parents got home sooner, saving time off work/school and making sure their hospital admission caused minimal disruption to their activities.

Conclusions This project demonstrates that implementing “good variation” in patient process whilst using sound methodology to investigate your tests of change, can results in improved child and family experience, systems change and financial efficiency.

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Patients’ perceptions of exercise as an intervention for postpartum depression

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Introduction Following recent studies mainly Daley (2017) which suggested that NICE guidelines should be altered to include the use of exercise at as an intervention of postpartum depression and that this should be discussed with patients during their care pathway. The aim of this service evaluation was to review whether patients had been advised to exercise both during and after their pregnancy as a view to the prevention and treatment of postpartum depression.

Patients and methods In total 54 mothers were selected at random from the post-delivery wards at the University Hospital of Wales between March 12th and April the 10th 2018. The selection Criteria was any consenting patient on the wards that had recently been through the pregnancy pathway. New mothers were interviewed about care and advice received along the care pathway from initial

scan to delivery. The Interviews were semi structured and informal allowing the mothers to share their experiences of the pregnancy pathway at University Hospital Wales.

Results From the 54 women recruited 53 (98%) had a discussion regarding the benefits of exercise during pregnancy with a healthcare professional, however only 7 patients (12.9%) had been advised of exercise in the prevention and management of postpartum depression. In addition to this 52 (96%) said that they were aware that exercise had a positive effect on mood, with 46 (85.2%) saying that they would prefer exercise as a first line intervention to pharmacological interventions.

Conclusions The results of this review would suggest that NICE guidelines for the treatment of patients with postpartum depression should be reviewed to incorporate more recent evidence and that healthcare professionals should incorporate this evidence into their management pathways.

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Prevalence of anxiety after stroke: an updated systematic review and meta-analysis of observational studies

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Introduction Anxiety is common and debilitating after stroke. A 2013 systematic review found the prevalence to be 18% when measured by interview and 25% when measured by rating scale.

Aims: To update the 2013 review and generate an updated measure of the prevalence of anxiety after stroke. Secondary aims were to measure the prevalence of subtypes of anxiety, and explore the influence on prevalence of the method of measuring anxiety, time post-stoke, and study setting.

Patients and methods A sensitive search of databases was performed. Studies were screened against pre-specified criteria. Study data were extracted using a pre-piloted form and risk of bias within studies was assessed using the Newcastle-Ottawa Scale. A second reviewer screened a sample of papers and checked data extraction and quality appraisal for errors. Interrater agreement was moderate to high. Meta-analysis, subgroup, and sensitivity analyses were performed, with results presented as forest plots.

Results 22564 unique records were obtained. 80 publications reporting 51 studies were included in the review; all 51 were included in meta-analyses. Based on 11 studies using clinical interviews, the prevalence of anxiety was estimated as 18.0% (95% confidence interval 13.3 – 22.6, I2 = 85%); the pooled prevalence from 40 studies using rating scales was 25.1% (95% confidence interval 21.4 – 28.9, I2 = 96%). Community-based studies reported a statistically significant lower prevalence than population-based studies. There was no statistically significant change in prevalence over time when measured by interview or rating scale. Higher quality studies tended towards lower prevalence. The relative importance of anxiety subtypes was not clear.

Conclusions The prevalence of anxiety after stroke is significant and in line with the results of the original review. Further research should focus on the prevalences of subtypes of anxiety, changes in prevalence over time, and on the effectiveness of treatments for anxiety after stroke.

Safety and Tolerability of Immunosuppression in non-IPF ILD: clinical experience from a tertiary ILD centre

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Introduction Interstitial lung diseases (ILDs) are a group of over 300 diseases affecting the interstitium.[1] Immunosuppressants e.g. corticosteroids, azathioprine (AZA), methotrexate (MTX), mycophenolate mofetil (MMF), and cyclophosphamide (CYC) have variable responses in effectiveness in slowing deterioration in some ILDs.[2][3]

Patients and methods Patients on immunosuppressants under the care of the ILD clinic at a tertiary referral centre in the North West were identified. Electronic records of clinic letters and lung function test results were retrospectively analysed from December 2009 to May 2018, with a focus on reports of AEs.

Results 99 patients (55% female) with a mean age of 60+10 years at the start of treatment undertook 131 courses of treatment. The most common diagnosis among the patients was NSIP (n=28, 28%). The breakdown of the other patients is as follows: HP 22 (n=22, 22%), Sarcoidosis (n=17, 17%), CTD-ILD (NSIP) (n=16, 16%), Uncertain ILD (n=11, 11%), COP (n=2, 2%), AIP (n=1, 1%), CTD-ILD (UIP) (n=1, 1%), UIP (n=1, 1%).

Of the 131 courses of treatment, 65 (49%) were with MMF, 48 (37%) were with AZA, 17 (13%) were with MTX, and 1 (1%) was with CYC. 122 courses of treatment had concurrent steroid therapy at initiation with an average dose of 15.5+9.2mg at commencement.

There were 95 reported AEs in total. Of the 131 courses of treatments, 61 (47%) reported an AE. The treatment that caused the greatest number of reported AEs was AZA (n=41, 43%), followed by MMF (n=40, 42%). The most common AEs among all treatments were abnormal LFTs (n=18, 18.9%), infection (n=15, 15.8%), and tiredness (n=9, 13.7%). The most common AE associated with AZA was abnormal LFTs (n=12) whereas MMF was most associated with infection (n=7).

The outcomes of AEs included temporary discontinuation (n=14, 19%) and dose reduction (n=13, 18%). 26 (26.3%) patients were started on a second immunosuppressant, 3 (3%) were given 3 courses of immunosuppressant therapy.

AZA led to no permanent discontinuations in immunosuppression treatment due to AEs as all patients permanently stopping AZA therapy due to AEs were switched to MMF. 10 (15.4%) MMF patients had treatment permanently discontinued due to AEs and 3 (17.6%) MTX patients were permanently discontinued due to AEs. The permanent discontinuation of all treatments was 30% when including AEs, disease progression and patient death.

Lung function outcomes showed the mean FVC % predicted declined by 4.2% per year with AZA and increased by 0.9% and 2.8% with MTX and MMF. AZA, MTX and MMF were steroid sparing with MTX achieving the greatest percentage decrease in steroid dose (36.3%).

Conclusions Patients mostly continued with second line immunosuppression for ILD, with a total permanent discontinuation rate of 30%. The evidence supports the use of AZA, MTX and MMF to achieve stability in lung function and a reduction in steroid doses.

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An analysis of the cross-sectional anatomy of the distal femur and its relation to through-knee amputations

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Introduction Although through-knee amputations hold numerous functional advantages over above-knee amputations; they are frequently rejected when both are viable options. Hospital Episode Statistics for 2003-2008 indicate that, during this period, just 727 through-knee amputations took place compared to 12,831 above-knee amputations (Moxey et al., 2010). Sectioning the femur in the axial plane in a through-knee amputation is often inevitable and can be done to improve poor primary healing rates. However, this often reduces the cross-sectional area of bone contributing to the distal surface of the amputation stump. Literature suggests that greater bony cross-sectional areas in the distal portion of amputations stumps improve functional outcomes (Kamman et al., 2014; Ferris et al. 2017). This project aims to analyse the cross-sectional anatomy of the distal femur in order to identify the level at which it is best to cut the femur to maximise the distal bony cross-sectional area in an amputation.

Patients and methods Cross-sectional area in the axial plane of the distal femur was measured at 4 levels in lower extremity CT angiograms (n=50), osseous specimens (n=4) and cadaveric specimens (n=2).

Results The results of all three components of this study indicated that the greatest cross-sectional area is at the level of the maximum height of the femoral intercondylar notch. Analysis of mean cross-sectional area across the osseous specimens and CT angiograms using a paired one-tailed t-test also indicate that the cross-sectional area at this level was significantly different from adjacent levels. Consistent trends of change in cross-sectional area across the distal femur were also noted.

Conclusions This data provides new anatomical knowledge that could be used to help modify existing amputation techniques by providing information as to at which level it is best to cut the femur to maximise distal bony cross-sectional area.

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Acute Oncology Support Application (AOS App) – a summative evaluation of its success in supporting medical professionals who treat oncological emergencies in Wales

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Introduction In the UK more than 360,000 cancer cases are diagnosed every year, that's a new diagnosis of cancer every 2 minutes (CRUK 2017).

Oncology patients arrive in A&E, acute wards, or the community with urgent problems as a result of their malignancy and treatments which can be difficult to manage, even for the most experienced Doctors. With this in mind, and the inevitable increase in patients who will receive cancer treatment in the future, Velindre NHS Trust has created the Acute Oncology Support App. The app is designed for use by all Doctors and trained healthcare professionals, with the aim of improving emergency cancer care in Wales.

"The Acute Oncology App is designed to provide easy, always there guidance, helping professionals to know what to do and who to contact for further advice. It's packed with expert knowledge, created with the help of oncology experts from across Wales, helping doctors back up their knowledge and strengthen their decision-making in an emergency. It's like having your own personal oncologist providing expert advice exactly when you need it." (Dr Hilary Williams, Velindre NHS Trust, October 2017).

This summative evaluation aims to quantify the impact Velindre's AOS App has had on medical professionals who provide emergency cancer care in Wales.

The evaluation also aims to highlight which content within the app users find most useful with future objectives of developing content further and marketing the app to a larger audience.

Patients and methods A longitudinal trend stud was used to establish confidence in treatment of oncology patients with a simple survey conducted prior to launch of the AOS App (September 2017) and then again post App launch (May 2018).

Participants were asked to rate their confidence in managing oncological emergencies, chemotherapy toxicities and immunotherapy toxicities between 0 (not at all confident) and 10 (fully confident).

Participants involved a variety of medical professionals including; medical students, nursing staff and Doctors of different grades.

Mean results and Z Scores were calculated for each survey question and results compared. Anonymised data regarding app use was also downloaded from Google Analytics and Apple's iConnect software for analysis of app content.

Results Results show medical professional's confidence in managing patients in an oncological emergency is significantly increased with use of the AOS app.

Mean confidence in treating general oncological emergencies prior to app launch was 5/10 (standard deviation=2.43). With use of the app, confidence increased further to 8/10 (sd=1.48), Z-

Score 14.42. Confidence in treatment of both chemotherapy and immunotherapy toxicities doubled; from 4/10 (sd=2.56 and 2.24) to 8/10 (sd=1.10 and 1.14) with Z-Scores 18.26 and 20.94 respectively. An alpha level of 5% (Z-score 1.645) was used to test significance of results obtained. Z-scores for all three scenarios were greater than 1.645 and so the null hypotheses could be rejected.

Conclusions The AOS app is an innovative creation by Velindre NHS Trust which has proven to be successful in aiding medical professionals who provide emergency cancer care in Wales.
The App's content has been viewed thousands of times; with users finding advice regarding immunotherapy and chemotherapy treatment most helpful.

6 months following launch, the app was used by 2000 different users - many of which return regularly. Although an impressive number, there is room for improvement in marketing of the app through social media as analytic data highlights little engagement from content seen via Facebook or Twitter.

Ultimately, the more support medical professionals have when providing treatment in an unfamiliar scenario the better the care will be. We hope more professionals will make use of the AOS app with the aim of improving emergency cancer care across the UK.

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siRNA as a medical therapy for Cushing's disease

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Introduction Cushing's disease is the result of an anterior pituitary corticotroph adenoma autonomously-secreting adrenocorticotrophic hormone (ACTH). Increased ACTH secretion stimulates excess cortisol production, which has devastating consequences and causes, diabetes, hypertension, osteoporosis, depression and psychosis, and increased infection risk. Untreated there is a 50% 5-year mortality. Surgical removal of the tumour is the only curative treatment, but the recurrence rate is high. There is a lack of suitable medical alternatives. RNA-interference is a naturally-occurring mechanism of post-transcriptional gene silencing that can be utilised to knock-down the expression of specific genes using small interfering RNAs (siRNAs).

Proopiomelanocortin (POMC) is coded for by POMC gene and is cleaved to form ACTH. We hypothesise that anti-POMC siRNA could be an effective treatment for Cushing's by silencing POMC expression and decreasing ACTH secretion. Current barriers to the use of siRNAs include lack of specific delivery to the target cell. We aim to increase the delivery specificity by targeting the corticotroph cells with an antibody-siRNA conjugate via corticotrophin-releasing hormone receptor 1 (CRHR1) a tissue-specific cell surface receptor.

Patients and methods AtT-20 cells are an immortalised cell line of murine anterior pituitary corticotrope tumour cells that secrete ACTH into culture media. The cells were used as an in vitro model of Cushing's to assess the effectiveness of transfection with 3 custom-designed siRNAs at reducing ACTH secretion. AtT-20 cells were transfected with one of 3 siRNAs specifically-targeting

POMC gene using Lipofectamine™-2000 transfection reagent and incubated for 24 hours. Culture medium was sampled for ACTH assay using an Immulite 2000® ACTH immunoassay. Controls included untreated cells, no-transfection-reagent and Lipofectamine™-2000-only. Control transfections were performed to investigate the sequence specificity of the anti-POMC siRNAs. Activation of the innate immune system was analysed by ELISA for IFN- α and -β. RT-PCR, a functional assay, flow cytometry and immunofluorescence were used to determine the expression of CRHR1.

Results Anti-POMC siRNAs caused a dose-dependent reduction of ACTH following treatment, compared to untreated cells, and did not induce IFN-α or -β. Control siRNAs had no effect on ACTH secretion. CRHR1 cell surface expression was confirmed in AtT-20 cells by functional assay, flow cytometry and immunofluorescence.

Conclusions Anti-POMC siRNAs decreased ACTH secretion by AtT-20 cells and could be a novel medical therapy for Cushing's Disease. CRHR1 expression in AtT-20 cells has been confirmed and this may provide a specific target for the delivery of anti-POMC siRNA conjugates to the corticotroph tumour cells.

Pharmacological Characterisation of Antagonists at Free Fatty Acid Receptor 2 (FFA2)

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Introduction Free fatty acid receptor 2 (FFA2) is a G protein-coupled receptor (GPCR) that is activated by short chain fatty acids (SCFAs). Presence of FFA2 in pancreatic beta-cells, adipocytes and leukocytes indicate its roles in energy regulation, metabolism and inflammation, although these functions require further elucidation. It is hypothesized that development of FFA2-targetted therapeutics would be beneficial for diseases such as type II diabetes, inflammatory bowel disease and obesity (1-4). To date, study of the FFA2 receptor and its physiological functions has been stalled by a lack of selectivity and potency of endogenous ligands at the receptor (5). Therefore, there is a requirement for development of synthetic ligands that are both selective and potent at FFA2.

Patients and methods The aim of this project was to test and characterise synthetic antagonist compounds at the FFA2 receptor. To do this, compounds were tested from two chemical series (Series 1 and Series 2) and a functional [35S] GTPγS binding assay was employed to create antagonist inhibition curves and perform Schild analysis. In this assay, radioactive, non-hydrolysable [35S] GTPγS accumulation is measured using scintillation counting.

Results Antagonist potency was estimated using pIC50 values and the most potent antagonist from each series identified. This was compound 1889 from Series 1 and compound 1890 from Series 2; pIC50 values are 7.24 ± 0.16 and 7.65 ± 0.21 respectively. Both of these compounds showed greater potency than the reference compound CATPB (pIC50 = 6.54 ± 0.12). Data from Schild analysis showed both 1889 and 1890 to be competitive antagonists at FFA2, as is the reference compound CATPB.

Conclusions Discovery of potent, selective antagonist compounds at FFA2 will allow further research into FFA2-mediated physiological roles and advance its candidacy as a potential therapeutic target for metabolic disease. Potent antagonists – such as compounds 1889 and 1890 – yield several advantageous properties as a clinical therapeutic including smaller doses and reduced drug-related side effects. Identification of potent antagonist compounds at FFA2 is a positive forward step in

therapeutics development for diseases involving the FFA2 receptor such as type II diabetes, inflammatory bowel disease and obesity.

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Investigating the Pharmacogenetics of Anti-TNF Response in Patients with Rheumatoid Arthritis Utilising the Re-weighted Disease Activity Score: Results from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate

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Introduction Anti-TNF drugs have revolutionised the treatment of rheumatoid arthritis (RA), but response is not universal. Genome-wide association studies (GWAS) have identified single nucleotide polymorphisms (SNPs) associated with treatment response. Unfortunately, many SNPS fail to be subsequently validated in independent studies. Response is measured using the disease activity score 28 (DAS28) which contains subjective measures (visual analogue score; VAS and tender joint count; TJC) that are influenced by confounding factors such as depression. This study used a reweighted DAS28 score that excludes the VAS and TJC to determine whether previously associated SNPs are associated with response to anti-TNF medications when compared to the original DAS28 in a prospective UK RA cohort of anti-TNF starters.

Patients and methods A literature review was conducted to identify SNPs with previous evidence of anti-TNF response discovered using a GWAS approach ($P<10\text{-}5$ or $P<10\text{-}3$ with validation in an independent cohort). Patients commencing anti-TNF therapy were recruited to the multicentre observational BRAGGSS study (n=1828). Clinico-demographic data were recorded at baseline and 6 months, including swollen and tender joint count, ESR or CRP and VAS and the original and reweighted DAS-28 were calculated. Treatment response was measured by change in DAS28 at 6 months, using the original and reweighted formulas. Donated samples underwent whole-genome genotyping. Linear regression analysis was conducted to investigate SNPs associated with change in DAS-28/re-weighted DAS, adjusting for baseline values using Plink 1.07.

Results Of the 36 SNPs previously associated with anti-TNF response, data for 26 were available for analysis after quality control. Using the original DAS28, at 6 months post anti-TNF initiation, one SNP was significantly associated with treatment response (rs12081765). Using the reweighted DAS28, five were significantly associated ($P\leq0.05$) (Table 1).

Conclusions More genetic associations were discovered when using the reweighted DAS28 which may reflect the exclusion of subjective measures. Further studies using larger independent patient cohorts are needed to validate these findings.

NLRP3 Inflammasome: Activation & Role in Neurodegenerative Diseases

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Abstract As part of the innate immune system, inflammasomes are cytosolic multiprotein complexes that regulate caspase-1 activity which is a protein that ultimately processes the pro-inflammatory cytokines IL-1β and IL-18. Nod-like receptors (NLRs) are a group of cytosolic receptors that include subtypes that control activation of the inflammasome. NLRP3 is the most versatile and extensively studied of these receptors. Whilst all inflammasomes recognise pathogens, NLRP3 can react to a remarkably large number of stimuli derived from both foreign pathogens and host tissue. This is one of the reasons that the NLRP3 inflammasome is the most clinically relevant. Excessive inflammation, which may be caused by inflammasome dysregulation, can result in a number of diseases. Research on mouse models, supported by evidence in humans, has suggested a role for NLRP3 in neurodegenerative diseases like Alzheimer's disease, Parkinson's disease and multiple sclerosis, amongst others. This report focuses on the activation of NLRP3, its role in neurodegenerative diseases and its potential as a promising therapeutic target.

The women-held antenatal card; potential for an effective handover tool on admission to maternity services in Banjul, The Gambia: A cross-sectional study

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Introduction Maternal mortality is particularly high in The Gambia[1] and effective communication of critical information from community to hospital services is a key safety issue[2]. The aim of this study was to assess the effectiveness of women-held maternal-health records as handover tools by examining the completeness of documents brought by women to hospital, including the government-issue antenatal card, and exploring the barriers and facilitators to effective document use.

Patients and methods 250 in-patients on maternity wards in Banjul were interviewed using a self-designed questionnaire and content analysis of all documentation brought by women on admission used World Health Organisation recommendations as 9 'minimum criteria'. The association of certain barriers, such as literacy, with effective document use was examined using logistic regression models.

Results Nearly all (97%) women admitted to maternity units brought some form of documentation - most frequently the antenatal card (94%). 84% of antenatal cards had at least one space incomplete and only 27% reported the estimated date of delivery. 25% of women arrived with all 9 items of the minimum criteria and antenatal cards were the only documentation to provide all 9. 60% of women referred carried structured referral sheets and 40% of women who had attended previous scans had an ultrasound report.

Conclusions This is one of the first studies to explore the contents and completeness of women-held maternal health records and has shown that accurate completion of antenatal cards should be encouraged to fulfil their potential as an effective handover tool. Adaptations to the card could take advantage of their reliable use by women and staff in the absence of competent use of referral forms and other documentation. Together this would ensure all essential information is available to

provide the smoothest handover to hospital-based care and prevent any delays to effective treatment and management of complications. Following WHO steps towards encouraging good quality care globally to extend beyond simple provision of services, the antenatal card has the potential to play a greater role in the effective information and referral systems in low-income countries and reduction of maternal mortality.

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Evaluating the suspected skin cancer (SSC) pathway in a New Zealand dermatology department

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Introduction New Zealand has the highest incidence of melanoma in the world.[1] Due to an ageing population, skin cancers are expected to increase.[1] Referrals for high suspicion of cancer must have a clinical assessment within 14 days. This target can be difficult to achieve due to administration delays and triaging. The current referral system does not separate general referrals from suspected skin cancers. In 2016, the referral pathway transferred from paper to electronic form, this provided an opportunity to introduce teledermatology as part of routine care. In the Waikato region, teledermatology is effective but not a part of usual care. In 2017, the dermatology referral form was inadequate due to the lack of clinical information provided when compared to the Quality Standards for Teledermatology. The SSC pathway is an advice-only referral system, which includes dermoscopsy images along with clinical information. The aim of this study is to evaluate the impact of the SSC pathway on dermatology referrals.

Patients and methods Data was analysed from 1st March to 30th April from 2016 to 2018. All data was included. Elective dermatology referrals are either accepted or declined. The accepted referrals are triaged for assessment in a semi-urgent appointment, routine appointment or virtual lesion clinic (VLC). These referrals should be completed within 6 days, whereas, SSC referrals should be completed in 4 days. To evaluate the referral system the data was analysed with and without the administration time.

Results A total of 1,869 referrals were analysed. There was a 245% increase in skin cancer referrals over the 2-year period. Accepted referrals decreased by 25.18% over 2 years. The 2018 referrals for SSC were all declined as designed by the referral system. 98.54% of referrals in 2018 were completed within the recommended time, however, including the administration time this decreased to 89.4%. 97.74% of SSC referrals were completed within 4 days, this process was not

delayed by administration time. In 2018, on average the dermatology referrals took 3.61 days. The SSC pathway averaged 1.46 days.

Conclusions The number of referrals being processed by the dermatology department has increased. Since the SSC pathway has been introduced the number of skin cancer related referrals has sharply risen. As more referrals are being declined with advice it suggests adequate information is being provided to make a diagnosis. This provides GPs with a quicker response, however, it is limited by their assessment. Currently, small quantities of GPs have the digital dermoscopy equipment which limits the use of the SSC pathway. Nevertheless, this pathway benefits patients as fewer will be required to travel to clinic and results can be obtained quicker, which decreases patient anxiety. The SSC pathway contains the most time critical referrals; therefore, it would be beneficial to streamline these referrals. The SSC pathway was quicker at providing expert opinions to the GPs compared to general dermatology referrals.

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Outcomes after Laparoscopic and Open Appendicectomy

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Introduction In the UK, the commonest abdominal surgical procedure undertaken in emergency setting is appendicectomy. Although more laparoscopic appendicectomies (LA) are performed compared to open appendicectomies (OA), there is no consensus regarding the gold standard for surgical approach of acute appendicitis.1,2,3 This study aims to look at clinical outcomes comparing LA and OA performed at the Royal Infirmary Edinburgh (RIE) and determine if a) LA reduces the length of hospital stay (LOS) compared to OA and b) to compare surgical post-operative complications (wound site infection, intra-abdominal collection and post-operative ileus) between LA and OA.

Patients and methods Prospectively pre-collected patient data from Lothian Surgical Audit was studied retrospectively. Patients who underwent appendicectomy in RIE between July 2014 and December 2016 were divided into two groups, LA and OA. Surgical and non-surgical complications documented on TrakCare™ during admission and up to three months post-surgery were noted as post-operative complications. Calculations were performed using SPSS software. Numerical data was presented as mean and standard deviation and evaluated using student t-test. Categorical data was

presented as frequencies and percentages and analysed using the Pearson Chi-Square test or Fisher's Exact Test. A p-value of 0.05 was considered statistically significant.

Results Of the 1138 patients who underwent an appendicectomy in RIE between July 2014 and December 2016, 1108 patients had LA and 30 patients had OA. 14 (1.3%) patients had a conversion from LA to OA. LOS was longer with OA (9.83 ± 4.05) when compared to LA (3.82 ± 2.41). A statistically significant difference was noted between LA and OA for post-operative complication ($p<0.001$). Of the recorded surgical complications, LA had statistically significant reduced rates of wound site infection ($p<0.001$), intra-abdominal collection ($p=0.006$) and post-operative ileus ($p=0.032$) compared with OA.

Conclusions LA has substantial benefits over OA including shorter LOS, significantly reduced wound site infection, intra-abdominal collections and post-operative ileus and should be routinely recommended if the required expertise and resources are available.

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The role of health visitors and midwives in the identification of perinatal anxiety: A qualitative study

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Introduction Perinatal mental health conditions effect up to 20% of women. The sequelae include maternal suicide, paternal mental illness and childhood developmental and conduct disorders. Perinatal anxiety (PNA) effects 13% of pregnant women, but is under-detected and under-researched. Women with uncomplicated pregnancies and deliveries are managed by midwives (MWs) and health visitors (HVs). This study explores the perspectives of MWs and HVs in the detection and management of PNA.

Patients and methods Ethics approval was obtained. Qualitative study using semi-structured interviews with MWs and HVs in the West Midlands. The interviews were digitally recorded with consent, anonymised and transcribed. An inductive thematic analysis using constant comparison was conducted.

Results Three linked themes will be presented: barriers to detecting PNA, communication, and working within limited resources. Barriers to detecting PNA included lack of continuity of care and perception that women will not disclose their symptoms. MWs and HVs reported poor inter-professional communications, partly due to lack of shared records. HVs and MWs described a lack of training about, and confidence in, the identification and management of PNA, a lack of resources to refer women to, but felt the voluntary (third) sector might have a role in supporting women.

Conclusions More training for HVs and MWs could improve detection of PNA. Sharing of records and face to face contact between HVs and MWs might improve communication. MWs and HVs would value knowledge of the available services, including third sector, to refer or signpost women to.

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Comparison of The *In Vitro* Effects of Local Analgesia with and Without Adrenaline on Osteoblast Proliferation and Metabolism.

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Introduction The aim of this study was to examine the in vitro effects of local analgesic reagents, such as bupivacaine and lidocaine, with and without adrenaline on human osteoblast proliferation and metabolism. This is to further examine the potential negative side effects of local infiltration anaesthesia.

Patients and methods Primary human osteoblasts were harvested from a femoral head and seeded into 96 and 24 well plates. These cells were then exposed to one of: Phosphate buffered saline, 1% lidocaine, 1% lidocaine + 0.0005% adrenaline, 0.5% bupivacaine, or 0.5% bupivacaine + 0.0005% adrenaline for 30 minutes. MTS assay was then used to measure cellular proliferation, OPG ELISA was used to measure respective quantities of OPG production, alkaline phosphatase assay was used to measure osteoblast enzyme activity and confocal microscopy was used to image cells.

Results Cell number and morphology: Cell number and morphology were negatively affected 216 hours post exposure to 0.5% bupivacaine and to an even greater extent when exposed to 0.5% bupivacaine alongside 0.0005% adrenaline. Alkaline phosphatase expression: Alkaline phosphatase is significantly reduced in both bupivacaine and bupivacaine with adrenaline both 24 and 168 hours after a 30-minute exposure. MTS assay: Reaffirmed the confocal microscopy finding that cell number is heavily reduced 24 hours and 168 hours after 30-minute exposure to both bupivacaine and bupivacaine with adrenaline. OPG assay: results showed a clear reduction in OPG levels 24 hours after exposure with a slight increase in comparison to PBS control 168 hours after 30-minute exposure to bupivacaine and bupivacaine with adrenaline.

Conclusions Combination usage of 0.5% Bupivacaine and 0.0005% adrenaline has a rapid and long-lasting negative effect on osteoblasts in vitro. Further study is required.

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Variations in Cerebrovascular Anatomy: perspectives of anatomists and clinicians: A Qualitative study

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Introduction Anatomy education has found itself debating the level at which to deliver content to medical undergraduate students. The core regional anatomy syllabus refers to one singular variant in anatomy despite other significant variants, particularly with the cerebrovascular vessels, which have direct implications with strokes – a debilitating pathology that most if not all doctors will face in their careers. AIM: What are the perspectives of neurosurgeons and anatomists in the teaching of common anatomical variants in vascular anatomy? Three research questions were asked: A) What are the importance, benefits and drawbacks of teaching and learning about vascular variants (with focus on cerebrovascular variants) in undergraduate medicine? B) How do perspectives of neurosurgeons and anatomists differ on the teaching of common variants in vascular anatomy and how clinically relevant / significant is it? C) What are their suggestions on how to deliver anatomy to medical students at undergraduate level?

Patients and methods This qualitative and interpretive research project was based at Hull York Medical School (HYMS) and recruited three anatomists that work with HYMS, and six clinicians (three registrars and three consultants) that have a connection with HYMS. Data was collected using semi-structured, in-depth interviews lasting an hour on average.

Results A) It is important to make students aware of variant 'hot-spots', without detracting from their grasp of 'normal'. B) With increasing specialisation, neurovascular variances only remain pertinent if consultants specialise in vascular neurosurgery. Utility is found in clinicians differentiating pathology from normal variant anatomy and thereby avoiding unnecessary referrals. C) A 'blended approach' of different anatomy delivery tools including virtual reality dissecting tables is suggested with implications considered.

Conclusions Variant anatomy should be touched on, without distracting students from learning 'normal' anatomy. In delivering anatomy content, a 'blended approach' is recommended. Future teaching may even involve virtual reality dissecting tables.

Is Diabetic Nephropathy a disease of misfolded proteins?

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Introduction Endoplasmic reticulum (ER) stress and a maladaptive unfolded protein response (UPR) have been established to play a role in the early pathogenesis of diabetic kidney disease (DKD). ER stress is accompanied by the build-up of misfolded proteins which can be found in the urine of patients with preeclampsia and theoretically DKD. The Congo red assay has been found to bind to misfolded proteins in previous literature in patients with preeclampsia and neurodegenerative disease. Recently, ER stress inhibitors such as ursodeoxycholic acid (UDCA) have been investigated in murine DKD models to show an amelioration of ER stress via the reduced expression of key components of the UPR. However, data on the use of ER stress inhibitors in patients with DKD is limited.

Patients and methods Clinical study: Urine samples were collected from 26 patients including those with and without DKD. The samples were tested for misfolded proteins using the Congo red assay to give a Congo red retention value. The Congo red retention values were compared across the two groups. Laboratory in-vitro study: Mice lung endothelial cells were induced with ER stress using tunicamycin. Some cells were pre-treated with UDCA, whilst others were not and acted as controls. The expression of ATF4 and XBP-1 were measured using real-time PCR in both groups and were compared.

Results Clinical study: Patients with albuminuria have a significantly higher Congo red retention value than those without albuminuria [49.8(26.6-102) vs 29.2(17-41.5), p=0.038], at a protein concentration of 6mg/ml. Laboratory in-vitro study: UDCA attenuates ER stress in mouse lung endothelial cells. The expression of ATF4 and XBP-1 were both reduced in cells pre-treated with UDCA compared to those that were not.

Conclusions Patients with DKD had significantly higher Congo red retention values than those without DKD. The detection of misfolded proteins using the Congo red assay in the urine of patients with DKD could have the potential to act as an early diagnostic marker for the disease, as well as used to monitor treatment with ER stress inhibitors. However, this study was cross-sectional and we can only determine an association. Hence, future work in the form of a prospective study is needed to establish a causative link between the detection of misfolded proteins and the development of DKD. The ER stress inhibitor, UDCA, attenuates ER stress in mouse lung endothelial cells as shown by the reduced expression of key UPR elements: ATF-4 and XBP-1. It will be of interest to see the potential renoprotective effects of UDCA in patients with DKD and future research investigating the mechanisms behind this will be needed.

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Investigating the Effects of BCR Stimulation on the Expression of CCR7 and CXCR5 in Chronic Lymphocytic Leukaemia

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Introduction Chronic Lymphocytic Leukaemia (CLL) is a malignancy of B-cells and is the most common form of leukaemia in the Western World. Signalling through the B-cell receptor drives accumulation of leukaemic cells. In addition, the receptor controls the “homing” of malignant cells to supporting tissue microenvironments by its effects on chemokine receptors, such as CXCR4 (i.e. receptor cross-talk). In addition to CXCR4, there are two less-studied chemokine receptors in CLL, CCR7 and CXCR5. In this work, I investigated effects of BCR stimulation on CCR7 and CXCR5 expression on CLL cells. Furthermore, I characterised effects of clinical kinase inhibitors of BCR on chemokine receptor cross-talk.

Patients and methods CLL samples were recovered for an hour at 37°C and stimulated with either soluble or bead-bound forms of anti-IgM to probe the effect of signal strength (i.e. weak versus strong signal, respectively). CXCR5 and CCR7 expression was quantified using multi-colour flow cytometry. Inhibitors tested were Ibrutinib (BTK inhibitor) and Idelalisib (PI3Kδ inhibitor).

Results Bead-bound (but not soluble) anti-IgM reduced CXCR5 expression at 24 hours (Mean=71.8%, SD=13.7, n=3). By contrast, soluble, but not bead-bound anti-IgM increased CCR7 expression at 8 hours (Mean=144.9%, SD=14.1, n=3). The inhibitors had some effect on anti-IgM-mediated CCR7 regulation, but overall, responses varied greatly between individual patient's samples (n=4).

Conclusions These results illustrate that the BCR modulates chemokine receptors in addition to CXCR4 in CLL cells. Interestingly, these chemokine receptors differ in their response to BCR stimulation in the same sample (i.e. induction versus downregulation, and susceptibility to strong versus weak signals). Further work is required to fully reveal the impact of the BCR on pathways controlling tumour cell tissue homing, and the effect of inhibitors on these pathways.

Investigating the Levels of Pro-apoptotic, Anti-apoptotic and Autophagy Markers in Ibrutinib-Treated Chronic Lymphocytic Leukaemia Patients

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Introduction Chronic Lymphocytic Leukaemia (CLL) is a cancer of B lymphocytes, the clinical behaviour of which is dependent on B cell receptor (BCR) signalling capacity and on anti-apoptotic mechanisms intrinsic to the tumour cell. BCR signalling is mediated by kinases that can now be targeted therapeutically and the first-in-class Bruton's Tyrosine Kinase inhibitor Ibrutinib has shown dramatic therapeutic efficacy with prolongation of survival. Interestingly, it also causes prolonged accumulation of CLL cells in peripheral blood.

This study aims to investigate levels of pro-apoptotic and anti-apoptotic molecules in these circulating CLL cells of patients receiving Ibrutinib treatment.

Patients and methods Levels of the pro-apoptotic protein Bim, anti-apoptotic proteins Bcl-2, Mcl-1 and Bcl-XL, and the autophagy marker LC3B2 were measured by immunoblotting on samples from nine CLL patients undergoing ibrutinib therapy. To indicate apoptosis of cells, PARP cleavage was used. Analysis was performed preceding therapy, at week 1, lymphocytosis peak and month 3/4 of treatment.

Results The levels of pro-apoptotic, anti-apoptotic and autophagy markers were variable between patients. The results showed a mean increase of Bim-EL isoform of 72.1% (p=0.004) at week 1, 127.4% (p=0.004) at lymphocytosis peak and 113.3% (p=0.004) at month 3/4 from pre-treatment levels. However, the levels of Bim did not associate with a significant increment of PARP cleavage.

Conclusions The increase in Bim-EL isoform suggests activated pro-apoptotic mechanisms in the circulating CLL cells during ibrutinib treatment. However, the absence of increasing PARP cleavage suggests that there could be other mechanisms counteracting the effects of Bim. This initial analysis warrants further investigations on the Bim pathway and additional mechanisms that may prolong tumour cell survival during ibrutinib therapy.

A Rare case of intra-parotid dermoid cyst

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Introduction Parotid masses need evaluation. In the paediatric population there is a slightly higher risk of malignancy though the majority of tumours are benign. We present a rare case of a congenital dermoid in a 13 year old girl.

Results A 13 year old female patient presented with a 4 month history of a gradually expanding left parotid swelling. On examination, there was a cystic swelling 2.5x2.5cm in size. Ultrasound and cytology were non-diagnostic. An MRI scan suggested branchial cleft cyst or first arch cyst. A left superficial parotidectomy was performed. Intraoperatively a small tail connected the cyst to the tragal cartilage with no sinus opening into the ear canal. Histology confirmed an intra-parotid dermoid cyst. In retrospect on re-evaluating the MRI scan, a small process extending from the lesion to the tragal cartilage was seen.

Conclusions Dermoid cysts are an ectodermally differentiated form of teratoma. They are rare in the parotid gland. Pre-operative diagnosis can be difficult. However, careful evaluation of cross-sectional imaging can be useful. A parotidectomy is the definitive treatment.

Engaging students with health system learning and structural inequities

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Introduction As healthcare students we have enormous pride in our health service (1). However, we often lack a clear understanding of its structure, its funding, and its inequities (2). Health system learning is often seen as unpalatable, peripheral and complex (3). Yet a significant amount of our work as consultants/GP's will involve leadership roles (4). The purpose of The Health Equity Challenge is to make systems learning accessible, and to increase awareness of the gaps in current service provision, whilst enabling healthcare students of all fields to become more effective advocates, better placed at ensuring health equity throughout their careers.

Patients and methods The campaign creates an interactive learning environment and involves a series of two-hour challenges held throughout the academic year in Manchester. These challenges emulate real life difficulties faced by leaders at different levels of the health service. They are open to students of all health-care fields, as well as prospective students involved with Widening Participation schemes. Experts from the field facilitate each session and provide a sounding board for the attendees as they navigate through the scenarios. The first challenge will be on October 18th, and involves a simulation of commissioning and DevoManc, the Health and Social Care devolution experiment currently occurring in Manchester. Attendees will evaluate their knowledge of NHS structure, resource allocation and inequities before and after the session, as well as evaluating the learning environment provided by the challenge.

Results Data will be collated and used to improve further sessions as well as to offer suggestions to similar initiatives. A more detailed description of the challenge, and findings from the first evaluation, will be presented in poster format.

Conclusions The poster will describe the multidisciplinary and interactive learning environment offered by the Health Equity Challenge, the experiences of the attendees at the first of the challenges and, based on these findings, offer suggestions for further engaging students with systems learning and structural inequities.

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Tpeak – Tend, Tpeak – Tend/QT ratio and Tpeak – Tend Dispersion for Risk Stratification in Brugada Syndrome: A Systematic Review and Meta-analysis

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Introduction Brugada Syndrome is an ion channelopathy that predisposes affected subjects to ventricular tachycardia/fibrillation (VT/VF), potentially leading to sudden cardiac death (SCD). Tpeak – Tend intervals, (Tpeak – Tend) / QT ratio and Tpeak – Tend dispersion have been proposed for risk stratification, but their predictive values in Brugada Syndrome have been challenged recently.

Patients and methods A systematic review and meta-analysis was conducted to examine their values in predicting arrhythmic and mortality outcomes in Brugada Syndrome. PubMed and Embase databases were searched until 1st May 2018, identifying 29 and 57 studies respectively.

Results Nine studies involving 1740 subjects (mean age 45 years old, 80% male, mean follow-up duration was 68 ± 27 months) were included. The mean Tpeak – Tend interval was 98.9 ms (95% CI: 90.5 to 107.2 ms) for patients with adverse events [ventricular arrhythmias or sudden cardiac death] compared to 87.7 ms (95% CI: 80.5 to 94.9 ms) for those without such events, with a mean difference of 11.9 ms (95% CI: 3.6 to 20.2 ms, P = 0.005; I2 = 86%). Higher (Tpeak – Tend) / QT ratios (mean difference = 0.019, 95% CI: 0.003 to 0.036, P = 0.024; I2 = 74%) and Tpeak – Tend dispersion (mean difference = 7.8 ms, 95% CI: 2.1 to 13.4 ms, P = 0.007; I2 = 80%) were observed for the event-positive group.

Conclusions Tpeak – Tend interval, (Tpeak – Tend) / QT ratio and Tpeak – Tend dispersion were higher in high-risk than low-risk Brugada subjects, and thus offer incremental value for risk stratification.

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Castro Hevia 2006; Mugnai 2017; Maury 2015; Letsas 2010; Wang 2007; Zumhagen 2016; Junttila 2008; Morita 2017; Kawazoe 2016.

Endovascular vs Open Surgical Repair for Isolated Ruptured Descending Thoracic Aorta: A Systematic Review and Meta-analysis

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Introduction The purpose of this study was to compare clinical outcomes between open and thoracic endovascular aortic repair in isolated ruptured descending thoracic aorta.

Patients and methods A comprehensive search was undertaken among the four major databases (PubMed, Embase, Scopus and Ovid) to identify all published data comparing open versus endovascular repair. Databases where evaluated to March 2018. Odds ratios, weighted mean differences, or standardized mean differences and their 95% confidence intervals were analysed.

Results A total of 29,133 patients were analysed in 19 articles. Patients undergoing open repair were younger (mean of 54 yrs vs 58 yrs, $p<0.01$). Cardiopulmonary bypass was used in 1% of open repair group. Duration of intensive care and total hospital stay were shorter in endovascular group (4.3 vs 9.9 days, $p=0.003$ and 16.7 vs 12.9 days, $p=0.009$ respectively). Although postoperative stroke and paraplegia were higher in endovascular repair group, but this didn't reach statistical significance 2.4% vs 1.6%, $p=0.47$, and 1.7% vs 0.84%, $p=0.62$ respectively. A rate of 9.5% of endoleak and 4.7% conversion to open was noted in the endovascular group. There was also higher rate of re-intervention at one year in the endovascular group ($p=0.01$). Lower in-hospital mortality noted in endovascular repair ($p=0.003$), while no statistical difference in mortality rates at one and five years ($p=0.51$ and $p=0.33$ respectively) between both groups.

Conclusions The present meta-analysis shows that ruptured descending thoracic aorta that is treated with endovascular repair have satisfactory perioperative outcomes with lower in-hospital mortality, however no differences in mortality rates noted at one and five years among both techniques.

Discussion about lifestyle in mental health consultations

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Introduction Mental health is a traditionally underfunded service, which has made it increasingly difficult for patients suffering with severe mental illness (SMI), to get the help they require. Evidence suggests that discussion of lifestyle during consultations with severely mentally ill patients is lacking and a missed opportunity to improve treatment and care. Research suggests these patients are more likely to undertake risky behaviours as a result of their mental illness. Conversely, patients diagnosed with serious physical illnesses are also at risk of developing mental illness and may then adopt risky behaviours.

Patients and methods The PubMed database was accessed and search terms 'SMI' and 'serious mental illness' were input. The studies retrieved were then filtered down and assessed for inclusion based on studies looking at physical illness in SMI patients. Moreover, how these patients were treated and managed in these different physical healthcare specialties were also considered. Statistics from publications on the Royal College of Psychiatrists website were found to support the findings of this literature review and were included. NHS publications were also referred too, as well as NICE guidelines for recommended treatments.

Results Accumulation of these behaviours and a lack of high quality care, has resulted in development of diseases such as cardiovascular and addiction, and a worsening of mental health symptoms leading to a shorter life expectancy. A disparity between physical and mental health care, poor organisation of these services and a lack of funds appears to contribute and underlie this issue.

Conclusions This review calls for more research and funding towards practitioner education, reorganisation of services and increased mental health screening. This will move mental health care towards parity with physical health care, improving services for all.

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Investigating Cardiovascular Disease in Systemic Lupus Erythematosus

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Introduction Patients suffering from systemic lupus erythematosus (SLE) are at greater risk of developing metabolic syndrome (MetS) and cardiovascular disease (CVD). This is due to traditional risk factors as well as disease-related factors. It is important to establish which aspects of the disease and its treatment cause this increased risk.

Patients and methods Overall, 26 flaring SLE patients (SLE-F), 37 stable SLE patients (SLE-S) and 30 healthy controls (HC) were recruited for a cross-sectional study. SLE-F was defined as BILAG A or B in one or more systems and SLE-S was defined as SLEDAI score ≤4. Traditional cardiovascular risk factors and inflammatory biomarkers were measured for all participants and disease-related factors were measured for SLE participants. The prevalence of each risk factor was compared between the groups.

Results The results confirmed that MetS is more prevalent in SLE and that SLE patients have a greater 10-year risk of cardiovascular events, shown by a significant difference in QRISK3 scores between SLE patients and healthy controls. There was a significant correlation between high-sensitivity C-reactive protein (hsCRP) and the QRISK3 scores ($r=0.271$; $p=0.043$). Univariate analysis showed inflammation and the treatment of SLE as factors driving MetS in SLE. Multivariate analysis of MetS showed a positive model driven by hsCRP (OR 1.183 (1.025-1.366)).

Conclusions Inflammation in SLE may be the cause of accelerated atherosclerosis and the prevalence of MetS in the population. More research needs to be carried out into how inflammatory biomarkers can be used to predict MetS and CVD in SLE.

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An audit of overweight and obese children admitted for surgery: implications for paracetamol overdose

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Introduction Childhood obesity has been established as one of the most detrimental public health concerns with its prevalence increasing at an alarming rate. Worldwide obesity has more than doubled since 1980 (1). Addressing the risks overweight individuals face prior to surgery must be

taken into consideration, such as the possibility of being administered the incorrect dosage of paracetamol medication, leading to a susceptibility to analgesic-induced toxicity (2). The aims of this audit include:

1. To identify the prevalence of overweight and obese children admitted for elective surgery at our institution
2. The incidence of intravenous paracetamol administered according to actual body weight in overweight children.

Patients and methods Following approval from our Trust wide clinical audit committee a prospective audit was undertaken of children admitted for elective surgery over a 4 week period. The age, gender, height and weight of all children admitted for surgery on the day-case ward at the children's hospital were recorded from the patient's admission notes, or through the investigator measuring the patient's height and weight following verbal consent from the patient and parents. The Medscape calculator was used to identify the exact BMI percentile for each child. In addition, the dose of intravenous paracetamol to each patient was obtained from the drug prescription chart. This allowed identification of the incidence of paracetamol over-prescribing in overweight children, by calculating the paracetamol dose according to ideal body weight and subtracting this from the actual dose administered.

Results 18% of boys and 22% of girls were classified as overweight or obese. 17 of the 19 and 15 of the 20 girls were over prescribed paracetamol. The average paracetamol dose over prescribed was 130 mg.

Conclusions The audit revealed that despite the high prevalence childhood obesity children 2-16 years old, less than a 3rd of the overweight and obese children were identified. Auditing children presented to the paediatric surgical department has identified the prevalence of childhood obesity. Secondly, it has been understood that there is a misconception into how to dose overweight children with paracetamol as well as there being a lack of understanding into the susceptibility of overweight children are to being overdosed.

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Perinatal events and atopy in the infant at one year of age

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Introduction Caesarean sections have become increasingly common, yet the long-term effects on the infant are largely unknown. Mode of delivery potentially impacts development of the immune system. Atopy is one of the first signs of abnormal immune function, but current data on the association between mode of delivery and atopy is inconclusive.

Patients and methods This is interim analysis of a recently established prospective birth cohort of 705 healthy, singleton, full-term infants recruited at birth. Infants were followed up at one year for assessment of eczema status and received skin-prick testing for allergic sensitisation.

Infants born by vaginal delivery were propensity-score matched to those born by pre-labour or in-labour caesarean section based on background characteristics. Sensitisation and eczema status at one year were analysed between the matched cohorts.

Results Before matching, 13.56% of pre-labour caesarean section infants had sensitisation at one year, compared to 25.77% of vaginal delivery infants (p=0.004). After matching, pre-labour caesarean section was associated with an 11% lower risk of sensitisation at one year in comparison to vaginal delivery. This difference was not significant using matched pairs analysis (p=0.061), but significant using proportional weighting analysis (p=0.017). This association is not seen in the in-labour caesarean section group. There is no evidence of an effect on eczema.

Conclusions Our findings indicate a weak association between pre-labour caesarean section and a lower risk of allergic sensitisation at one year of age. This supports the theory that reduced exposure to physical and hormonal stress at birth influences immune system development. This is the first mode of delivery cohort study to utilise propensity score matching to reduce the impact of confounding variables, which could be used as a model for future studies.

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Comparison of body composition measurements of breast cancer patients using bioelectrical impedance along with CT derived data: The CANDO-2 Study

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Introduction Agreement between multiple methods of measuring body composition in order to identify those at risk of sarcopenia has not been adequately determined. The hypothesis for this study is that the ability to categorise patients as sarcopenic is not dependent on the choice of

method used to assess body composition, in this case by bioelectrical impedance (BIA) and CT scan analysis.

Patients and methods Twenty women with early stage breast cancer were recruited (age=54±10, BMI=29±6). They had CT scan and BIA measurements after diagnosis but prior to starting chemotherapy. Body composition data was collected and analysed to provide whole body measurements and sarcopenia was classified using cut-offs.

Results Differences between CT and BIA measurements showed significant variability for all individuals for all body composition parameters ($p<0.001$) but there was statistically significant agreement between FFM results from BIA and CT at group level ($p=0.880$). There was variation in classification of sarcopenia between methods (L3 muscle CSAi = 8/20, BIA FFMi = 3/20, BIA SMMi = 4/20).

Conclusions Measurements of body composition and sarcopenia categorisation by CT and BIA are not synonymous. They provided different results and CT was more likely to put patients in the 'at risk' category for sarcopenia. Therefore one method cannot be substituted for the other clinically and it remains unknown which method is correct.

Comparing staff and student neuroanatomy knowledge as a way to inform teaching practices

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Introduction Neuroanatomy is commonly perceived as a difficult topic, although some students choose to attend the annual National Undergraduate Neuroanatomy Competition (NUNC) which tests neuroanatomy beyond the level of the typical medical curriculum. One challenge of teaching anatomy to medical students may be understanding areas of weakness as areas of perceived difficulty may vary between staff and students. The aim of this study is to compare staff versus student performance data in the 2017 NUNC anatomy spotter examination.

Patients and methods 109 students and 13 staff (neuroscientists, anatomists, neurologists and neurosurgeons) completed the 84-part neuroanatomy spotter examination. All questions were assigned a subtopic (Cerebrum, Diencephalon, Cerebellum, Vascular, Brainstem/CN, Spinal Cord or Other). Student and staff scores were compared for each subtopic. Ethical Approval was not required.

Results Staff significantly outperformed students (72.3% vs 54.6%, $p<0.05$). Of the 84 questions asked, the distribution of questions was 17 Brainstem/Cranial Nerves, 3 cerebellum, 30 cerebrum, 8 diencephalon, 11 other (mostly ventricular system, meninges and skull), 3 spinal cord and 12 vascular. Students performed best (>60%) on diencephalon and other, moderately (50%-60%) on spine, vascular, cerebrum and brainstem/cranial nerves, and poorly (<50%) on cerebellum. However, staff performed best (>70%) on spinal cord, other and diencephalon, moderately (60-70%) on cerebellum, cerebrum and vascular, and poorly (<60%) on brainstem/cranial nerves.

Conclusions While staff outperform students in our neuroanatomy spotter, areas of relative strength and weakness differ between the two cohorts. Further study is required to facilitate teachers understand areas of weakness and better direct their efforts in improving student knowledge and understanding.

Medical student attitudes to undergraduate palliative care teaching

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Introduction All doctors face death – however, UK medical schools provide varying levels of palliative care (PC) exposure. Prior studies have found that PC experience promotes reflection and a more holistic approach to patient care; additionally, clinical knowledge of PC is a GMC requirement for new doctors. We aimed to quantify student PC exposure at one UK medical school, determine which methods of teaching students prefer in PC, and what factors affect student thanatophobia ("fear of death") score; likelihood of specialising in PC; and student views on involving terminally ill patients in teaching.

Patients and methods Students from the 2017-2018 Medicine cohort in years 1-5 at Hull York Medical School (HYMS) were surveyed using Qualtrics software. This survey included questions on student background, teaching methods (experiences, effectiveness, and personal preference), and outcomes (likelihood of specialising in PC, thanatophobia score, reflection on involving terminally ill patients in teaching).

SPSS software was used to analyse quantitative data. Qualitative data were coded and extracted into themes.

Results >50% of medical students at HYMS responded to our survey.

Small group seminars, bedside teaching, and speaking to patients were rated most useful; textbooks, e-learning and reflective essays were rated least; compared to other specialties, lectures, speaking to patients and textbooks were considered less useful, and student-selected modules, reflective essays and observing professionals preferred in PC.

Likelihood of specialising in PC was higher in females, after PC-related student-selected modules, or speaking to patients (male students only), but significantly lower in males with no PC experience. Mean thanatophobia score decreased from Year 1 (23.9) to Year 5 (19.83), but extracurricular PC experience significantly lowered Year 1 scores.

"Exposure to terminally ill patients is useful for students" was the most prevalent theme in student reflections across all year groups.

Conclusions Teaching preferences differ slightly in PC compared to other specialties, however teaching involving patients and in small groups appears to be preferred. Several factors, including gender and experience of PC via student-selected modules (indicating a special interest) affect a student's likelihood of specialising in PC. The decrease in student thanatophobia from 1st-5th year may be due to increasing PC exposure over time; this is supported by the fact that 1st years with extracurricular experience had significantly lower scores.

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Uptake of Statin Therapy following Recent Episode of Myocardial Infarction (MI) as a Secondary Prevention of Coronary Heart Disease at a Primary Care Centre in Birmingham

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Introduction Previous episode of myocardial infarction (MI) significantly increases the risk of recurrence and one's mortality by 6-fold[1]. Statin is a lipid-lowering drug used for both primary and secondary prevention of CHD[2]. WHO estimates that patients with CHD on statin therapy experience 30% mortality benefit for every 1 mmol/L decline in cholesterol level[3]. However, following recent controversy in 2013 regarding the efficacies of statin[4], many patients have stopped taking statin for the fear of adverse side effects and are reluctant to be started. One article in Lancet[5] reports a 12% increased risk for patients to discontinue statin for secondary prevention and projects further 2,000 adverse episodes occurring as a consequence. Nevertheless, an updated NICE guideline on lipid modification[6] recommends not to delay statin therapy in secondary prevention of CHD. This project aims to assess the uptake of statin therapy in patients following recent MI.

Patients and methods All patients with history of MI and acute coronary syndrome (ACS) at a primary care centre in Birmingham were extracted from EMIS. After excluding patients who were previously on statin, patients' medication history (along with discharge letter from secondary care hospital and consultation notes) were reviewed to quantify the uptake of statin therapy as secondary prevention of CHD.

Results Of 56 patients with previous episode of MI, almost all patients (except for one) were started on high-intensity statin therapy. In 62.5% (35/56) of patients, statin therapy was initiated either upon discharge from secondary care or within 3 months of initial episode of MI. The remainder of patients were started on statin therapy over the course of few years following their initial MI. Muscle pain was reported in few patients, but this was controlled by lowering the dose of statin and did not result in discontinuation of statin. Statin therapy was discontinued in 14.5% (8/55) of patients as per deranged liver function tests, worsening comorbidities, and patients' request.

Conclusions In secondary care setting, statin is routinely prescribed for all patients with recent episode of MI. Nevertheless, seeing that only 2/3 of patients were on statin therapy at 3 months following an episode of MI, there appears to be continued scepticism toward statin among subset of patients. Continued patient education regarding efficacy and safety of statin as a multidisciplinary effort between cardiologists and GP's will be necessary to bridge the gap in statin therapy.

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Are glucocorticosteroids or beta blockers more effective in treating severe dermal haemangiomas in neonates and infants?

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Introduction Infantile haemangioma is the most common type of birthmark seen in infants. In the past the first line treatment used for the condition was oral glucocorticosteroids. However, since 2008, the use of β-blockers such as oral propranolol has become more popular as a first line treatment. The primary aim of this structured review was to compare the efficacy and safety of oral propranolol in comparison to oral glucocorticosteroids by systematically reviewing current literature on the subject.

Patients and methods The search engines PubMed, Medline and Scopus were used to obtain relevant journal articles. In all cases the search terms 'infantile haemangioma' and 'treatments' were used. Four papers were chosen, these included randomised control trials, meta-analysis and case series. The papers were all published in the last 5 years, written in English, free to access and directly relevant to the title.

Results All four journals which were analysed suggested that propranolol is the most effective treatment for infantile haemangioma and had a higher rate of clearance than glucocorticosteroids. Propranolol also showed fewer side effects when compared to prolonged use of glucocorticosteroids. However, in approximately 10% of cases propranolol was not effective. In such scenarios glucocorticosteroids was shown to be an appropriate alternative treatment choice.

Conclusions It can be concluded that oral propranolol is more effective as first line treatment in most cases. However, in infants who failed to respond to propranolol, short, intermittent, high doses of glucocorticosteroids have shown to be effective.

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Audit assessing the use of Glasgow Coma Scale observations following unwitnessed inpatient falls across a West Midlands Hospitals trust

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Introduction Inpatient falling is a serious issue in hospitals, it can lead to patients feeling unsafe during their stay, lower their confidence and in some cases, even increase their risk of mortality. Where a patient fall was unwitnessed, the possibility of head injury cannot be ruled out and therefore the Glasgow Coma Scale, must be carried out thoroughly to ensure the patient does not deteriorate. NICE guidance recommends the minimum frequency of observations with a GCS equal to 15 post fall should be as follows: Half hourly for 2 hours, hourly for the next 4 hours, 2 hourly thereafter until 24 hours has passed since the fall and If the GCS drops below 15 at any point, GCS measurements should be carried out every half hour until GCS reaches 15 or 24 hours has passed. I aimed to assess whether these guidelines were being adhered to at a west midlands hospitals trust.

Patients and methods Data was collected on patients who had an unwitnessed fall over the month of August 2018, sample size n=89. Study type – a cross-sectional study looking at inpatient falls over the month of August 2018. Study setting – Worcestershire hospitals trust – including Worcester Royal Hospital, Alexandra Hospital and Kidderminster Treatment centre. Data collection – using eZ notes to obtain patient information from notes scanned into the database. Data collected – time and frequency of GCS measurements. Analysis – Data was coded and analysed using Microsoft excel. Inclusion/exclusion criteria – only unwitnessed falls were included in this audit, only falls that had been documented in the patient notes online could be included in this audit.

Results Where GCS post fall was 15/15 it was found that 52.4% of the audit sample had the correct GCS measurements for the first 2 hours, 19% of the sample had the correct GCS measurements for the first 6 hours and 0% had the correct measurements for the full 24 hours. Where GCS post fall was below 15/15 it was found that 13.3% had the correct procedure followed.

Conclusions Adherence to NICE recommendations and hospital guidelines is sub-optimal over the hospitals in this trust. Where wards are often being understaffed and busy, healthcare professionals may prioritise other jobs over regular checking of patient observations, especially if a patient appears well. Therefore, the importance of neurological observations should be promoted among health care professionals as if neurological observations such as the GCS are not regularly checked, a patient who sustained a head injury could deteriorate with negative consequences for the patient and would add to workload for healthcare professionals. Re-audit of this topic should be done annually to assess improvement.

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What Neurodevelopmental Outcomes Are Being Measured In Congenital Infections Including Zika – A Systematic Review Of The Literature

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Introduction There has been emerging interest in outcomes of children affected by congenital infections since the outbreak of Zika virus in Brazil. The virus has been linked to congenital neurodevelopmental disorders in children in LMIC settings where few tools are adapted and standardised to assess children appropriately.

Patients and methods We conducted a systematic review of the literature to identify what outcome measures have been used in children affected by congenital infections (including Zika). We searched Pubmed, Scopus, Google Scholar and Cochrane from 1960 to 2017 to identify studies where outcomes were measured secondary to in-utero viral infections at birth. We collated studies to evaluate coverage of outcomes against the framework of the International Classification of Functioning and Disability (ICF), synthesizing an outcome matrix to understand extent of coverage of domains in the framework.

Results 53 studies were identified with information relating to outcomes measured in children exposed to viral infections in utero from the preterm period to 19 years of age. The most populated ICF-CY domain measured was structure which included microcephaly, eye, ear and neurological structures (using imaging techniques). The functioning domain was also well reported with a wide range of tools used (Bayley Scales of Infant Development (BSID), Teller acuity cards, Auditory Brainstem Responses (ABR), Gross Motor Function Classification, sleep patterns). Few studies reported outcomes in the activities and participation domain and the environmental outcomes of the ICF-CY. 34/53 studies concentrated on microcephaly (58.8% defining microcephaly as OFC ≤2SD, 20.6% as OFC <3%, 3 studies using both definitions and some had no definition). Only 24.6% of studies measured other factors. Almost all of these focused on child development using (BSID) for 0-2 years and cognitive functioning utilizing the Wechsler Intelligence Scale for Children (WISC) (6-17 year olds). Other outcomes measured included; motor functions, vision and hearing but methods of measurement and validity of those measures are vastly under-reported.

Conclusions The review demonstrated lack of cohesiveness and consistency in reporting and measurement of outcomes. Studies focus more on health structure and functioning rather than the other relevant social, psychological and participatory parts of the ICF which may be more relevant for families and children.

A review of the efficacy of TNF biologics used in psoriatic arthritis

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Introduction PsA is an arthritis associated with psoriasis. It is a chronic and debilitating condition with a large burden of disease: mortality is 62% higher in those with PsA, compared to the general population (1). Several treatments are available for PsA such as NSAIDs, conventional DMARDs and biological DMARDs (2).

Patients and methods The Web of Science database was searched for trials of each drug in patients with psoriatic arthritis. Studies with less than 50 patients and studies which were solely open-label were excluded. Most studies assessed drug efficacy by the percentage of drug-recipients and placebo-recipients achieving PsARC, PASI50/75/90 and ACR20/50/70.

Results All drugs reviewed have evidence supporting their efficacy in both the short and long term, as reflected by changes in PASI scores and the increased percentage of those receiving drugs achieving PsARC and ACR20/50/70, compared to the placebo.

Discussion: All studies were double-blind, randomised placebo-controlled trials, which eliminate selection bias and are a rigorous way to assess causal relationships. However, the maximum length of the double-blind portion of these studies was 24 weeks. Furthermore, aspects of some trials such as the dosing regimen and eligibility criteria were not in line with NICE guidelines and the assessment tools for drug efficacy have their limitations.

Conclusions While all drugs are effective, etanercept appears to be less effective on skin manifestations; the most effective drug cannot be ascertained as no studies directly compare the drugs to each other. Various factors will affect the drug prescribed to a patient, such as the patient's needs and preferences, the drug's safety-profile, cost-effectiveness and NICE guidelines. Further research needs to be conducted to test the long-term efficacy of these drugs, as there are no double-blind randomised controlled trials lasting more than 24 weeks.

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NPI-0052 induces apoptosis in patient derived medulloblastoma cells from the most aggressive sub-groups

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Introduction Medulloblastomas are among the most common malignant brain tumours in the paediatric population and consist of at least four distinct subgroups (WNT, SHH, G3 and G4), with unique molecular and genetic features, and clinical outcomes. Current therapy involves aggressive treatment that often leaves survivors with significant neurological and intellectual disabilities, largely due to the effects of nonspecific cytotoxic therapies on the developing brain. Hence, more targeted and less toxic therapies are vitally needed to improve the quality of life of survivors.
NPI-0052 is a second-generation proteasome inhibitor that is able to cross the blood brain barrier and exerts anti-tumour effects in glioma and haematological malignancies.
In the present study, we evaluate the anticancer activity of NPI-0052 in the most aggressive medulloblastoma sub-group.

Patients and methods For this project we use human medulloblastoma cell line and patient derived G3/G4 medulloblastoma cells. In these cells we measure proteasome activity, cell viability, cell cycle, apoptosis and reactive oxygen species, alone and after treatment with NPI-0052.

Results We show that NPI-0052 inhibits proteasome activity in patient derived G3/G4 medulloblastoma cells. Importantly, we demonstrate that proteasome inhibition reduces cell viability and induces apoptosis in a dose-dependent manner. We also observe that NPI-0052 mediates its cytotoxic effects through oxidative stress, p53 stabilization and caspase-3 activation. Finally, we demonstrate that the combination of radiation and NPI- 0052 leads to a synergistic effect on medulloblastoma cell death.

Conclusions The findings of this project raise the possibility that NPI-0052 can be used as an adjunct to radiation for G3/G4 medulloblastoma to minimize treatment related side effects.

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Patient-level factors and short-term postoperative outcomes associated with the conversion of laparoscopic colectomies: secondary analysis of two international multicentre audits

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Introduction The use of laparoscopy for performing colectomies is currently a widely utilised surgical technique. However, despite the frequent nature in which laparoscopic colectomies require conversion to open surgery, the risk-factors and postoperative outcomes associated with laparoscopic conversions remain unclear. This study aimed to identify which patient-level factors predict the need to convert a laparoscopic colectomy, and to compare short-term postoperative outcomes following completed laparoscopic, converted and open colectomies.

Patients and methods Using data collected during the European Society of Coloproctology 2015 and 2017 audits, data on adult patients who underwent a colonic resection, distal to the ileum and proximal to the rectum were extracted. Multivariable multi-level logistic regression analysis was performed to identify patient-level predictors of conversion and to compare adjusted postoperative outcomes (rate of anastomotic leak, surgical site infection, major postoperative complication, mortality and hospital stay >4 days) between groups.

Results Data on 5,148 patients, from 596 centres, across 48 countries were analysed (n=2,369 completed laparoscopic, n=461 converted and n=2,318 open colectomies).

Patient-level factors that independently predicted the need to convert a laparoscopic colectomy were; being aged 50-59 years, male gender, underweight or obese, a current smoker and having an

emergent/urgent surgical indication (all P<.05). When comparing postoperative outcomes, completed laparoscopic colectomies were associated with a reduced rate of all postoperative complications compared to open colectomies (all P<.01). Compared to completed laparoscopic colectomies, converted colectomies were associated with an increased rate of surgical site infections (P=.008) and an increased proportion of patients requiring hospital stays >4 days (P<.001). There were no significant differences in outcomes between converted and open colectomies.

Conclusions Using a large-scale, international database, the need for a laparoscopic conversion was predicted by patient age, gender, body mass index, smoking status and surgical urgency. However, results of this study suggest that, where possible, a laparoscopic colectomy should be attempted in all patients, despite their conversion risk. This is due to the superior postoperative outcomes associated with a completed laparoscopic colectomy and the non-significant differences in outcomes between converted and open colectomies.

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A thematic qualitative analysis of the advantages and challenges of introducing a GP Longitudinal Placement into the second-year medical curriculum

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Introduction The UK population in 2016 was at its largest ever, of which 18% of the 65.6 million were aged 65 and over, set to increase to 24.7% by 2046 (1). With an increasing demand on provision of care for the elderly in the community setting, the capacity of the General Practice (GP) workforce in delivering this mandate is insufficient at present (2). As only 20-30% of UK medical graduates in the last 20 years have indicated their first career choice as a GP, medical schools promoting the primary care setting to students early on in their medical careers is paramount (2) (3). Longitudinal placements in the community setting provide opportunities for students to be involved in continuity of patient care as well as the management of chronic illnesses, showing that students value learning from a defined patient group over a length of time (4)(5).

As part of the new MBBS Curriculum 2020 at GKT Medical School, Year 2 medical students embarked on a longitudinal placement at the same general practice for one day a week (24 days at GP and 6 campus day learning sessions). Commencing in September 2017, 378 students were placed in groups consisting of 6-14 students in general practices based in Central and Greater London, with the same GP tutor acting as an educational supervisor. Learning consisted of teaching clinics, home visits from a patient bank and a humanities group assignment. This analysis evaluates the advantages and challenges of introducing a new GP longitudinal placement into the second-year medical curriculum.

Patients and methods Data was collated from feedback received by GP tutors and students. Data from GP tutors: GP Satisfaction questionnaire, 2 x focus group campus days, Stage 2 evaluation (18 GP Tutors). Data from students: 4 x student focus group, Student Evaluation (242 students). Qualitative data was coded and analysed using NVivo 11. Ethic Approval Code: LRS-17/18-4884 (KCL).

Results Four themes were identified from the GP tutor data:

- Tutor-student relationship, Organisation of the programme, Esteem of GP tutors, Benefits to patients

Four themes were identified from the student feedback:

- Tutor-student relationship, Student's personal development, Changing perceptions of General Practice, Patient encounters and experiences

Findings showed an increase of double in the number of students who would consider GP as a future career after this placement, 83% of GP tutors felt enthusiastic about delivering the programme again next year and 88% of students rated the placement as either "good" or "excellent". Improvements were identified as clearer guidance for the clinical humanities task, more flexibility of the GP programme for tutors on clinical teaching as well as combating disparity in teaching.

Conclusions The longitudinal placement allowed for the development of strong tutor-student relationships, providing both educational and pastoral support, with the satisfaction of GP tutors raised due to observing student progression throughout the year as well as the insight to primary care positively influencing students' perceptions of general practice as a career choice. GP retention rates for the next cohort was 78%, showing the enjoyment by tutors in not only delivering the programme but also the chance to be involved in teaching medical students. The continuity provided to students by having a GP tutor as an educational supervisor throughout the placement saw student's confidence in their clinical and communication skills increase, as well as patients valuing the extra time spent with medical students. These findings strongly support the value of inclusion of the GP longitudinal placement in the second-year medical curriculum and the benefits of exposing students to primary care early in their careers.

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Central vestibular dysfunction mediates imbalance in acute head trauma

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Introduction Imbalance is one of the most commonly reported sequalae following traumatic brain injury [1]. Post-concussion dizziness and imbalance increases the risk of unemployment three fold compared to non-dizzy patients [2].

The brain mechanisms mediating acute post-concussion imbalance are unclear as there are few studies exploring balance in acute head trauma.

Patients and methods This was a single-centre cross-sectional study with adult patients over 18 years of age with a closed head injury and normal peripheral vestibular function admitted to a Major Trauma Centre.

All 10 patients were identified as suffering from imbalance in the acute phase of head trauma (average 13 days since injury). The majority were male (average 57, M:F (7:3) with severe to mild head injury (GCS range 3-14).

Posturography testing [3] and Sports Concussion Assessment Tool 3rd Edition (SCAT3) [4] were used to assess patients. Assessment of balance was defined by the limits of postural stability, under 4 test conditions (Williams' balance order), vision present/absent (Vi+/Vi-), and joint position sense present/absent (Pr+/Pr-); vestibular input was always present.

Results All patients complained of moderate imbalance, dizziness and fatigue. Patient sway was consistently worse than the controls during the vestibular dependent condition (Vi-/Pr-). A three-way interaction was described between group, visual feedback, and proprioceptive feedback. [2x2x2 ANOVA: interaction $p < .05$ for Group Pr Vi].

All patients undertaking the balance component of the SCAT3 (Balance Error Scoring System/BESS) made significantly more errors on the single leg stance and tandem stance than controls where Vi and Pr are challenged (vestibular dependent). (main effect for group test: 2x3 ANOVA; $p < .05$) with the tandem stance the best differentiator between controls and patients ($P<0.0001$; Bonferroni corrected).

Conclusions All acute head concussion patients experienced balance problems manifested a vestibular ataxia, by definition of central aetiology given normal peripheral vestibular functioning. Imbalance is less visible when walking and more prominent under static balance conditions, opposite to that of cerebellar ataxia. Balance dysfunction is more sensitive than cognitive and symptom domains in the SCAT3 assessment.

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Clinical audit of short synacthen tests performed at the Queen Elizabeth Hospital Birmingham

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Introduction The short Synacthen test (SST) is used to diagnose adrenal insufficiency, a condition that can be fatal if untreated (1). The diagnosis is often delayed because symptoms are non-specific, common, and overlap with many other conditions (2). At the Queen Elizabeth Hospital Birmingham, the usage of the SST has been on the rise with associated resource implications. We performed an audit to assess whether the SST was being implemented as efficiently as it could be by reviewing two aspects of SST practice:

1. Patients with traumatic brain injury, cranial irradiation or exogenous steroid use are routinely screened with an SST. We investigated whether the 9.00am cortisol measure could be used to exclude patients who are not likely to benefit from a SST.
2. Patients with vague symptoms which may be attributed to adrenal insufficiency are also tested. We investigated whether there were any particular symptoms, or number of symptoms, associated with failure of the SST, and whether a 9.00am cortisol was checked prior to the test being carried out.

Patients and methods Data on SSTs performed at QEHB over a 12 month period (January 2016 to January 2017) was gathered from hospital databases. With regards to the cohort of patients who are routinely screened (indicated by traumatic brain Injury, cranial Irradiation or exogenous steroid), the sensitivity and specificity of an arbitrary 9am cortisol level cut off in predicting the result of the subsequent SST was calculated. The exogenous steroid group was further analysed with binary logistical modelling. For the cohort with non-specific symptoms, the clinicians' referral reasons were analysed to identify relationships between symptoms/number of symptoms and likelihood of SST failure. It was also verified that each of these patients had a 9.00am cortisol taken prior to referral for a SST.

Results The binary logistical analysis provided a statistical basis to implement a 9am cortisol cut off value in clinical practice. Fatigue, headache, and postural symptoms were the most common reasons for SST referral. There did not appear to be a relationship between any particular symptom and failure of the SST, nor any number of symptoms and failure. A small number of patients were referred for a SST without having had a morning 9.00am cortisol checked.

Conclusions Generally, there is correct usage of the SST although a small number of referrals were identified which appear to be inappropriate and based on limited clinical information. No single symptom or particular number of symptoms are associated with failure of the SST, therefore this should not influence a clinician's decision to test a patient.

Furthermore, we find a statistical model by which to determine a cut off threshold based on the 9am cortisol test in order to optimise SST usage in patients taking exogenous steroids.

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Novel interaction between HSV-1 and host proteins: indication of intrinsic cellular defence mechanism?

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Introduction Herpes viruses are unique amongst viruses in that they exit the cellular nucleus by forming an enveloping bud from the inner nuclear membrane, through the course of the perinuclear space (1).

In the case of herpes simplex virus 1 (HSV-1), this budding is mediated through a nuclear egress complex (NEC) consisting of the viral proteins UL31 and UL34 (2).

The topology of this budding mechanism bears resemblance to the targets of membrane remodelling processes carried out by the cellular ESCRT machinery (3).

In this study, we characterise the localisation patterns of UL31 and UL34, both individually and conjointly. We next aimed to establish whether the NEC interacts with the cellular ESCRT pathway in order to resolve the viral budding process.

Patients and methods The HSV-1 strain KOS proteins UL31 and UL34 were tagged with fluorescent markers and expressed in HeLa cells.

Wide-field fluorescence microscopy was used to visualise the cellular distributions of these proteins.

Finally, yeast two-hybrid assays were used to identify direct interactions between the viral proteins with a library of cellular proteins directly involved in or accessory to the ESCRT pathway

Results Wide-field fluorescence microscopy visualising the fluorescently tagged UL31 and UL34 confirmed that the two viral proteins to interact and localise to the nucleus, in accordance to the formation of the nuclear egress complex.

The yeast two assay showed negligible interaction between both UL31 and UL34 and the ESCRT machinery proteins. However, high levels of interaction was established with an accessory protein named CC2D1A, which is known to be implicated in inhibiting a similar budding process HIV-1 (4). Furthermore, UL31 and UL34 showed little interaction with a homologous protein CC2D1B, which is not implicated in antiviral activity.

Conclusions While this study found that that UL31 and UL34 did not directly interact with any components of the cellular ESCRT machinery, this does not rule out an indirect means of interaction

The key finding of this study was the discovery of the interaction between CC2D1A and the viral nuclear egress proteins. Since CC2D1A is known to be involved in inhibiting a similar budding process HIV-1, it is possible that this interaction is indicative of a cellular defence mechanism against HSV-1 infection. Further investigation is required to further elucidate the nature of this interaction.

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Evaluating current practice of genetic testing offered to breast cancer patients with comedo necrosis and HER-2 positive disease

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Introduction In 2012, it was suggested that comedo necrosis with DCIS or comedo necrosis and HER-2 positive disease is a feature of breast cancer in patients with Li-Fraumeni Syndrome. This condition is an autosomal dominant condition caused by germline p53 mutations, first proposed by Frederick Li and Joseph Fraumeni. It is characterised by an increased risk of breast, bronchus, blood, brain, adrenal and bone tumours, with a life-time penetrance of over 90% in women. It is unclear whether testing women with comedo necrosis and HER-2 positive disease at a young age, or those with a family history with autosomal dominant transmission of early-onset tumours for germline p53 mutations will help detect this condition. We set out to determine whether the Tp53 testing criteria could be used to detect women with germline mutations in Tp53.

Patients and methods (1) A database search of the University of Leicester's Electronic Document and Records Management (EDRM) was used for identifying the audit population through retrospective data collection with a target of reviewing 100% of the sample size for eligibility. (2) A review conducted of all family files used within the last two years and any file number generated from 18000 onwards, from when the Masciari et al paper was published-June 2012. The time used to identify the population was from the 01/01/2012 to 01/01/2018. (3) Using suggested TP53 criteria to determine individuals of the total population whom are eligible for germline testing. We considered germline testing in all referred breast cancer patients with comedo necrosis and DCIS or comedo necrosis and HER-2 positive disease (under the age of 35 at diagnosis or in association with a suggestive family history).

Results From the database search of the University of Leicester's EDRM, within the timeframe specified, 170 individuals (n=170) were deemed eligible for consideration in the time decided upon. Of these, 49 patients (29%) fit the criteria. 12 of the 49 were appropriate for testing and 9 of these have already been tested. Of the 12 individuals, 8 were negative for p53 mutations, 1 was positive

for a mutation in the BRCA2 gene, and 2 declined testing or DNA screening. There are a further 6 individuals who will most likely be tested for p53 and results are awaited.

Conclusions It can be drawn that it is worth evaluating current practice of genetic testing offered to breast cancer patients with comedo necrosis and HER-2 positive disease, with accounting for the Tp53 criteria. Whilst the yield may be small, it is sufficient to argue that without the evaluation, a population of patients with genetic mutations could be missed. There is a precedent to factor this criteria into current determination of eligibility for testing because of the identification of a present positive genetic mutation. It is sufficient enough to warrant a further study of more women in this category.

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A retrospective analysis of patient outcome following surgical excision of axillary Hidradenitis Suppurativa, using split skin graft and vacuum-assisted closure

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Introduction Hidradenitis suppurativa is a chronic, idiopathic condition. It is characterised by inflammation in areas of skin containing apocrine sweat glands, such as the axilla and groin, leading to abscess formation, and scarring. Severe or persistent disease requires wide surgical excision. Methods of wound closure include, but are not limited to: vacuum-assisted closure (VAC); and a combination of split skin graft (SSG) and VAC.

Patients and methods A single-centre retrospective analysis was conducted, evaluating outcomes for all patients receiving surgical excision of axillary hidradenitis suppurativa, with SSG and VAC, or VAC alone. Data was collected from 2014 to July 2018 inclusive. Subjective outcomes measures were obtained through IMPARTS: Integrating Mental and Physical Healthcare: Research, Training and Services, which provides resources for routine collection of patient reported outcome. Data collected include the Dermatology Life Quality Index (DLQI), the Generalised Anxiety Disorder Assessment (GAD-7), and the Patient Health Questionnaire Depression Scale (PHQ-9).

Results 38 patients received SSC and VAC, and 28 patients received VAC alone. Of those, 17 (45%) and 11 (39%) patients, respectively, completed IMPARTS both before and after their procedure. The outcomes for this cohort of 28 patients have been evaluated using paired t-tests. We have found a 17% (p=0.05) improvement in DLQI after intervention. However, while there were improvements in PHQ-9 and GAD-7, of 30% and 7% respectively, and modest improvements in disease severity (4%), and odour severity (6%), these findings were not statistically significant (p=ns).

Conclusions Our study results demonstrate quality of life improvement following excision of axillary hidradenitis suppurativa, with SSG and VAC, or VAC alone. However, our analysis was limited by the low the number of cases for which IMPARTS data collection had been fully performed. We therefore aim to evaluate current practice to ensure that a greater population of patients are offered the opportunity to provide feedback.

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A systematic review and meta-analysis of gender-based differences in the uptake of colorectal cancer screening using flexible sigmoidoscopy.

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Introduction Colorectal cancer (CRC) is the second and third most common cancer in women and in men respectively globally (1). CRC is a major burden on society and there are gender-based differences in incidence and mortality. Incidence is higher in men (746,000) than in women (614,000), and this is reflected in the mortality statistics with men (374,000) having higher mortality than women (320,000) globally (3). In the UK, 22,800 men and 18,400 were diagnosed with CRC, and 8,600 men and 7,300 women died of CRC according to the latest figures in 2014. (2). Screening for CRC is an effective way to reduce its incidence and associated mortality. Systematic reviews have been carried out for gender-based differences in uptake for stool-based test screening but there have no systematic reviews for screening using flexible sigmoidoscopy (FS).

Patients and methods A protocol was written for this study, based on the PRISMA statement. A systematic search on five medical databases (MEDLINE, EMBASE, SCOPUS, Web of Science and the Cochrane central database of controlled trials) was carried out. Screening and data extraction were performed by two independent reviewers at all stages. Data analysis, including the meta-analyses, were performed on the Review Manager 5.3 software. Risk of bias within studies was assessed using the Cochrane Collaboration and the Newcastle-Ottawa scale for randomised and non-randomised studies respectively. Risk of publication bias was assessed and displayed on a funnel plot.

Results Our search resulted in 18 articles from 9 separate studies. 14 of the articles were from large randomised trials from the US-based PLCO trial, from the UK-based FSST trial, from Norway-based NORCCAP trial, from Italy-based SCORE trial and one from the UsK-based Bowel Scope Screening programme. Two articles were from were cohort studies from the UK, one was an observational study from the Netherlands, and one was a randomised study from Sweden. Across the studies, a total of 187,917 individuals were invited and 133,215 attended FS screening (uptake = 70.9%). The overall uptake for women and men was 68.9% and 72.9 % respectively. Women were less likely than men to attend FS screening although this was not statistically significant (odd ratio = 0.90; 95% CI: 0.80 to 1.03; P = 0.12). Two studies reported higher uptake for women and argued that the higher

uptake for women may be due to a female nurse endoscopist in the study. There was significant heterogeneity and inconsistency in the direction of effect across the studies. None of our subgroup analyses, including by use of reminders, age groups, deprivation levels and marital status, provided an explanation of the heterogeneity among the studies.

Conclusions It can be concluded that there is a trend for women to have lower uptake than men for FS screening, although this did not reach statistical significance, and remains to be confirmed in future studies. The main limitation of this study was that gender-based data on uptake were not available for all the studies, which led to several papers being excluded despite involving primary FS screening. Nonetheless, our findings are important in terms of generating a hypothesis, which is whether participants being informed of a female endoscopist will help improve women uptake. Gender-based differences in uptake for screening programmes translate into gender differences in incidence and mortality. It is of utmost importance for future studies and screening programmes to report gender-based data as part of a preventive approach to reduce the colorectal cancer burden on society.

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Cellular Metabolism of Different Macrophage Phenotypes: a Lipidomics Study

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Introduction This research aimed to identify chemical markers of lipid metabolism pathways in 'classically activated' (M1) vs. 'alternatively activated' (M2) bone marrow derived macrophages compared to ‘inactivated’ (M0) macrophages in vitro (historically generated samples). Macrophage polarisation has many medical applications and some pathologies are associated with dynamic changes in macrophage activation. Current research in this field suggests that M1 cells are implicated in initiating and sustaining inflammation and M2 cells resolve or minimise chronic inflammation.

Patients and methods Firstly, we measured the presence and relative concentrations of different glycerophospholipids produced by each distinct macrophage phenotype sample. We then analysed the glycerophospholipid profile of each macrophage phenotype to conclude which type of metabolism had occurred and traced it back to work out whether the macrophage had been classically (M1), alternatively (M2) activated or not activated at all (M0 standard).

Results From our results, we found that the levels of Phosphotidylcholine, Phosphatidylglycerol and Phosphatidylinositol glycerophospholipids were statistically significantly higher in M1 than M2 and that M1 macrophages had a significantly higher level of lysophospholipids. However, the level of Phosphotidylglycerol glycerophospholipids was higher in M2 macrophages.

Conclusions These results seem to suggest that the different macrophage states had undergone a different pathway of metabolism to remodel glycerophospholipids to produce distinct glycerophospholipid profiles in order to meet the specific biochemical requirements of each polarised state. This meant that each macrophage phenotype could perform their opposing functions. Research into macrophage polarisation has exciting potential in medicine and further research into macrophage manipulation may prove therapeutic benefits to patients in many areas of disease.

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The use of clozapine in treatment of early treatment-resistant schizophrenia

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With thanks to National EDEN studies' authors: M. Birchwood, H. Lester, L. McCarthy, P. Jones, D. Fowler, T. Amos, N. Freemantle, V. Sharma, A. Lavis, S. Singh and M. Marshall

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Introduction Clozapine is the only drug with proven efficacy for patients with treatment-resistant schizophrenia. According to NICE guidelines, clozapine should be used to treat "schizophrenia that has not improved despite the sequential use of adequate doses of at least 2 different antipsychotic drugs. At least 1 of the drugs should be a non-clozapine second generation antipsychotic" (NICE, 2014). However, in the UK, only 14-50% of patients with treatment resistant schizophrenia eligible for treatment with clozapine are offered the treatment (Stroup et al., 2009).

This audit aims to provide greater insight into the prescribing patterns of psychiatrists in the UK and help to understand any delays in commencement of clozapine for early treatment-resistant schizophrenia.

Patients and methods Data for this audit was obtained from the national EDEN studies. The EDEN studies enrolled patients from Early Intervention Services across England (Birchwood et al., 2014). The EDEN studies included all patients aged 14-35 with a first presentation of psychotic symptoms. 'Ultra– high risk' patients were excluded from the study, as these patients are not treated as part of Early Intervention Services. The data collected included full drug history (including dosage), number of anti-psychotics prescribed and PANSS (Positive and Negative Syndrome Scale) score; this data was used to assess adherence to NICE guidance when prescribing clozapine.

Results Out of the 61 patients demonstrating treatment-resistance schizophrenia (PANSS >16) and eligible for clozapine treatment; only 5 were being treated with clozapine by 12 month follow up.

Some patients were trailed on up to 5 different anti-psychotics before being prescribed clozapine; despite NICE guidance stating patients are eligible for clozapine after not responding to 2.

Conclusions This audit concluded that, nationwide, there are significant delays in commencement of clozapine treatment for eligible patients with early treatment-resistant schizophrenia. Recommendations include education for psychiatrists on the known efficacy of clozapine and alteration of the NICE guidelines to discourage delays in prescribing clozapine and encourage greater continuity in prescribing practice in the UK.

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Haplotype Analysis of the LOC400706 and Caecam 16 region at the Myotonic Dystrophy Type 1 locus

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Introduction Myotonic dystrophy type 1 (DM1) is an autosomal dominant disorder which affects the skeletal muscles, heart, eyes and brain. The disorder is caused by an expanded CTG trinucleotide array in the 3'-untranslated region of the DMPK gene.

Patients and methods Genomic DNA of 2 Mb around the DMPK gene was sequenced, where tandem repeats and multiple SNVs were detected as new variants in two regions, Caecam 16 and LOC400706. These SNVs were subsequently analysed and found to be present in unrelated DM individuals, however not shared among related DM individuals. This unusual phenomenon was therefore investigated through haplotype analysis of these two regions. This project aimed to investigate the ancestral origin of mutation, at the same time find a new genetic marker linked to DM1.

A total of 355 DNA samples were analysed for three different groups- Generation Scotland, a large collection of human control DNA samples, and DMGV and Quebec population, which consist of DM1 patients from Scotland and Saguenay-Lac-Saint-Jean region of Canada respectively.

Results The results showed high variability in the LOC400706 region but not in the Caecam 16 region. DNA sequencing revealed that the repeat units of 24 base pairs in LOC400706 were 100% homogenous whereas the repeat units of 42 base pairs in the Caecam 16 region exhibited sequence polymorphisms.

For LOC400706 region, our analyses showed an overrepresentation of 12 and 13 repeat units in the DMGV population, and an overrepresentation of 14 repeat units in the Quebec population. Generation Scotland showed a wide spread of values, which was expected from an unbiased sample.

Conclusions The overrepresented alleles were suggested to be the alleles linked to DM1 chromosome, and therefore LOC400706 can potentially serve as a new genetic marker for DM1, and will be able to help map the relatedness of DM1 families in the general population.

Relevance of thrombophilia testing in patients undergoing ilio-femoral venous stenting for post-thrombotic occlusion

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Introduction Inherited and acquired thrombophilias increase the risk of venous thromboembolism (VTE), and the antiphospholipid antibody syndrome (APS), an acquired thrombophilia, is associated with a high risk of recurrent VTE. Post-operative anticoagulation therapies remains tailored, with APS patients requiring long-term vitamin K antagonists (VKA) compared with direct oral anticoagulants (DOACs) for patients with inherited thrombophilia. As such, ilio-femoral venous stenting in patients with thrombophilia is controversial. The aim of this study was to examine the association of thrombophilia with cumulative patency and re-intervention rates following stenting for post-thrombotic occlusion.

Patients and methods Consecutive patients (2012-2017) receiving a nitinol venous stent for post-thrombotic disease with a minimum of one-year follow-up were included for analysis. Thrombophilia testing was performed when VTE occurred at a young age with: weak provoking factors; or strong family history; or recurrence. Patients with strong risk factors for VTE were not tested, and excluded from analysis. All patients were given therapeutic dose low molecular weight heparin divided twice daily for 2wks post-procedure, followed by a VKA for 6mths. Patients with APS continued on long-term VKA therapy at 6mths, while all other patients were transitioned to DOACs. Stent patency was assessed using duplex ultrasonography 24hrs, 2wks, 6wks, 3mths, 6mths,1yr and yearly post intervention, and re-interventions performed when there was a reduction in stent diameter of >50% or occlusion.

Results Of 205 patients treated, 138 (67%) were tested for thrombophilia, of which 59/138 (43%) had an inherited 30/59 (51%) or acquired 29 (49%) thrombophilia (Table 1). Cumulative patency was 88% for patients with thrombophilia, and 89% in patients without (median follow-up 1.7yrs; range 52-258wks). Additionally, 64/138 (46%) patients required re-intervention to maintain patency, of which 28/59 (47%) occurred in patients with thrombophilia, and 36/79 (45%) without. Inherited or acquired thrombophilia was not associated with cumulative patency loss (P=0.402), or higher risk of re-intervention (P=0.255).

Thrombophilia Type	Patients tested for thrombophilia n=138
Thrombophilia negative	**79 (57%)**
Inherited	**30 (22%)**
Factor V Leiden	22 (16%)
Prothrombin gene mutation	0 (0%)
Protein C	2 (1%)
Protein S	2 (1%)
Antithrombin	4 (3%)
Acquired (Antiphospholipid antibody syndrome)	**29 (21%)**

Table 1. Outcome of thrombophilia testing in patients without strong provoking factors for VTE

Conclusions Thrombophilia assessment for APS should be performed in patients undergoing ilio-femoral venous stenting without strong provoking factors for VTE as prolonged anticoagulation with VKA is advised in this patient group due to their increased risk of VTE recurrence. Furthermore, patients with inherited or acquired thrombophilia should not be excluded from ilio-femoral venous stenting as patency outcomes are good in conjunction with appropriate post-operative anticoagulation therapy.

The use of wearable technology to monitor patients receiving chemotherapy

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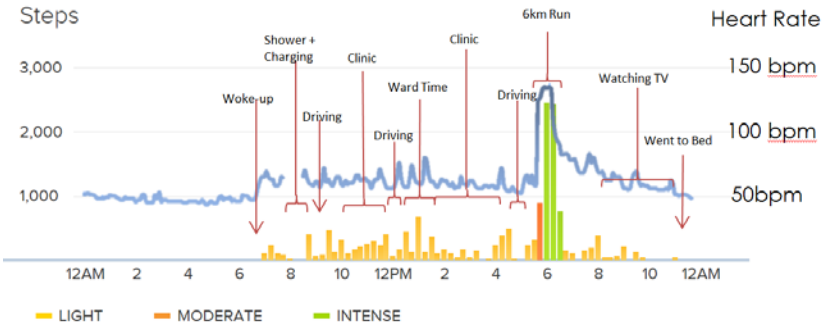
Introduction The explosive rise in demand for wearable technology over recent years has sparked significant interest in its use in remote monitoring of patients. Chemotherapy causes complications that occur predominantly in an out-of-hospital environment. This study aimed to investigate the potential for the remote monitoring of patients, to enable earlier detection of complications, such as neutropaenic sepsis, thereby eliminating delays in intervention, reducing admissions and costs, increasing patients QoL and ultimately reducing mortality.

Patients and methods To test patient enthusiasm, questionnaires were developed for chemotherapy patients and their carers to record their opinions on overall care and follow-up, levels of anxiety and depression during treatment and desire for further monitoring. Following a review of commercial fitness monitors, three devices (Fitbit Charge-HR, Jawbone Up-3 and Pulse-Ox) were chosen for head-to-head comparison, which resulted in selection of the Fitbit. Subsequently, healthy volunteers wore the device for 1 week, while keeping a diary of activities and completing a questionnaire.

Results 39 patients (average age 62 years, 24 men) and 29 carers (average age 59 years, 7 men) completed the questionnaire. Responses confirmed 67% of patients and 68% of carers were very willing to allow biometric data to be remotely monitored. While 64.1% of patients agreed that closer monitoring would directly improve their care. Interestingly, greater levels of treatment-related anxiety were recorded in carers compared to patients (GAD-7 7.11, 95% CI 6.23 – 7.99 vs 4.78, 95% CI 3.74 – 5.80, P=0.0004).

Pilot studies in 11 volunteers demonstrated the Fitbit's ability to accurately capture data on heart rate, activity levels, and sleep (see figure). However, problems were encountered during this study, primarily around the software available to remotely access and interrupt live data.



Conclusions This study demonstrated a clear enthusiasm among oncology patients and carers for remote monitoring through the use of wearable technology. Furthermore it has confirmed the capability of existing monitors to capture objective and quantifiable data accurately. The technology is advancing rapidly and becoming more affordable, and it can be anticipated that soon it will be possible to monitor further parameters such as temperature, glucose, ECG and oxygen saturation. The imminent roll-out of 5G technology will also enhance remote data capture. Further studies are required to confirm patient benefit but the greater challenge moving forward will be real-time data analysis. With 8000 patients per year receiving chemotherapy at the Christie, automated algorithms will be required to reliably recognise a deteriorating patient and trigger an appropriate response.

Ancestry differences in T-wave symmetry of 58,858 individuals from the UK Biobank Study

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Introduction Malignant arrhythmias are associated with sudden cardiac death (SCD), which accounts for ~20% of mortality in the general population (1). Previous studies have demonstrated that the electrocardiogram (ECG) is a powerful non-invasive diagnostic tool for the prediction of arrhythmic risk (2). Spatial dispersion of ventricular repolarisation is associated with higher arrhythmic risk (3) and is reflected on the T-wave symmetry and morphology (4). SRarea is a parameter reflecting the T-wave morphology and describes the symmetry ratio between the T-onset-to-peak area and the T-peak-to-end area. It represents both the spatial symmetry and temporal synchronicity of the whole repolarisation process. Higher heart rate (inverse of RR) alters the dispersion of ventricular repolarisation (5), and results in a more symmetrical T-wave (6). This makes the symmetry of the T-wave a promising arrhythmic risk predictor. Langley et al. reported the SRarea in healthy individuals to be 1.68 ± 0.25 (mean ± SD) (7). However, the sample size was very small (N = 20) and only included individuals of European ancestry. We aim to determine the reference values of SRarea in a significantly larger cohort and investigate differences related to ancestries.

Patients and methods UK Biobank (UKB) is a prospective study of volunteers from the general population with baseline and follow-up data on clinical, biochemical, genetic and outcome measures. We have approvals from UK Biobank (application number 8256) to perform analyses of the ECG dataset. For this project, we analysed 1-lead ECG recordings during 15 seconds at rest from 58,858 individuals. Individuals with a history of cardiovascular conditions and those taking heart-rate altering medications were excluded prior to analysis. We first located the onset, peak and offset

timings of the waveforms within each heartbeat using in-house processing algorithms. Then, we derived a representative average heartbeat using all the available heartbeats. SRarea, RR and T-wave amplitude (TAmp) were derived from these average heartbeats. Correlation was evaluated with Spearman's correlation coefficient and multi-linear regression models were applied including these covariables: age, BMI, systolic and diastolic blood pressure, sex, diabetes, cholesterol, smoking and ancestry. The Mann Whitney U test was used to test the statistical significance of the difference between groups.

Results The mean (±SD) SRarea was 1.400 (± 0.633) and showed a low correlation ($\rho<0.5$) with TAmp, RR or any of the continuous covariables, p-value < 2.2e-16. SRarea was lower in females (p-value < 2.2e-16), diabetics (p-value < 2.2e-16), individuals with high cholesterol (p-value < 2.2e-16) and non-smokers (p-value = 1.725e-06). The ancestry of the population was as follows: 92.7% European, 2.46% African, 2.77% Asian, 0.60% Chinese and 1.51% mixed. The SRarea was found to be significantly lower in Europeans (1.382 (± 0.630) compared to other ethnicities; 1.738 (±0.624) in Africans, 1.508 (±0.617) in Asians, 1.725 (±0.606) in Chinese and 1.559 (±0.647) in mixed, p<2.2e-16. Multilinear regression analyses revealed the resting RR interval to be the only covariate significantly contributing to SRarea irrespective of ancestry. Mean (±SD) values of resting RR were significantly higher in Europeans (0.861 (±0.142) sec) compared to Africans (0.852 (±0.135) sec, p=0.006), Asians (0.851 (±0.136) sec, p=0.001), and mixed (0.851 (±0.140) sec, p=0.026). In contrast, we did not find significant differences in RR between Europeans and Chinese (0.867 (+/-0.132), p=0.415). A likely explanation is the low sample size of this population.

Conclusions We observed SRarea to be lower than previously reported by Langley et al. (7). SRarea values were significantly different across ancestries and it was significantly modulated by the RR interval for all ancestries. These observations across different ancestries will need to be validated in additional samples, but future works are warranted that ancestry and RR interval should be taken into consideration when using T-wave symmetry or other T-wave morphological parameters from an ECG for arrhythmic risk prediction.

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Incidence and risk factors for acute kidney injury after total joint arthroplasty; a retrospective cohort study

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Introduction Acute Kidney Injury (AKI) is a common complication post-arthroplasty, although it has not been extensively studied. We carried out a retrospective study to determine the incidence and risk factors of AKI in patients undergoing total joint arthroplasty (TJA).

Patients and methods We reviewed the medical records of all patients who underwent elective TJA from December 2014 to January 2017 at the Salford Royal Hospital, UK. AKI was defined using the AKIN, RIFLE and KDIGO criteria in patients with worsened renal function post-arthroplasty. We analysed the association of the demographics, risk factors, medications and use of peri-operative IV fluids with AKI. A logistic regression was performed to find any correlation between these factors and incidence of AKI.

Results 197 patients were included in our study, the mean age was 70.2 and male to female ratio was 6:5. Of these, 32(16.2%) developed an AKI. The multivariate logistic regression revealed 4 independent factors associated with the risk of AKI; age (P =0.0011, OR 1.07, 95% CI 1.03-1.18), obesity (P =0.003, OR 6.4, 95% CI 2.34-17.5), smoking (P =0.0482, OR 3.76, 95% CI 1.01-14.0) and COPD (P =0.0253, OR 3.85, 95% CI 1.18-12.5).

Conclusions The incidence of AKI post-arthroplasty was found to be much higher than stated in other literatures. The recognition of the high incidence and multiple independent risk factors will allow a better approach to peri-operative management, limiting the risks of AKI. Our study also highlighted the importance of documenting urine output and the need to repeat the renal function test 3 months after an AKI to assess recovery.

GP Perceptions of Perinatal Anxiety in Women: Implications for Medical Education

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Introduction Perinatal mental health describes conditions that start during pregnancy and the first-year post-partum. The most common conditions are depression and anxiety disorders. Perinatal anxiety (PNA) is under-reported but may have higher prevalence than depression, however, research and clinical attention typically focuses on the latter [1]. Poor management of PNA is associated with negative impacts on both maternal health and the child's cognitive and emotional development, in addition to increasing demand on services [2]. Currently the National Institute for Health and Care Excellence (NICE) have not developed guidelines for the identification and management of PNA in women; PNA has therefore been identified as a research priority. This study aims to explore GP experiences and perceptions of current practice in the provision of care to women with PNA and their impact on contemporary medical education.

Patients and methods Secondary qualitative analysis of semi-structured interviews with GPs in the West Midlands about their experiences and perceptions of managing women with PNA. Consent to use research data in future research was obtained in the original study and transcripts were already

anonymised. Thematic analysis using principles of constant comparison was conducted with key themes agreed with the research team.

Results Nine transcripts were analysed identifying key themes: awareness of PNA and use of diagnostic tools; relationships between GPs and other clinicians; communication with women and need for training.

Conclusions This study has implications for undergraduate and postgraduate medical education, emphasising the importance of integrated professional education (IPE) and the value of continuous reflective practice.

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Care of the paediatric solid organ transplant patient in the UHNM surgical day-case

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Introduction In response to a solid organ transplant patient having a surgical day-case procedure at the University Hospital of North Midlands (UHNM), we assessed the preparedness of the unit to appropriately care for such a patient.

Patients and methods A questionnaire was produced asking staff (unit nursing/allied staff and consultant paediatric anaesthetists) how they feel that the unit is able to care for such patients.
A single-page questionnaire was completed by volunteers on the UHNM paediatric day-case unit and collected over a 3-week period during July and August 2018.

10 staff members responded.

Deductive analysis of the feedback comments was undertaken.

Results The results showed that there is little experience amongst the staff on the unit with caring for transplant patients. They also lack confidence in their personal ability to care for these patients. Only one respondent had undergone specific training for care of transplant patients – they detailed that this was whilst working for a different Trust. The majority felt that UHNM is able to provide safe care despite staff having little experience with this group of patients, comments relating to this question highlighted a of ‘lack of training’ and ‘infection exposure risk’. The staff detailed the changes that they would like to see implements within the unit as ‘infection control protocol’ and ‘creation of guidelines’. Qualitative feedback analysis of the free comments section identified the themes of deficiencies in ‘training’ and ‘ward facilities’ which have led to staff members experiencing a ‘lack of confidence’.

Conclusions The staff have little overall experience in caring for transplant patients and have not received any specific training from the Trust. This has therefore led to a lack confidence in their

ability to care for this group of patients. However, the majority felt that UHNM was able to provide safe care despite this.

The implications of this review of the quality of care the unit provides suggests that staff may feel that they can provide better quality care to transplant patients if they were to receive specific training, ward facilities were modified to cater for them and/or Trust guidelines were created in order to assist their work.

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Reduced thalamic and putamen volume associated with autistic traits and depressive symptoms in First Episode Psychosis: A Voxel-based Morphometry study

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Introduction Schizophrenia, autism spectrum disorders (ASD) and depression exhibit a significant elevated co-occurrence compared to the general population. Due to the elevated symptom co-occurrence within all three conditions, an exploratory investigation was undertaken to reveal any underlying neuroanatomical commonality between ASD traits and depressive symptoms, within first episode psychosis (FEP), due to poorer health outcomes these comorbidities can lead to.

Patients and methods A sample of 20 individuals with first episode psychosis (FEP) were recruited from early intervention services. Severity of ASD traits and depressive symptoms were assessed using the: Autism Spectrum Quotient (AQ) and Positive and Negative Syndrome Scale (PANSS). Participants also underwent a T1 weighted MRI scan. A conjunction whole brain analysis was conducted to explore an association between severity of ASD traits and depressive symptoms with changes in total grey matter volume (GMV).

Results A significant negative correlation was revealed between both an increase in AQ social deficit and an increase in PANSS depressive scoring with GMV reductions in the right thalamus, extending into the right putamen.

Conclusions Dysfunction within these structures can lead to impaired reward prediction and failure to assign reward value to social interactions. This could manifest itself in FEP as both the social deficit traits seen in ASD and social anhedonia associated with depression.

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When doctors are patients: identity, illness, and idealism in twentieth-century medical autobiography

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Introduction Over the last hundred years, the number and prominence of physicians writing about their own illnesses (especially mental illness) has increased. This research presents a history of physician illness narratives over the twentieth century; exploring their emergence in social and historical context.

Patients and methods The research aims to demonstrate the changes in physician illness narratives and examine the experience of mental illness in physicians. It is interdisciplinary in nature; applying principles of history, sociology, phenomenology, and critical theory.

Results Vignettes in the early century have progressed to dedicated memoirs in the modern day. The use of anonymity and the nature and choice of wording give insight into historical and current stigma associated with mental illness in physicians. These narratives provide evidence that the transition from 'doctor' to 'doctor-as-patient' is significantly stigmatised, particularly from within the medical profession. Early texts justify their publication in the combination of objective and subjective knowledge gained by the ill doctor, but this shifts to a rationale based on combatting stigma and offering support to colleagues. Ideals of the physician as strong and resilient appear to persist across the century, and medical culture often continues to hold the individual accountable for their illness and the impact of this on their career.

Conclusions Where the voice of the ill doctor is gaining power, this research emphasises the importance of addressing the challenges they face. Despite increased support services for doctors experiencing illness, many of these texts describe an oppressive nature of medical culture, recount stigmatising attitudes from colleagues, and ineffective treatment methods. These narratives highlight the consequences of a profession resistant to change.

Confirming Transcription of Clinically Relevant P. knowlesi Pknbpxa Variant in Experimental Parasites Genetically Modified at the Pknbpxa locus.

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Introduction Plasmodium knowlesi is a protozoan parasite that mostly causes simian malaria but has also been found to infect a large number of humans in South Eastern Asia in recent years. Four other human malarias not including P. knowlesi have been recognized and studied but an effective in vivo model that can be translated into clinical medicine has not yet been produced from these. There is an overwhelming burden of malaria around the world with no adequate prophylaxis and drugs that struggle to successfully get rid of the disease. As P. knowlesi both affects humans and primates and lends itself to stable transfections, it is an ideal species to manipulate in hope of developing efficacious malaria therapies. By observing P. knowlesi invasion characteristics we believe we have

the best chance of finding a mechanism to target malaria, in particular the Pknbpxa gene which expresses a protein key in blood stage P. knowlesi erythrocyte invasion.

Patients and methods Our aim was to confirm transcription of a previously transfected clinically relevant allele at the Pknbpxa locus in an experimental line of P. knowlesi adapted to long term human erythrocyte culture. We achieved this by amplifying cDNA from harvested PkTF2-8 parasites with Pknbpxa site specific primers. The amplicons were then run in agarose gel electrophoresis and resulting nucleic acid fragment migration compared along a 100bp DNA ladder to ascertain whether any transfected PkTF2-8 cDNA was amplified.

Results We were thus able to confirm that the knocked in allele was transcribing and functional.

Conclusions As the transfected allele was sequenced from parasites associated with higher disease severity, we can look to associate function of this allele with clinical outcomes in the hope to contribute towards a malaria vaccine and further drug development. With resistance to drugs on the rise and no current viable alternative, it is vital to find an appropriate translational model and solution to the global health malaria dilemma.

Postgraduate abstracts

Maternal and Perinatal Outcomes in Teenage Pregnancy Between Indigenous & Non-indigenous. Is there a difference?

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Introduction Teenage pregnancy is a worldwide problem. There are about 16 million teenagers between the age of 15-19 years old giving birth every year, contributing to 11% of total deliveries worldwide(1). This is becoming a greater concern not just in developed countries, but more so in developing countries, where social welfare support may be lacking. According to World Health Organisation (WHO), teenage pregnancy is defined as 'teenaged or under aged girl, usually within the age of 13-19, becoming pregnant'. Teenagers or adolescence (Latin = to grow) is the transition at which the carefree child becomes a responsible adult. It is often characterized by rapid somatic changes of sexual maturation as well as personality and biological maturation. Pregnancy in teenagers is a common occurrence worldwide and its rated vary between countries due to the differences in level of sexual activity, law and policies in teen marriages, sex education provided and access to contraception. There seems to be quite significant variation in teenage pregnancy and birth rates worldwide, with developing countries significantly higher than that of developed countries(2). By far, UK has the highest incidence of teen pregnancy in Europe while USA has the highest incidence among other developed countries which ranges from 0.9% to 21%(3). This study was conducted in Sarawak, which is a state in Borneo of Malaysia. It focused to look into both maternal and perinatal outcomes in teenage pregnancy among indigenous and non-indigenous group.

Patients and methods It is a retrospective analysis of case records of teenage pregnancies from January to December 2014. The subjects gave birth in the Department of Obstetrics and Gynaecology, Sarawak General Hospital (SGH), Kuching, Malaysia. Maternal and perinatal outcomes of teenage <19 years old were compared between indigenous and non-indigenous group. A total of 970 teenage pregnancies were analysed using Chi Squared test and Logistic Regression analysis in SPSS Version 24.

Results The overall teenage pregnancy rate in 2014 in SGH was 8.3%. Indigenous population has a higher teenage pregnancy rate with 10.2% rather than 7.9% among non-indigenous. This study has also shown that indigenous teens are more prone to be single than married during pregnancy and that they have significant risk of going into caesarian section delivery and having low birth weight babies.

Conclusions In conclusion, the study shows that overall teenage pregnancy rate among indigenous population is higher than non-indigenous. It was also found that indigenous teenage have higher caesarean section rates and low birth weight.

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Identifying High Density Mineralised Protrusions (HDMPs) in Human Spines using MRIs and CT scans from Public Databases

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Introduction High-density mineralised protrusions (HDMPs) arise as extrusions of the mineralised matrix into clefts of the hyaline articular cartilage. HDMPS are believed to significantly contribute in the mechanical destruction of the joint. Being previously identified in hip and knee joints of AKU patients, this research aims to identify HDMPs in other weight bearing joints, in particular the spine. Previous techniques used to investigate the joints using decalcification and embedding in paraffin did not reveal these projections, therefore using imaging method was considered to be an alternative technique to further investigate these projections. The novel aspect of this research lies on using public databases as its main resource, allowing the coverage of a larger number of images.

Patients and methods Radiopedia.org was the main online resource. Covering a total of 350 static & 3D images, the age of the patient, gender, the level where HDMPs were identified and the relation of these projections to any pathological changes that might have occurred at the vertebrae were all taken into consideration. The number of slices that showed HDMPs in 3D images was also recorded.

Results HDMPs were identified in both genders, commonly among the adult group with 85% of them in the thoracic and lumbar spine. HDMPs were also found not to be related to any spinal pathological changes.

Conclusions This research provides evidence that HDMPs are not related to ageing, as expected, and that they have the potential of being normal micro-anatomical structures within the spine.

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Exploring non-clinical staff experiences of participating in Yorkshire and Humber patient safety huddles: A qualitative study

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Introduction Communication errors are the leading cause of patient harm in the National Health Service - causing 255,000 patients to suffer serious disability or die annually. In attempt to provide safer and better quality care, implementation of patient safety huddles (PSH) has been rising in the UK, specifically Yorkshire and Humber (Y&H). These PSH are unique in including non-clinical staff. Hence, there is a global paucity of research regarding non-clinical staff experiences, all conducted in North America. Transferability of these findings cannot be inferred to the Y&H PSH hence, empirical research is important.

Aims To explore the common themes non-clinical staff experience participating in PSH and the perceived effect they have on the patients, wards and staff.

Patients and methods Wards (n=3) were recruited within Leeds Teaching Hospitals NHS Trust (LTHT). All wards recruited had sustainable PSH with continual non-clinical staff participation. These staff were approached and semi-structured interviews (n=8) were conducted. All interviews were audio- recorded, transcribed and thematically analysed. Ethical approval was received from University of Leeds, SoMREC.

Results Nine themes were identified in relation to the study aims. Three themes address PSH staff experiences: 1) Role and contribution 2) PSH barriers and 3) PSH facilitators. Six themes address the perceived PSH effects: 1) Saving time, 2) Awareness 3) Integration through communication 4) Personal development through new opportunities 5) Supportive, level playing field and 6) Our patients and the NHS.

Conclusions Non-clinical staff experiences revealed implementation of PSH favourable on our patients, wards and LTHT. Furthermore, barriers and facilitators non-clinical staff experienced are key to the valuable learning in making PSH a sustainable intervention.

The length of time taken to provide written feedback in mini-Clinical Evaluation Exercises (mini-CEXs) in the e-portfolios of foundation doctors

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Introduction Supervised learning events (SLEs) are tools used as part of the online e-portfolio (HORUS) to record the progress of foundation doctors and give the opportunity for trainers provide feedback (1). The mini-Clinical evaluation exercise (mini-CEX), first described in 1995, is an SLE where the foundation doctor is observed performing a clinical exercise; it was introduced because of growing evidence at the lack of feedback doctors in training received (2). Good quality feedback is paramount to the development of foundation doctors and it has been shown that systematic feedback can lead to improvements in clinical performance (3) (4). Participant responsiveness is one of two key characteristics of mini-CEXs that are positively associated with its educational impact (5). While it is often recommended that feedback should be given in a timely manner (6), there are no guidelines on the definition of timely feedback. The aim of the study is to assess the length of time taken to provide written feedback for a mini-CEX in the portfolio of foundation doctors at the Royal Liverpool and Broadgreen University Hospital.

Patients and methods 50 foundation year one (FY1) doctors at the Royal Liverpool and Broadgreen Hospital NHS Trust, employed between 01st August 2017 and 31st July 2018, were sent email invitations to take part in the study. 30 FY1 doctors replied to the email invitation and gave their consent for their mini-CEXs to be analysed. The dates between the clinical event and the sign off by the trainer were analysed in Excel.

Results 30 (FY1) doctors were included in the study. 281 mini-CEXs were collected from the trainees, 260 of which were signed off by a trainer. 22 days was the mean number of days from date of clinical event to sign off by the trainer. 8% of mini-CEXs (n=21) were signed off on the same day as the clinical event. 33% of mini-CEXs (n=87) were signed off between 2 and 7 days, 17% (n=45) were signed off between one week and two weeks and 20% (n=52) were signed off between two weeks and four weeks after the clinical event. 21% (n=55) of mini-CEXs were signed off more than 4 weeks after the clinical event with the longest date to sign off being 207 days.

Conclusions This study demonstrates great disparity in the length of time taken for trainers to provide written feedback to foundation doctor trainees. Feedback may be less effective if it is not given to the trainee promptly and with enough time to implement meaningful change. 21% of mini-CEXs were signed off greater than 4 weeks after the clinical event. We propose that a 4-week interval could be considered too long for reliable recall of the clinical event from both the trainer and trainee, which may reduce the effectiveness of feedback. Further education for trainers and trainees on the importance of timely feedback is required to ensure that every mini-CEX provides the trainees with effective feedback and the time to improve their performance. There is further scope to assess the relationship between the quality of written feedback and the length of time take to provide written feedback.

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Interdisciplinary Dementia Teaching

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Introduction According to the General Medical Council's guidance "it is essential for good and safe patient care that doctors work effectively with colleagues from other health and social care disciplines" (1).

Despite this many of the undergraduate health care degrees rarely incorporate interdisciplinary teaching opportunities into their curriculum. Healthcare students are expected to work with other disciplines and understand the integration of their roles despite there being little formal undergraduate experiences of this (2).

Patients and methods An interdisciplinary dementia crash course was designed to allow all undergraduate healthcare students to work collectively to better their understanding of dementia care. The two-hour course was established in 2016 and continues to run twice per year. The course incorporates the Alzheimer's Society initiative 'Dementia Friends' which aims to promote a

'dementia friendly' society with increased awareness about dementia and motivation to improve the lives of those living with dementia. In addition to addressing health promotion and reducing stigma the course includes a review of the aetiology, history, examination, investigations, categorisation of and management of dementia. The sessions also offer students the opportunity to share their experiences in caring for patients living with dementia.

Results A total of 5 courses have been conducted, attended by a total of 118 students. Feedback was collected on the content, relevance and delivery of the sessions. Additional feedback across the 5 sessions was collected on the perceived benefit of interdisciplinary teaching and the demand for further multidisciplinary teaching. Amongst the randomised sample of 40 students feedback, 100% of students 'strongly agreed' that multidisciplinary teaching is beneficial and also that it should be conducted more commonly.

Conclusions Dementia is an appropriate topic for an inter professional teaching approach. Interdisciplinary teaching has many well documented challenges but can be extremely rewarding once this resistance is overcome. This paper demonstrates that interdisciplinary dementia teaching can be beneficial to all professions involved and that there is a demand for further interdisciplinary teaching.

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Mechanical thrombectomy: comparative cases in the context of neurointervention provision in the North West of England

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Introduction Following numerous recent clinical trials, mechanical thrombectomy has been incorporated into the National Clinical Guideline for Stroke, NICE guidance and the American Heart Association Stroke Council's guidance on early stroke management. However, despite the identified efficacy of thrombectomy in selected patients inadequate service provision is resulting in missed opportunities for reducing the stroke related disabilities and improving quality of life for patients with ischaemic stroke in the North West of England. The North West of England is the third most populated in the United Kingdom and is home to three neurointervention centres. These three neurointervention centres provide a '9-5' weekday service for a population of over 7 million people.

Patients and methods A comparative case report of two young stroke patients demonstrates the physical, economic, psychological and social impacts of mechanical thrombectomy and the impact of inadequate out-of-hours service provision in the North West of England.

Results Case reports include Mr A who received IV thrombolysis which was followed by mechanical thrombectomy and Mrs B did not. The thrombectomy patient, Mr A, returned to near normal functioning whilst Mrs A, unable to receive thrombectomy; experienced a 7 months hospital stay complicated by a venous thromboembolism requiring tracheostomy in the high dependency unit.

Conclusions Stategies to improve mechanical thrombectomy provision include improved education on thrombectomy and rapid patient selection which must be paralleled by increasing availability of services. An increasing demand will result in an inexcusable need for increased neurointerventionist training and posts to increase the capacity of the current neurointerventional centres in the North West of England which will translate to better patient outcome as demonstrated in the comparative case reports.

THE INTRODUCTION OF AN OPT-IN SYSTEM FOR COMPRESSION STOCKINGS AND ITS IMPACT ON VTE RATES IN PATIENTS WITH NECK OF FEMUR FRACTURES

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Introduction Compression stocking are widely implemented as part of VTE prophylaxis in patients admitted with neck of femur fractures. However, a recent multicentre randomised control trial in stroke patients presented data advocating review of such practices with high levels of stocking associated complications (skin tears, ulcers, skin necrosis) whilst demonstrating a non- significant risk reduction in the VTE rates in stroke patients[1]. As such, we trialled the introduction an 'opt-in' system for the prescription of compression stockings in the NOF patient population.

Patients and methods NOF admission data was collected retrospectively using a computer generated randomised sequence in stage one of the audit. The opt-in system for compression stockings was then introduced as standard practice across the department. Stage 2 of the study collected data in a prospective manner re-auditing rates of VTE, mortality, prescription/application rate of compression stockings and compression stocking associated complications following the introduction of the 'opt-in system'.

Results The rate of both prescription and application of compression stockings was reduced with the introduction of an 'opt-in system'. No statistically significant difference in rate of VTE ($P>0.05$) and mortality was noted with the introduction of an 'opt-in system'. However, the data demonstrated a statically significant reduction in compression stocking associated skin tears ($P=0.0002$).

Conclusions The data supports the use of an 'opt- in system' for compression stocking prescriptions in patients with neck of femur fractures and prompts review of automated use of compression stockings in similar patient populations.

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An Audit on Trastuzumab for the Treatment of HER2-Positive Gastric and Gastro-Oesophageal Junction Cancer

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Introduction Trastuzumab is a monoclonal antibody against human epidermal growth factor receptor 2 (HER2) used for many years in breast cancer. It has recently been shown to significantly improve progression-free survival (PFS) when included alongside chemotherapy in patients with metastatic gastric and gastro-oesophageal junction (GOJ) cancers: a breakthrough finding for patients with otherwise poor prognosis. The same large multicentre randomized controlled trial (ToGA 2010[1]) also showed no significant increase in adverse events using Trastuzumab. We studied the effectiveness of Trastuzumab in our own patient population, audited against the findings of ToGA.

Patients and methods All twenty-three patients on trastuzumab for HER2-positive gastric and GOJ cancer were followed up for 24 months. The gold standard was ToGA's median PFS of 6.7 months. Data were extracted from electronic patient records including: demographics (age, gender, ECOG performance status [2], ethnic origin), histology (primary tumour site, HER2 expression status), radiological assessment (computed tomography-defined staging, metastatic sites and date of disease progression) as well as any adverse effects recorded in clinic letters or hospital discharge summaries. Findings were analysed using Kaplan-Meier curve and calculation of median PFS (with 95% confidence interval).

Results Similar to ToGA, our study population was on a regime of trastuzumab, cepecitibine and cisplatin as well as being a predominantly male population (87%), ECOG performance status 0-1 (90%) and with HER2 overexpression (93-100%).

Differences between our population and ToGA include: ethnicity and primary tumour site.

- Ethnicity: 96% Caucasian and 4% Asian compared to ToGA's 39% Caucasian, 51% Asian and 10% Other
- Primary tumour: 87% GOJ, 13% gastric compared to ToGA's 20% GOJ, 80% gastric.

A single patient reported nausea and vomiting. There were no other adverse effects reported. Over a median follow-up period of 24 months, our study showed a significantly increased median PFS of 10.5 months (95% CI 9.6 - 14.5), compared to ToGA's 6.7 (95% CI 6.0 – 8.0).

Conclusions Our study has reaffirmed the benefit of trastuzumab inclusion in chemotherapy regimens for metastatic GOJ and gastric cancers. Additionally, it raises the important discussion of whether GOJ tumours benefit more from HER2 targeted therapy than gastric tumours – a finding to be explored in future research.

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Quantified three-dimensional characterisation of the ultrastructure of decellularised unscarred and scarred human dermis using a combined atomic force microscopy and multiphoton imaging approach with future implication for human skin substitute design

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Introduction The three-dimensional (3-D) spatial arrangement of dermal tissue plays a crucial role in directing cellular behaviour during wound healing. Thus, it is crucial to elucidate a better understanding of the three-dimensional dermal architecture of the human skin. The aim of this project was to understand the configuration in morphological structure of decellularised human dermis between unscarred skin and normal cutaneous scars.

Patients and methods Skin samples were obtained from ethically consented volunteer patients undergoing Abdominoplasty surgery. All skin samples underwent decellularisation (DNA removal = 88%.). Histological sections of cellular and decellularised dermis were subsequently analysed using standard haematoxylin and eosin (H&E), and 4',6-diamidino-2-phenylindole (DAPI) stains. In addition, extent of decellularisation was quantified using an Easy-DNATM isolation kit. Biomechanical and structural evaluations were performed using atomic force microscopy (AFM) and Multiphoton Microscopy (MPM).

Results Interestingly, there was no change in the gross morphology of decellularised unscarred and scarred dermis, under light microscopy. However, MPM and AFM showed that collagen fibers in unscarred decellularised dermis were arranged randomly. Collagen fibers of decellularised unscarred dermis appeared to have a significantly rougher (Rq-16.5, Ra-12.5, Rmax-198; $p<0.0001$) surface topography. Based on AFM reduced modulus values, collagen fibers of unscarred decellularised dermis were less stiff (mean 2.155 MPa ± 0.9595; $p<0.0001$) compared to decellularised scarred dermis. MPM demonstrated that collagen fibers in unscarred dermis are interwoven, akin to a mesh-like structure. Furthermore, scarred dermis had a higher collagen volume density (papillary dermis, $p<0.0082$; reticular dermis, $p<0.0332$).

Conclusions Decellularisation of unscarred and scarred dermis was successfully achieved which enabled evaluation of unique micro-architectural differences between intact and injured skin. The parameters addressed in this study may help in developing engineered scaffolds for dermal wound repair. Ideally, the scaffolds should exhibit a mesh-like structure with a rough surface and low stiffness, which represents the microenvironment of unscarred dermal tissue.

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Non-purulent low-grade infections in nonarthroplasty shoulder surgery: from skin commensals to opportunistic pathogens, impacting diagnosis and treatment

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Introduction Recent studies have identified the diagnostic challenge of low-grade infections after shoulder arthroplasty surgery. Infections after nonarthroplasty procedures have not been reported. This study assessed patient-related risk factors, outcomes, and clinical presentation of low-grade infection after open and arthroscopic nonarthroplasty shoulder surgery.

Patients and methods The cases of 35 patients presenting with suspected low-grade infection were reviewed. Biopsy specimens taken at revision surgery were cultured in the sterile environment of a class II laminar flow cabinet and incubated for a minimum of 14 days at a specialist orthopaedic microbiology laboratory. Patient-related factors (age, occupation, injection), index surgery, and infection characteristics (onset of symptoms, duration to diagnosis, treatment) were analysed.

Results Positive cultures were identified in 21 cases (60.0%), of which 15 were male patients (71%). Of all patients with low-grade infection, 47.6% were male patients between 16 and 35 years of age. Propionibacterium acnes and coagulase-negative staphylococcus were the most common organisms isolated (81.1% [n = 17] and 23.8% [n = 5], respectively). Of 14 negative culture cases, 9 were treated with early empirical antibiotics (64.3%); 7 patients reported symptomatic improvement (77.8%). Of 5 patients treated with late empirical antibiotics, 4 stated improvement. Patients presented with symptoms akin to resistant postoperative frozen shoulder (persistent pain and stiffness, unresponsive to usual treatments).

Conclusions Young male patients are at greatest risk for low-grade infections after arthroscopic and open nonarthroplasty shoulder surgery. P. acnes was the most prevalent organism. Patients presented with classic postoperative frozen shoulder symptoms, resistant to usual treatments. Interestingly, 78.6% of patients with negative cultures responded positively to empirical treatment. Clinical Relevance: In patients with a resistant and persistent post-operative pain and stiffness surgeons should consider and investigate for low-grade infection, particularly in young males. The causative organism should be sought with tissue biopsies and cultured in extended cultures in a sterile laboratory. The most common organisms are Propionibacterium acnes and coagulase negative staphylococcus, but empirical treatment is still successful in most cases when cultures are negative.

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Comparison of two Severity screening tools (PSI VS. CURB65) in adult patients with Community Acquired Pneumonia (CAP)

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Introduction Community acquired pneumonia (CAP) is one of the most common presentations to secondary care. There are two main risk-stratification systems for patients with CAP, CURB-65 commonly used in the UK and PSI in the North America. There are very few studies carried out to compare these two scoring systems. (1,2)

We conducted a retrospective observational study to review the superiority be-tween the two named systems. This was completed on a cohort of patients admit-ted to an NHS District Teaching Hospital with a definite diagnosis of CAP from May/17 to Dec/17.

Patients and methods Total of 65 cases were delivered by random selection from the Trust's medical records as the diagnosis of "pneumonia", out of which only 35 cases had the definite diagnosis of CAP. 60% of the cases were male and the mean age was 58+/-38 (ranging from 20 to 96). Each case's calculated CURB-65 score was confirmed followed by retrospective calculation of their PSI score, which was then classified into the four main PSI categories accordingly.

Results In our NHS Trust, CURB-65 was calculated for 80% of patients ranging from minimum of 0 to maximum of 4 with no patients scoring 5 on their initial assessment. There was a total of 13 cases scoring 0 and 1 which according to the national guidelines all should have been discharged and dealt with in the community; however, they all needed an acute bed after clinical assessment. (1)

There was found to be a positive correlation between the severity of score and both mortality and length of stay (LOS) with 0% mortality for those scoring 0 and 100% for those scoring 4. The morality in those with score of 3 was as high of 50%. The total number of mortality was reported as 12 claiming nearly one-third (34%) of the entire cohort. The average length of stay for the cohort of patients was approximately 10 days. Furthermore, it was noted that those who were admitted with lower CURB scores were most likely to be either on higher spectrum of age or to be suffering from multiple co-morbidities, especially COPD, renal or heart failures. This would align with the room for "the clinicians judgement" in the NICE/BTS guidelines on the destination of care and the choice of antimicrobial therapy. (1,3)

As per PSI scoring system and its respective categories, out of the 35 cases, five were classified as category 1 with 0% rate of mortality. There was a total of 10 patients in category 2 with 10% mortality rate following IV ABx therapy. Categories 3 and 4 constituted most of the admissions (total of 20, i.e., 57%) and indeed had the highest number of mortality (91%). (2)

Conclusions While both the PSI and CURB-65 lacked in correctly risk stratifying the least severe cohort of the patients, PSI was indeed a more accurate representation of the dis-ease severity amongst the inpatients with CAP. This is most likely for correctly taking into account firstly the patient's co-morbidities and next their further laboratory and radiological findings. Nevertheless,

there still needs to be more comprehensive, multi-centred clinical trials evaluating the use of PSI scoring for the UK cohort of patients.

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The Value Of The Frozen Section as a Diagnostic Tool For Intraoperative Management Of Ovarian Lesions

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Introduction Ovarian cancer is one of the most common cancers affecting females worldwide. Traditionally, ovarian lesions were histologically analysed postoperatively due to the time involved to prepare the paraffin slides (Srinivasan et al., 2002). Alternatively, a 'frozen section' is a fast histological analysis that allows the clinical team to alter a treatment plan during surgery (Novis and Zarbo, 1997). Despite the benefits of a frozen section, the diagnostic accuracy may be reduced (Ratnavelu et al., 2016).

The aim of the project was to complete an audit of all ovarian frozen section cases performed in Auckland City Hospital, New Zealand, in order to determine its diagnostic suitability in cancer management and its effect on patient management.

Patients and methods The pathology records, multidisciplinary meeting notes and surgical operation notes of cases which involved ovarian frozen section between 01/01/2014 and 31/12/2017 were searched electronically, and the data analysed.

Results A total of 123 cases had an ovarian frozen section. 12.2% of cases had a discordant diagnosis between frozen section and paraffin slides. The sensitivity and specificity of the frozen section for benign are 97.96% and 90.16%, for borderline 82.35% and 93.68%, and for malignant 82.00% and 98.41% respectively. In 12.2% of cases, the diagnosis was deferred to paraffin slides. Only in 44.7% of cases, the frozen section was mentioned in the surgical operation notes. In 17.4% of cases, the frozen section did not appear to have any impact on the patient intraoperative management.

Conclusions The results of this study are comparable with the results presented in other published studies. Utilising a frozen section when diagnosing borderline tumours is challenging and has the greatest potential for error. Some of the cases demonstrated that the frozen section was not utilised appropriately.

Frozen section is a valuable and accurate diagnostic tool which can aid intraoperative decisions, however, the surgeons and pathologists should be aware of its limitation and be selective when to utilise it.

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Analysis of ATR Mutations and Expression in HPV-positive and -Negative Head and Neck Cancers

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Introduction The Human Papilloma Virus (HPV) infection is an important risk factor for head and neck squamous cell carcinomas. Previously, the lab had identified mutations in the ataxia-telangiectasia and rad3-related (ATR) kinase, a mediator of the DNA damage response. Notably, these mutations were only present in HPV-negative, but not –positive HNSCCs. However, the role of ATR and the subsequent effect of its mutations in HNSCCs remain unknown. This investigation aimed to study and compare the role of ATR signalling in HPV-positive and –negative HNSCCs, after its activation by UV radiation.

Patients and methods Using the COSMIC database, HPV-positive and -negative HNSCC cell lines with wild-type ATR, were identified. To investigate changes in ATR signalling over time, UV-treated cells were harvested at different time-points. Western blot was conducted to analyse the expression of ATR and its downstream effectors, checkpoint kinase 1 (Chk1) and phosphorylated histone H2AX (γ-H2AX). Additionally, the effect of increasing UV dose on ATR signalling was also studied using Western blot.

Results Results from the experiments indicate a previously unseen biphasic expression of ATR after 25mJ of UV radiation, with a peak at 15 minutes and 8 hours. Conversely, there was a relative reduction of γ-H2AX expression at all time-points except at 30 minutes, and 16 and 24 hours compared to untreated cells. In UV dose studies, the HPV-negative HSC3 cells were shown to have a lower expression of ATR and Chk1 compared to the HPV-positive HeLa cells at all doses.

Conclusions Preliminary results from this investigation provide an exciting insight into the pattern of ATR signalling induced by DNA damage in HNSCCs. This study also identified differences in ATR signalling between HPV-positive and –negative tumours. Further work will help elucidate the role of wild-type and mutated ATR in tumours. The ultimate goal is comprehensive understanding of the genetic heterogeneity of HPV-positive and -negative HNSCCs.

Investigating the Potential of a Novel ER Stress Indicator in Breast Cancers

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University of Southampton (Research taken place at King's College London)

Introduction Multiple stressors can cause disruption to the normal protein folding process in cells. The subsequent dysfunction results in aggregation of unfolded proteins at sites such as the endoplasmic reticulum (ER). This is known as ER stress and if uncontrolled, would eventually result in cell death. However, cells utilise the unfolded protein response (UPR) to prevent apoptosis from occurring. This process is beneficial in normal cells but is exploited by cancer cells to promote survival and treatment resistance. To examine the role of UPR within cancer cells, a sensor to detect ER stress is required. Therefore, this study aims to generate and evaluate an ER stress biosensor through which quantitative data can be gained for analysis.

Patients and methods To create the sensor, XBP1, a mediator of ER stress, and the fluorescent protein mCherry were amplified and ligated into the green fluorescent protein vector, p-EGFP-C1. The sensor was then subsequently transfected into cells and ER stress was induced using tunicamycin. The sensor discriminates cells under ER stress through the splicing of XBP1, which occurs as part of UPR. The expression of mCherry is reliant on the successful splicing of XBP1. Hence only cells under ER stress express both GFP and mCherry, whereas all other cells with the vector would solely express GFP.

Results When analysing results, GFP expression in cells was used as a measure of sensor uptake, while mCherry expression was used to indicate ER stress. Treatment with tunicamycin resulted in increased mCherry expression compared to no treatment, indicating the successful construction and validation of a novel ER stress indicator.

Conclusions The successful creation of an ER stress biosensor for quantitative analysis holds great promise. Now the sensor can be utilised to progress studies examining the role of ER stress in oncogenicity. This would help address the issue of therapeutic resistance in cancer, resulting in improved outcomes of patients.

Change in BMI (Body Mass Index) after Total Hip or Knee Replacement

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Patients and methods To identify the trend in BMI in patients who undergo sequential consecutive knee/ hip replacement in ipsilateral/contralateral lower limb based on BMI recorded during pre-operative assessments to improve counselling patients and meet their expectations regarding their BMI status prior to and after surgery. We studied 362 patients with 2 sets of BMI's. They all had knee or hip replacement consecutively over a variable time scale. We used their pre-operative assessment BMI's and compared the change with respect to time and overall result.

Results As we studied over 200 patients, it was a parametric distribution. We analysed the data by linear regression and found that the BMI value increases over time suggesting that patients by and large gain weight over time after consecutive lower limb arthroplasties.

Conclusions In conclusion, patients need to be counselled properly regarding outcomes of arthroplasty. Patient may have pain relief, may or may not have improved mobility which may or may not necessarily improve BMI status post surgery.

An audit of compliance with guidance for pathological examination of sentinel lymph nodes.

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Introduction Patients presenting with primary breast cancer require sentinel lymph node biopsy for staging. Histological samples form the basis of diagnosis and treatment of primary breast cancer. This audit reviewed the compliance of histological sentinel lymph node samples to a nationally-agreed criteria by the Royal College of Pathologists.

Patients

- 20 patients with sentinel lymph node histology were randomly selected from a local pathology centre over one calendar year (2015/16).

Methods

- Two researchers reviewed all sentinel lymph node histology blocks to assess for appropriate sectioning. This was achieved by counting the number of slices on each patient's histopathology slides.
- Data was compiled using an Excel spreadsheet.
- The nationally-agreed standard is that a sentinel node >5 mm in size should be sliced at intervals of 3mm or less. Sentinel nodes <5 mm in size should be bisected and blocked in their entirety.
- Expected compliance was 100%.

Results

- The 20 patients produced 21 sets of histological slides.
- 13 samples had ≥1 slice per 3mm (62%).
- 8 samples had <1 slice per 3mm (38%).
- Only 62% of patient received the correct amount of histological slices based on nationally-agreed criteria.
- Expected compliance was 100%.

Conclusions In conclusion, only 62% of patients received the correct number of histological slices, with 38% having inadequate slices per mm.

Possible contributing factors include:

- Lack of familiarity with standard
- Quality of biopsy specimen
- Incorrect measurement of lymph node at cut up

This research project highlights the need for vigilance in monitoring nationally-set criteria, and ensuring that this is widely publicised and adhered to. Following presentation and education to the department, we aim to re-audit using the updated histological dataset published by the Royal College of Pathologists.

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Time-Limited Trials (TLTs) and the role of time on the Intensive Care Unit (ICU): a qualitative study

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Introduction When patients on the Intensive Care Unit (ICU) do not improve with invasive treatment, it may be in their best interests to withhold (i.e. not start) or withdraw (i.e. stop) treatment. These decisions are fraught with uncertainty, but observing the patient's treatment response over a period can be helpful. Time-Limited Trials (TLTs) are 'an agreement…to use certain medical therapies over a defined period to see if the patient improves or deteriorates'[1]. They aim to prevent inappropriate treatment and improve communication with the family[2]. Time in healthcare is often portrayed negatively by clinicians, especially in the context of political targets (e.g. 4-hour A&E waits). However, time on ICU appears to have a more complex role. TLTs are uncommon in the UK, with limited research on TLT length and clinical perspectives. This study offers perspectives of ICU clinicians, explores barriers to TLT uptake, time required for treatment response and the role of time on ICU.

Patients and methods Eighteen participants (nine doctors and nine nurses) were recruited from ICUs at two small teaching hospitals within the same trust in North West England. Recruitment was voluntary, using poster and email adverts to ICU staff, and staff had varying levels of experience. Participants were doctors or nurses with experience of withdrawing or withholding care on ICU. Ethical approval was successfully sought. One-to-one semi-structured interviews were conducted, lasting 25 to 90 minutes, in Jan-Feb 2014. Interview transcripts were loaded on to Nvivo 11.4.1.1 and thematic analysis was performed. Other members of the research group validated codes and results.

Results Intensivists already use time to see whether patients respond to treatment and to give the family time to process their experiences. Thus, some participants saw TLTs as no different from current practice. Potential barriers are that TLTs are not appropriate for all, it will increase the number of end of life decisions, treatment may prolong the patient's life inappropriately and they can lack continuity. Timeframes for TLTs ranged from 1-10 days, though these were generally not disease specific. Nurses believe they reach conclusions quicker than doctors and participants would be quicker to withdraw treatment for family members than as a professional. The roles of time are manifold: as a tool, a message, a gift, as evidence and as a connection. Different clinicians value time differently.

Conclusions The role of time on ICU, compared to other specialties, is unique. TLTs ensure decisions are made in a timely fashion by providing explicit time limits, preventing "plodding along" (S1-D3-C). TLTs were not completely understood by intensivists on these units and teaching intensivists would maximise the effectiveness of TLTs. Communication is key and involving palliative care colleagues in difficult discussions may help shift focus to relationship-building with families[3]. Research is required to decide on disease-specific TLT durations.

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The Role of Autophagy in Breast Cancer Progression and Angiogenesis

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Introduction Autophagy maintains intracellular homeostasis, through a complex process of self-digestion of cell contents within autophagosomes. It has been extensively associated with breast cancer, acting as both a tumour-suppression mechanism, and a driver of tumour progression. Additionally, autophagy has been associated with physiological angiogenesis, however little is known of its influence on tumour angiogenesis. Tumour angiogenesis is a well-known necessity for tumour growth and progression to metastasis, and has been targeted to improve outcomes in cancer, unfortunately with mixed results. Breast cancer survival is drastically reduced in the metastatic stage; therefore, prevention of metastases through inhibition of tumour angiogenesis may improve survival outcomes.

Patients and methods Mice with Atg16L1ΔWD mutation were injected with MMTV-PyMT-derived breast cancer cells. This specific mutation impaired function of Atg16L1, an essential protein for autophagosome formation. Tumour volume was measured to compare growth of tumours. Immunohistochemical staining of endomucin within tumour sections was used to assess growth of blood vessels. In addition, endothelial cells were studied in vitro with either Atg16L1ΔWD mutation or siRNA depletion of Atg16L1. Western blotting was used to analyse expression of key proteins within angiogenesis pathways, while endothelial cell motility was assessed using random migration assays.

Results No effect was observed on growth or vascularisation of tumours when Atg16L1 function was impaired in mice. However, in vitro analysis of endothelial cells showed expression of eNOS was significantly reduced with impairment of autophagy ($p<0.05$), while a random migration assay showed reduced motility with impairment ($p<0.01$) or depletion of Atg16L1 ($p<0.05$).

Conclusions These findings demonstrate a potential pro-angiogenic role of autophagy, via expression of eNOS and effects on endothelial cell migration. Further study of this role in physiological and tumour angiogenesis may reveal novel targets for anti-angiogenic therapy in breast cancer.

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Does early versus late initiation of RRT for patients with AKI improve patient survival outcome?

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Introduction Acute kidney injury (AKI) is a common disease affecting approximately 13–18% of all hospital inpatients(1) and has a mortality rate between 25-30%.(3) Studies have shown that AKI is poorly recognised by clinicians, with 43% of patients having a late diagnosis.(13) The National Confidential Enquiry into Patient Outcomes and Death (NCEPOD) showed that half of all patients who died with AKI were not managed appropriately.(13) Given that one fifth of patients who are diagnosed with AKI could have been prevented, there has been a large drive within healthcare to ensure high quality guidelines for AKI based upon robust evidence.

NICE argues that early initiation of RRT may increase patient overall outcomes such as a reduction in morbidity.(16) However, this must be balanced against the risks and side effects of RRT that patients would be exposed to such as infection or haemorrhage. Since the evidence behind NICE's guidelines was between the years 2002 to 2010,(16) this review aims to critically appraise current research on whether early versus late initiation of RRT in patients with AKI improves patient outcomes.

Patients and methods The methodology consisted of entering search items such as [Renal Replacement Therapy AND early initiation] into the following databases: Pubmed, Medline and Web of Science. Strict exclusion criterion such as articles publication dates between 2015 and 2017 provided the most up-to-date research. Early RRT was defined as immediate whereas late was greater than 72 hours after randomization.

Results The findings from this review found that one out of the three studies found statistically significant reduction in mortality with early initiation of RRT. (table 1). The Zarbock et al. also noted significant secondary outcomes of reduced hospital stay and improvement in renal function. The remaining studies found statistically significant secondary outcomes that included a reduction in hospital stay by 31 days, an enhanced recovery of renal function and a decreased duration of RRT.

Study	Study Design	Sample Size		Primary outcome		Significance value
		Early	Late	Early	Late	
Gaudry et al. (2016):	RCT, multi-centre	312	308	48.5%	49.7%	P=0.79
Zarbock et al. (2016)	RCT, single-centre	112	119	39.3%	54.7%	P=0.03
Wald (2015)	RCT, multi-centre	48	52	38%	37%	P=0.92

Conclusions Overall, the findings on early initiation of RRT in AKI were inconsistent. Given that the evidence behind NICE's recommendations for RRT in AKI are graded low to moderate quality as well as the discrepancies found from this review, it would be appropriate for further studies evaluating survival impact from early RRT.

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A feasibility study investigating the Rotation Illusion Test for Age-Related Macular Degeneration (RITA) using tablet technology

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Introduction The aims of this study were to investigate the feasibility of the tablet-based Rotation Illusion Test for Age-related Macular Degeneration (RITA) in eyes with neovascular Age-Related Macular Degeneration (nAMD). The properties of RITA that were investigated include the relationship between RITA scores and other measurements of visual function (visual acuity, VA, and optical coherence tomography, OCT) and the test-retest repeatability.

Patients and methods A sample of 39 participants with an established diagnosis of nAMD in at least one eye were recruited from a UK ophthalmology clinic. The first two weeks of the study involved preliminary testing. 8 of the 39 participants were involved and only recommendations for RITA development were collected during this period. During the final testing phase, 31 participants performed RITA followed by VA testing in their study eye. RITA was then repeated. Participants then continued along their usual treatment pathway, including OCT imaging. Participation was for a single visit only.

Results Patient acceptability and practicality was good following RITA developments made during preliminary testing. 1 participant was excluded from the study analysis due to difficulties testing VA. The mean age of participants was 79 years and no relationship was found between age and RITA score. Gender analysis revealed men scored slightly higher in RITA. With increasing structural damage on OCT, participants scored lower in RITA. A weak relationship was found between RITA and VA. The test-retest repeatability over two measures revealed good agreement (bias= -0.5).

Conclusions RITA has demonstrated feasibility for monitoring nAMD disease activity. This study contributes to the ongoing advancements in tablet technology and their use in home-monitoring. The relationship demonstrated between RITA, OCT and VA support the idea that RITA may be able to detect para-central vision loss, independent of changes in VA. Further research is required to demonstrate the sensitivity and specificity of RITA.

Using tablet technology for the monitoring of disease activity in Age-related Macular Degeneration

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Introduction Age-related macular degeneration (AMD) is a common ophthalmic disorder and the leading cause of visual impairment (VI) and blindness in the Western World (1). Prompt initiation of treatment is the primary predictor for improved outcomes in AMD (2). Under existing treatment

regimes, there is potential for visual deterioration in between appointments. With a healthcare system already under immense pressure (3), home testing using computerized systems could allow patients to independently and objectively monitor disease.

Patients and methods This study aimed to investigate a tablet-based vision test, the Rotation Illusion Test for AMD (RITA) for monitoring disease activity in neovascular-AMD (nAMD). It aimed to investigate the validity of RITA by comparison to existing, objective measures of visual function and by investigating the test-retest repeatability. A prospective observational study was performed in patients with established nAMD. 40 participants were recruited from a UK ophthalmology clinic. Participants performed RITA testing and then continued along their usual treatment pathway, including visual acuity (VA) and optical coherence tomography (OCT).

Results Participants found RITA easy to use, requiring minimal examiner involvement. Peripheral damage on OCT corresponded to lower RITA scores, demonstrating validity for testing para-central vision. Changes in para-central vision may act independently of changes in central VA. A weak relationship was found between RITA and VA measurements. RITA demonstrated good levels of agreement when tested for test-retest repeatability.

Conclusions This study contributes to the ongoing advancements in tablet technology and their use in home monitoring. RITA was compared to validated measures with promising results. There is a clear possibility that RITA could have a role in monitoring and the reduction of the socioeconomic burden of AMD.

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An audit of the Heywood, Middleton & Rochdale Minor eye conditions service

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Introduction The Heywood, Middleton and Rochdale Minor eye conditions service (HMR MECS) is an optometrist-led service, established in 2013 with the aim of managing patients with minor ophthalmic complaints within the primary care setting (1). The service aims to provide timely assessment and management of these patients, delivered by accredited optometrists from optometry practices across the 3 regions.

The service is available to patients of all ages registered with a general practice in Heywood, Middleton or Rochdale. Referral to the service may come from a number of sources including; self-referral, general practice or other NHS services. The set-up of this service reflects a wider shift towards a more primary-care-led NHS, as a response to the increasing demands and funding restraints within secondary care services (2).

Patients and methods This audit aimed to identify the effectiveness of this service in reducing the secondary care burden by investigating accessibility, referral source and consultation outcomes. Retrospective data from 2241 MECS appointments in the year 2015 was collected.

Appointments were divided into 'urgent' and routine'. Data was collected on the time taken for patients to be seen to demonstrate service accessibility. Data was also collected on referral source and consultation outcomes including referral rates to secondary care.

Results 99.33% of 'urgent' cases were seen within 24 hours and 99.91% within 2 working days. Of the 1115 'non-urgent' cases, 98.75% were seen in 5 working days. 99.11% of appointments were initiated within 30 minutes of appointment time. The majority of patients self refer into the service. 73.27% of patients were managed within the service, and only 14.42% required referral to secondary care. The majority of patients would have accessed their GP or emergency if MECS had not been available.

Conclusions This service fulfils its aim of assessing patients with minor eye conditions and preventing their inappropriate attendance to A&E, or even general practice. The service should continue at its current standards by ensuring patients and service providers are correctly informed on how and when to use the service, and that there is continuous monitoring of the service to ensure this.

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Using STAR Tool to Improve Clinical Notes in a General Surgery Department

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Introduction The quality of clinical notes is an important aspect of healthcare. Complete and accurate notes are needed to optimise patients' care and ensure continuity of care[1]. Inadequate documentation is a known causal factor to adverse events[2]. We aimed to investigate the adequacy of our notes as well as highlight the importance of good record keeping in a cohort of new doctors at the time of August changeover.

Patients and methods We identified patients admitted and discharged within the first three weeks of August from each of four general surgery wards in our hospital. We retrospectively searched their electronic records to find and assess their initial clerking, subsequent entries, consent form, anaesthetic record, operative note, and discharge summary. The STAR score[3] was used to assess these note sections. We raised awareness among junior doctors by sharing our findings, developing a "model" entry, and creating a clerking proforma for patients admitted directly from the day surgery unit. A second cycle of data collection following these ongoing interventions is planned to start in November.

Results 85 patient files were reviewed with an average score of 82.9%. All sections had an average score of >85%, except for the initial clerking that scored 76.8%. All sections had been completed for

every patient, except for the initial clerking where 9 patients didn't have one completed. 5 of these patients had been admitted directly from day surgery without an initial clerking.

Conclusions Our first cycle shows a good baseline of record keeping with room for improvement, particularly in the initial clerking. Our 3 best section results are >90% and come from notes with available sample templates. We aim to improve our initial clerking results in the second cycle following the implementation of a clerking proforma for patients admitted directly to the wards following day surgery.

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Audit of cognitive screening of elderly vascular patients and subsequent pilot intervention of a pre-operative MOCA

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Introduction It has been found that the prevalence of undiagnosed cognitive impairment (CI) is high in vascular patients and is linked to adverse outcomes such has post-operative delirium (POD) and increased length of stay 1,2. Multiple studies suggest that a preoperative Montreal Cognitive Assessment (MOCA) has been effective in identifying patients with cognitive impairment who are at risk of POD 1,3. In this study our aims/objectives were to audit the completion of cognitive assessments in elderly patients admitted to the Vascular Unit and to introduce a cognitive screening tool at the point of admission to help detect previously undiagnosed CI and identify patients at risk of developing POD.

Patients and methods Part 1. Retrospective case note review. Admissions over a one-month period aged over 65 were studied and baseline characteristics were recorded, including previous diagnosis of CI and the rate of cognitive screening with 4AT/ AMT.

Part 2. Pilot intervention using Montreal Cognitive Assessment (MOCA) over a two-week period. Emergency and elective patients admitted to the vascular ward >65 were asked to complete a pre-operative MOCA conducted by FY doctors within 24 hours of admission. The scores were recorded (<24 indicating impairment) as well as any previously documented AMT/4AT or history of CI.

Results Part 1. 32/51 admissions were screened using the 4AT score. 0/51 were screened using other tests such as AMT or MOCA.

Part 2. 33/42 patients were screened for cognitive impairment. 11/14 consented to complete the MOCA. Cognitive impairment was found in 7/11 of these patients but was only previously documented in 2/11.

Conclusions MOCA is an effective screening tool in identifying CI but due to time pressures is not feasible to complete routinely in the ward setting. It has been demonstrated in other studies that when cognitive impairment is recognised and accommodated for this can lead to better post - operative outcomes 1,3. Therefore in the future it would be useful assess the implementation of MOCA screening in pre-operative clinics.

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Are medical students taught how to teach? A Systematic Review

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Introduction 'Teaching and learning are the foundation of the professions' (1) and the General Medical Council stipulates in its guidance document 'Outcomes for graduates' (2) that doctors must 'reflect learn and teach others' and 'function effectively as a mentor and teacher' (3). To teach professionally in the UK, one requires specialised qualifications (4) implying that subject knowledge alone is insufficient to be a proficient teacher. Thus, doctors and medical students, it could be argued, should be formally taught how to teach.

Methodology MEDLINE, Scopus, PsycINFO, SAGE and the Education Resource Information Centre (ERIC) databases were searched for articles relating to Medical students being taught how to teach. Hand-searched abstracts were generated, their titles reviewed and inclusion criteria applied in an iterative screening process. Published quality appraisal criteria (5) determined which high quality papers to discuss in detail.

Electronic literature searches yielded 3231 citations of potential relevance. Applying limitations, removing duplications and reviewing the title and full text articles reduced this number to 29. 6 additional papers were identified after hand-searching the relevant papers' bibliographies, totalling 35 papers.

Teaching on how to teach - The time period over which students were 'taught how to teach' ranged from a few hours (6) to 240 hours over a 6 week period (7). Facilitation and feedback skills were taught in 56.7% and 63.3% of the studies.

Participants - Teaching on 'how to teach' was primarily delivered to senior medical students; Only 5 papers suggested that junior students alone received such teaching. Most studies involved <50 students, suggesting that formal instruction on how to teach was available only to a minority medical students and only 6.7% of these papers (n=2) (8) (9) delivered entirely mandatory training.

Country of origin - papers were from a range of counties, heightening external validity. Most papers originated from western, developed countries which may limits representativeness of medical education in eastern or developing count.

Although there are examples of some Medical students being taught how to teach, the literature indicates this tends to be an elective pursuit offered to interested, academic or competent individuals. The majority of medical students globally are not receiving such training, and arguably, it may be the less proficient, less academic students who are most in need of it.

Further study - there is scope to further explore medical students being taught how to teach in developing countries as minimal papers in this review were from such regions.

An additional qualitative study would be to interview junior doctors to ascertain their opinions regarding what educational teaching as an undergraduate might improve their postgraduate teaching.

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