ASRS Symposium

23 November 2016
IMS Level 7 Conference Room

UNIVERSITY OF ABERDEEN

ACKNOWLEDGEMENT

Professor Phyo K Myint
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& Chair, ACAT Executive Board

Programme Outline

Location: IMS Level 7 Conference Room

Activity	Time
Introduction (Prof. Phyo Myint)	17.00-17.05
Oral presentations	17.05-17.55
Poster viewing & Refreshments	17.55-19.00
Oral presentations	19.00-19.50
Break	19.50-20.00
Prizes (Prof. Alan Denison)	20.00-20.10
Wrap up (Prof. Phyo Myint)	20.10-20.15

A high anti-cholinergic burden is associated with falls and low bone mineral density at Ward's triangle in middle aged women of Aberdeen Prospective Osteoporosis Screening Study

Andrew Ablett

1 Background

There are limited data on use of anticholinergic medications and their effects on falls and bone health in middle aged women. We aimed to examine the cross-sectional association between anticholinergic medication burden (ACB) and falls, bone mineral density (BMD), and low trauma fractures in Aberdeen Prospective Osteoporosis Screening Study (APOSS) participants.

2 Methods

ACB score (0 = none, 1= possible, 2= definite) was calculated for each medication in 3883 Caucasian women (mean age (SD) =54.3(2.3) years) who attended the second APOSS study visit (1997-2000). ACB burden was calculated by combining the ACB score of each medication participants were taking at the time of questionnaire. Incident falls during the preceding 12 months and prevalent low trauma fracture data were ascertained from self-reported questionnaire. BMD was measured at the hip (Ward's triangle, neck of femur and trochanter) and spine (L2-4) using dual energy X-ray absorptiometry. Outcomes were examined using logistic regression controlling for anthropometry, menopause, physical activity, comorbidities, and medications.

3 Results

From 3883 participants, 3292 had ACB score = 0, 328 had ACB score = 1, and 262 had ACB score ≥2. High ACB burden (≥2) was associated with increased odds (ACB=0 reference) for falls (fully adjusted OR (95% CI) = 1.81(1.25-2.62);P=0.002), and having low BMD (bottom 20%) at Ward's triangle (3.22 (1.30-7.99);P=0.011). Incidence of falls over 12 months for participants with ACB score ≥2 was 319 per 1000. For ACB categories 1 and 0, falls incidence per 1000 was 214 and 215 respectively. ACB ≥2 was not associated with BMD at other hip sites, lumbar spine, nor fracture. Confining analyses to fractures at ≥50 years of age showed similar results.

4 Conclusion

Our findings provide potential mechanistic links between ACB and falls risk in older age.

Validation of a novel transgenic mouse model with selective loss of intra-articular adipose tissue

Serena Banh

1 Background

The infrapetellar fat pad (IFP) has been proposed to play a role in the development of knee osteoarthritis (OA), of which the cause remains unknown. Based on lineage-tracing studies in our group, adipocytes in IFP is selectively targeted and modified in the knee joint to develop a novel mouse model, Gdf5-Cre;Bscl2fl/fl. The aim of this study was to validate the loss of intra-articular adipocytes and the use of this mouse model as an investigative tool for OA research studies.

2 Methods

Genotyping was performed by PCR and gel electrophoresis using DNA extracted from ear clips. Hindlimb knee joints were collected at 14 weeks of age, fixed and embedded in paraffin, and serially sectioned (5 um sections). H&E and Safranin O staining were performed to analyse the IFP and joint cartilage respectively. Adipocytes in IFP were identified by immunohistochemistry using perilipin antibody. Images of stained sections were acquired using AxioScan Slide Scanner, and the IFP size and adipocyte number were manually quantified using ZEN 2012 software. Data was analysed for statistical significance using Graphpad Prism.

3 Results

Of 14 transgenic mice analysed, 7 were Gdf5-Cre;Bscl2fl/fl (cKO, Male n=4; Female n=3) and 7 were Bscl2fl/fl littermate controls (Male n=3; Female n=4). H&E staining demonstrated that while IFP was reduced in size, extra-articular subcutaneous fat appeared normal and unaffected. Preliminary results from Safranin O staining indicated no obvious cartilage damage other than reduced IFP. Quantitative analysis showed significant decrease in IFP size, adipocyte number and adipocyte density in cKO mice compared to WT littermate controls.

4 Conclusion

Our findings confirm a selective loss of intra-articular adipocytes in Gdf5-Cre;Bscl2fl/fl mice. Longitudinal and interventional studies of these mice can provide an understanding of whether the loss of joint fat cells is detrimental to knee joint and elucidate the underlying mechanisms of the role of IFP in OA.

Supervisors: SM Clarke, Cosimo De Bari, AJ Roelofs

Clinical predictors of ankylosing spondylitis: novel analysis of a primary care database

Mohammed T Bashir

1 Background

Ankylosing spondylitis (AS) is associated with delays between first symptoms and diagnosis with potential diagnostic opportunities being missed in primary care. We aimed to examine feature patterns in GP records during the 5 years before diagnosis.

2 Methods

We conducted a matched case-control study using data from the Primary Care Clinical Informatics Unit Research (PCCIUR) database of anonymised records from Scottish GP practices. Cases were defined as patients with a coded diagnosis of AS and were matched with controls by age, sex and GP practice in a 1:4 ratio. We defined a symptomatic subset of cases and controls with at least one back pain related code. We searched data for all instances of the following; musculoskeletal symptoms & disorders (axial and non-axial), non-specific symptoms (e.g. fatigue); medication and investigations. We examined these individually and in composite features, either as combinations (ESR within 30 days of axial pain) or recurrences (2 or more back pain episodes separated by at least 6 months). We compared the incidence of each feature in cases and controls as odds ratios (ORs) with 95% confidence intervals calculated over the 5 years before diagnosis and shorter time periods to analyse temporal patterns.

3 Results

Main analysis included 932 cases and 3700 controls and symptomatic analysis 448 cases and 932 controls. Typical features were all more common in cases in whom the first coded episode of axial pain occurred within 18 months of diagnosis in over 40%. Composite features more common in cases than symptomatic controls included ESR within 180 days of axial pain (OR 3.6, 1.6-8.2) and recurrent episodes of axial pain or enthesopathy (OR 3.2, 2.2-4.7).

4 Conclusion

This is the first study to demonstrate the predictive value of composite variables for AS in routine data and to examine temporal patterns in the 5 years before diagnosis.

Supervisor: Christopher Burton

The impact of rurality on cancer survival: a systematic review and meta-analysis (study ongoing)

Raphae Barlas

1 Background

Cancer is one of the leading causes of morbidity and mortality worldwide. While 47% of the world's population reside in rural areas, studies assessing the the association between cancer mortality and rurality have yielded contradictory findings. The current review therefore aims to comprehensively assess the association between cancer survival and rurality.

2 Outcomes

The primary outcome under assessment is survival. Secondary outcomes under consideration include the association between rural residence and; diagnostic delays, treatment delays, late stage of presentation and cancer morbidity.

3 Inclusion and Exclusion Criteria

Articles will be included if they report cancer survival outcomes in rural communities and compare cancer survival between different types of geographical areas, and/or explore theories of mechanisms for the impact of rurality or geography on cancer. The types of participants will be human subjects of any age who have been diagnosed with or treated for cancer in remote or rural areas; however, defined. Regarding the exposure, studies assessing any type of cancer (excluding non-melanoma skin cancer) in remote or rural conditions or geographical isolation, however defined, will be included. List of sources that will be excluded are studies not published in English and papers that have not included comparative data from urban and rural populations.

4 Methodology

Electronic databases (MEDLINE, Embase, CINHAL) were searched for qualitative and quantitative studies published between 1946 and 2016. Two reviewers independently screened titles against the inclusion/exclusion criteria to identify potentially relevant publications. Following title screening all potentially relevant abstracts were obtained and screened for eligibility. Full text articles were then obtained for further examination. Articles fully meeting the inclusion criteria are currently proceeding through quality assessment and data extraction.

Supervisor: Peter Murchie

Evaluation of the Aberdeen University Summer Research Studentship (ASRS) Programme

Shona Boyle

1 Background

ASRS is an eight-week research mentorship programme for 1st and 2nd year medical students. Since its inception in 2010, the programme has never been formally evaluated and there is a distinct paucity of information on how such an early experience in medical school can have an impact on future academic activity and aspiration during medical education.

2 Methods

Previous ASRS recipients were invited to complete a questionnaire via email in order to assess the respondents' views on various aspects of the programme. The survey was designed to explore individual experiences, personal outcomes, and recipients' general feedback, including any recommendations for the future.

3 Results

66 out of 117 recipients (56%) completed the questionnaire. Almost all (>95%) of the respondents would recommend ASRS to students in early years of medical education. The majority (70%) continue to be involved in research and 50% went on to do an intercalated degree. 66% of students who were undecided about intercalating before ASRS, decided to intercalate after doing ASRS. From the 66 students that completed the survey, their work was presented at a national meeting or conference on 29 occasions, with a further 9 presentations at an international level. Moreover, 34 successful publications have been produced, 14 of them original research articles. Commonly reported benefits of the programme included learning new skills such as data handling and analysis, and laboratory techniques as well as gaining experience with a research team. However, about of quarter of the recipients felt unsupported by their supervisor for varying reasons.

4 Conclusion

While these results indicate that short term research experience programmes such as ASRS, early on in medical school, are generally positive and influential experiences, they also highlight that individual ASRS experiences are dependent on allocated supervisors and the resources available.

Supervisors: Georgina Hold, Phyo Myint, Seonaidh Cotton

Cumulative live-birth rates following miscarriage in an initial complete cycle of IVF: a retrospective cohort study of 113,870 women

Natalie Cameron

1 Background

Miscarriage following IVF is a setback for couples who are uncertain about their ultimate prognosis. Cumulative live-birth rates (CLBRs), which are better indicators of overall chances of IVF success, have not previously been reported in couples who miscarry an IVF pregnancy.

2 Methods

Data from the Human Fertilisation and Embryology Authority (HFEA) register on IVF/ICSI treatments using autologous gametes started from 1999-2008 were analysed. CLBRs were estimated in women who a) had miscarriage (and no live-birth), b) at least one live-birth or c) no pregnancy in their first complete cycle (including fresh and frozen embryo transfers following a single oocyte retrieval).

3 Results

In their first complete cycle, 9,321 women had at least one miscarriage (and no live-birth); 70,076 had no pregnancies and 33,152 had at least one live-birth. After three complete cycles, conservative CLBRs (which assume that women who discontinued treatment subsequently never had a live-birth) were 40.9%, 49.0% and 30.1%, while optimal CLBRs (which assume that women who discontinue have the same chance of live-birth as those treated) were 49.5%, 57.9% and 38.4% in the miscarriage, live-birth and no pregnancy groups respectively. Odds of cumulative live-birth for women who miscarried in their first complete cycle were 43% higher than those who had no pregnancy [odds ratio (95% confidence interval) = 1.43 (1.35, 1.52)], and twice as high for live-birth versus no pregnancy [2.10 (1.95, 2.26)]. Significant predictors for live-birth in all women included tubal infertility [0.88 (0.87, 0.93)] and increasing age [18-40 years = 0.94 (0.94, 0.95); >40 years=0.63 (0.60, 0.66)].

4 Conclusion

After 3 complete cycles of IVF/ICSI, women who miscarried or had a live-birth in their first complete cycle had a higher chance of live-birth (40.9% and 49.0% respectively) than those who had no pregnancies (30.1%). Our findings will reassure couples who experience miscarriage in their first complete cycle of IVF/ICSI.

Supervisors: S Bhattacharya, David McLernon

Docosahexaenoic acid as a treatment for acute stroke: a systematic literature review

Lily Fulton

1 Background

The number of stroke patients arriving at hospital within a therapeutic timeframe is increasing, enabling earlier and more successful intervention. Currently, this involves thrombolysis and thrombectomy in the hours immediately following the ischaemic incident. Animal studies have shown that protection of the penumbra during this time could reduce cell death and improve clinical outcome. Brain tissue contains a high amount of polyunsaturated fatty acids, particularly docosahexaenoic acid (DHA), an omega-3 fatty acid, found in the phospholipid fraction of the grey matter and synaptosomes. DHA is essential for normal brain growth and cognitive function, and dietary supplies are required for membrane replacement, maintaining synaptic integrity, gene regulation and synthesis of docosanoids and neuroprotectins. DHA circulates in plasma bound to albumin. As DHA plays a critical role in neuronal survival and synaptic function, and is also a potent modulator of brain inflammation, it is a strong candidate for a successful neuroprotectant in stroke. The Stroke Therapy Academic Industry Roundtable (STAIR) consortium has published recommendations for the guidance of animal research studies to ensure that they maximise the potential for successful transfer into clinical practice.

2 Methods

I conducted a systematic literature review of papers reporting administration of DHA in animal models of acute stroke. Relevant papers were selected based on pre-defined criteria; those assessing the effect of DHA on neurobehavioural score and infarct volume in animal models of acute stroke. Data were extracted manually, and collected, organised and analysed using the CAMARADES database.

3 Results

Results show significant improvement in neurobehavioural score and infarct volume in DHA treated groups compared to control animals.

4 Conclusion

These findings demonstrate that the STAIR criteria have been met, and provide a basis for progression to translational clinical trials of DHA as a treatment for acute stroke.

Supervisor: Mary Joan MacLeod

Clinical epidemiology of invasive fungal infections in children and neonates: interim results of a multi-center national prospective study

Rekha Gurung

1 Background

Invasive fungal infections (IFI) cause significant morbidity and mortality in children. Although the number of infections have steadily increased over the last decade, diagnostic difficulties and the increasing prevalence of azole resistance in Aspergillus fumigatus, have forced clinicians to reconsider the management strategy for these infections. The purpose of the study was to prospectively study a new management strategy for IFI with increased use of diagnostic tools to enable a causative diagnosis of the IFI being made.

2 Methods

Eight Dutch University Hospitals participated by entering clinical data anonymously from 53 paediatric patients treated with a suspected or proven IFI. Data were prospectively collected since 2013 in a secure web-based registry 'PedMyc' into an electronic case report form. The registry was structured by separate pages to facilitate data entry during the AF treatment course. The following data were collected: age, sex, underlying disease, risk factors, results of fungal diagnostic tests (including imaging), dosing schedules, plasma levels of azole AF, modification of AF therapy, and outcome.

3 Results

The study comprised of 51 children and 2 neonates (36 m; 17 f; median age = 10.42 years). At inclusion, 47 patients had suspected infection and 5 patients had proven infection. Diagnostic tests were performed on patients with suspected infection (GM = 47, CT = 46, culture = 10 and biopsy = 11). The results from diagnostic tests led to the following outcomes: No infection (1), proven fungal infection (7) and probable fungal infection (24). [Data for 21 patients were not available]

4 Conclusion

Our study suggests an important role for diagnostics in the management of IFI. The data was not sufficient to conclude on the effects of treatment change on patient outcomes. Further data collection is needed to determine whether it is feasible to modify AF treatment for better outcomes, based on the algorithm proposed.

Supervisor: Adilia Warris

Novel NHS Grampian patient database for Inflammatory Bowel Diseases (IBD) highlights clinical association between asthma and IBD

Stavroula Lila Kastora

1 Background

Inflammatory bowel disease (IBD) embodies the dysregulation of immune reaction to the non-pathogenic commensal microbial antigenic factors at the mucosal level in a susceptible genetically host. While several genetic and environmental factors have been identified to foster the deregulation of both innate and adaptive immunity in the gastrointestinal tract, the exact pathophysiological mechanism of IBD development remains elusive. Under the umbrella of IBD, two distinct pathological conditions exist which non the less share symptomatological manifestations as well as treatment regimes. These conditions are Cohn's disease (CD) and Ulcerative Colitis (UC). In Europe, the IBD population is estimated to 0.1% with increasing prevalence and incidence in westernized areas.

2 Methods

In this work, we introduce a novel way of patient data registration that bypasses the necessity of letter dictation via a live datasheet introduction as well as share important findings regarding the NHS Grampian IBD population.

3 Results

We have developed a live patient specific sheet that evolves upon each consultation via information entry and allows simultaneous update of the referring GP while cataloging patient information in a numerical scheme enabling for statistical analysis of the IBD population as a whole. Our database catalogues information such as the specifics of IBD condition (UC or CD), classification of disease and date of diagnosis as well as co-morbidities, therapeutic regimes, previous surgical interventions, key diagnostic investigations, dated extra-intestinal manifestations and up-to-date clinical assessment that incorporates previous, dated consultations.

4 Conclusion

In this work we have established a direct clinical link between asthma and IBD conditions while via bioinformatics analysis we have highlighted putative neutrophil specific pathways that may be deregulated in both of these conditions giving rise to a co-morbidity phenotype.

Supervisor: Georgina Hold,

Evaluating Primary Care Risk Prediction Tools used in the Referral of Suspected Colorectal Cancer

Jonathan May

1 Background

Colorectal cancer is the fourth most common cancer in the UK. Patients suffering from this disease can present in a diversity of ways, often with only un-differentiated symptoms. With early referral associated with best prognosis, assuring GPs have the best tools to support their decisions is vital. Our aims were to compare the sensitivity of the RAT and Qcancer risk prediction tools against referral data, and investigate causes of delayed referral.

2 Methods

This was done by establishing a database of patient information from a cohort with confirmed cases of CRC. We analysed consultations and background data in order to assign a risk prediction score at first presentation and point of referral based on the Qcancer and RAT criteria. These scores were cross-checked to establish quality assurance, before proceeding with analysis.

3 Results

The most surprising of our preliminary findings is that the Qcancer prediction criteria has a far higher sensitivity (both at first presentation and referral) than the RAT. This is particularly worthy of further investigation as the RAT is currently the more widely used tool in Primary Care. Based on our findings, less than a quarter of CRC patients would be eligible for emergency referral at first presentation under the RAT (based on Scottish guidelines of >3% risk), versus around 40% following Qcancer. Another interesting discovery was that the average time between first presentation and referral was found to be 66 days.

4 Conclusion

One of our next steps will be to look at potential trends in those experiencing the greatest delays in referral, as well as those scoring lowest at first presentation and point of referral. If patients within these respective groups share certain symptoms, co-morbidities, or other characteristics this could potentially be of use in facilitating earlier intervention.

Supervisors: *Peter Murchie*

Sexual Function Problems in Ankylosing Spondylitis Patients: A Systematic Review

Bethany McLoughlin

1 Background

Numerous studies have investigated sexual function in Ankylosing Spondylitis (AS), reaching differing conclusions. This review aims to investigate, and clarify, the prevalence of sexual problems in AS patients, and associations between these problems, disease measures or psychological variables.

2 Methods

A systematic literature search was conducted on the Ovid databases, with the last search on 31st May 2016. Excluded studies didn't give specific AS patient data. The prevalence of problems, associations with disease measures (BASDAI, BASFI and BASMI) and quality of life/psychological status were extracted.

3 Results

29 studies were included. The prevalence of sexual problems varied from 12.3% - 100%, due to the range of definitions and assessments of sexual dysfunction used. Rezvani et al reported sexual dysfunction was common in male patients, but didn't significantly differ from controls. Pirildar et al however reported erectile dysfunction was characteristic of male patients. Akkurt et al reported sexual dysfunction was more common in female patients, however found no associations with disease activity, yet Demir et al did find negative associations between disease activity and sexual function. In male patients Dong et al reported similar relationships, yet Dincer et al reported a relationship between spinal mobility. Ozgul et al reported differences in intercourse frequency and sexual drive according to patient's anxiety levels. Healey et al reported depression was associated with an increased impact on patient's sexual relationships. Akkurt et al reported desire and arousal were significantly lower in female patients with depression, mirrored by Rostom et al who found male sexual problem patients significantly differed from those without regarding depression.

4 Conclusion

Further studies are required to clarify the exact prevalence, yet sexual dysfunction appears to be common. Physicians should consider the effects of AS on sexual function for holistic management.

Supervisor: Gareth Jones

Sexual function problems in ankylosing spondylitis patients - Results from the Scotland Registry for Ankylosing Spondylitis (SIRAS)

Bethany McLoughlin

1 Background

AS is a chronic rheumatic condition that can impact upon physical and sexual functioning. This analysis aims to clarify the prevalence and characteristics of sexual problem patients and to assess potential associations.

2 Methods

SIRAS is a disease registry which collected data on AS patients from 2010 - 2013. A postal questionnaire collected patient information. Associations were assessed using descriptive statistics and logistic regression. A small number provided information therefore, a p value <0.10 was considered relevant. Results are percentages, mean values with standard deviation and odds ratios with 95% confidence intervals.

3 Results

125 patients provided information. 61.6% reported problems, with no significant difference regarding gender (72.4% males vs 53.8% females) or age (mean 53yrs (SD 1.44) vs 52 (2.05)). However, higher BASDAI scores (mean 4.51 (SD 2.38) vs 2.85 (2.37)) and BASFI scores (4.64 (2.76) vs 2.93 (3.05)) were observed. Patients who reported: joint/back stiffness (OR 5.58; 95% CI 1.65 – 18.92,), reduced joint/back movement (5.08; 1.75 – 14.74,), back pain (4.26; 1.46 – 12.46,), joint and muscle pain (3.78; 1.28 – 11.15,), swollen joints (3.05; 1.31 – 7.09) and fatigue (2.67; 1.06 – 6.74,) were more likely to report problems. The odds of reporting problems increased in patients reporting BASDAI scores ≥ 4 (2.81; 1.17 – 6.77,) or BASFI scores ≥ 4 (2.23; 0.86 – 5.78). Patients appear reluctant to seek help; 94.5% reported not approaching consultants, 52% reported non-discussion with their partner. Physicians also appear disinterested, with only 5.5% of patients reporting a consultant had approached them.

4 Conclusion

Sexual dysfunction is common in this cohort, with associations with increased BASDAI and BASFI scores. Healthcare professionals should consider sexual issues in their AS management and develop strategies to open communication.

Supervisor: Gareth Jones

Patterns for Earlier Diagnosis of Crohn's Disease

Mahrukh V Mirza

1 **Background**

Crohn's disease is a lifelong inflammatory bowel disease with vague symptoms and no simple test to diagnose it so there is often a delay in diagnosis. This delay could mean missing the therapeutic window to intervene before disease complications occur. We hypothesised that data in GP computer records might include clinical features which could be used to shorten diagnostic delay.

2 **Methods**

We carried out a matched case control study using anonymised GP records. Cases were patients diagnosed with Crohn's disease and controls were matched by age, sex and GP practice. We analysed all cases and controls and a symptomatic subset of cases and controls who presented with abdominal pain or gut symptoms in the period before diagnosis. We searched the data for features including age at diagnoses, symptoms, prescriptions and diagnostic tests. Composite features were then created as combinations of these (e.g. lower GI symptoms and prescription of tricyclics). Results were reported as Odds Ratios (OR) in the 5 years before diagnosis and in shorter time periods in relation to diagnosis.

3 **Results**

Data was obtained from 294 cases, 1150 population controls and 890 symptomatic controls. There was no correlation between occurrence of the disease and patient characteristics such as age of diagnoses and deprivation levels. Approximately 45.3% of cases waited >2 years to be diagnosed from their first coded cardinal symptom and 39% waited < 1 year. The OR for lower GI pain and inflammatory markers was significant only in the 12 months prior to diagnosis. In contrast, for lower GI function, IBS, anti-diarrheal and anti-spasm medications, the OR was significantly increased for several years.

4 **Conclusion**

A substantial number of patients diagnosed with Crohn's disease consult their GP with symptoms, particularly diarrhoea and IBS, in the 2-5 years before diagnosis. Therefore patterns in the GP record could be used to facilitate earlier diagnosis.

Supervisor: Christopher Burton

Aspergillus nidulans in chronic granulomatous disease: an in vitro study

Muhammad S Rajab

1 Background

Chronic granulomatous disease (CGD) is an inherited immune disorder characterized by NADPH oxidase dysfunction. The CGD patient often encounters recurring episodes of bacterial and/or fungal infections, which are often life-threatening. Normally rare, Aspergillus nidulans displays an anomalous affinity for the CGD host - invasive aspergillosis (IA) cases involving A. nidulans are much more common in CGD; infective episodes are more aggressive and lethal than those caused by the relatively commonplace A. fumigatus. We seek to elucidate this anomaly by studying the immune responses of healthy and X-linked CGD (X-CGD) hosts when exposed to A. nidulans and A. fumigatus. We depart from previous similar studies by using bone marrow-derived macrophages (BMDMØs) to mimic host immune machinery in vitro.

2 Methods

BMDMØs were cultured from murine marrow obtained from wild-type and X-CGD (gp91−/−) phenotypes. To emulate physiological conditions, BMDMØs were stimulated with interferon gamma (IFN-γ). BMDMØs were then infected with clinical strains of A. nidulans and A. fumigatus obtained from CGD patients. XTT and ELISA assays were then performed to study BMDMØ fungicidal activity and cytokine response, respectively.

3 Results

Upon IFN-γ stimulation; XTT showed that both BMDMØ phenotypes were much more effective against A. nidulans than A. fumigatus, albeit at similar levels. However, stimulated gp91−/− BMDMØs showed a 3 to 4-fold higher release of pro-inflammatory cytokine IL-1β than wild-type when infected with Aspergillus; IL-1β levels from gp91−/− BMDMØs were 3 times higher for A. nidulans than A. fumigatus.

4 Conclusion

Results are consistent with emerging hypotheses of IA pathophysiology in CGD attributing exaggerated inflammatory host damage rather than impaired pathogen clearance as the main cause. Results may also explain the increased virulence and aggressiveness of A. nidulans infections compared to A. fumigatus in CGD.

It must be stressed however the study is still very preliminary; more optimization and experimental repeats are needed to concretise any trends observed.

Supervisors: Adilia Warris, Jill King

Infective Endocarditis is associated with worse outcomes in stroke: a Thailand National Database Study

Katie A Reid

1 Background

Infective Endocarditis (IE)is a rare, but not uncommon condition associated with increased risk of cerebrovascular events. There is little data on the prognosis of stroke patients with IE including risk of complications.

2 Methods

We examined the association between IE and both serious and common stroke complications in a cohort of hospitalised stroke patients in Thailand. Data were obtained from a National Insurance Database which covers ~75% of the Thai population. All hospitalised strokes between 8th January 2003 and 31st December 2013 were included in the current study. Characteristics and outcomes were compared between stroke patients with or without IE. Logistic regression models were constructed to assess study outcomes controlling for age, sex, stroke type and co-morbidities.

3 Results

A total of 590, 115 stroke patients (mean (SD) age=64.2(13.7) years) (ischaemic= 51.7%; haemorrhagic= 32.6%; undetermined= 15.7%) were included in this study, of whom 2129 (0.4%) had stroke associated with IE, and they contributed to 314 (0.05%) deaths. After controlling for potential confounders, we found that IE was significantly associated with the following post-stroke complications: arrhythmias (adjusted odds ratio (AOR) (95% CI)= 6.94(6.29-7.66), sepsis =1.24(1.01-1.52), pneumonia = 1.34 (1.17-1.53), respiratory failure = 1.43(1.24-1.66) and in-hospital mortality 1.29(1.13-1.47) (p for all<0.001). In-hospital mortality appears to be driven by complications. Among those who survived to discharge, IE patients were less likely to have had a long length of stay (>14 days) in hospital (OR0.76 (0.63-0.92)).

4 Conclusion

Early recognition and appropriate management of IE associated complications in stroke has potential in preventing stroke related deaths in people with IE.

Supervisors: Phyo Myint , Raphae Barlas

Surgical modality and tumour stratification as predictors for perioperative, oncological and quality of life (QoL) outcomes in renal cell carcinoma; T1-2N0M0

Michael Scott

1 Background

Renal cell carcinoma (RCC) is the most common malignancy of the kidney and accountable for 2-3% of cancers globally. Since the inception of minimally invasive nephrectomy, advancement in imaging has heralded increased serendipitous detection of early stage RCC; and localised RCC now constitutes over half of all RCC cases. Due to this in part and the possibility of metachronous disease, minimally invasive surgery is emphatically encouraged, and indeed, there has also been a gradual repudiation of radical nephrectomy in favour of its nephron sparing counterpart for localised cancer. There is global acceptance that preservation of the kidney reduces risk of sequelae such as renal replacement therapy dependency, and this drives surgery catechisms for small renal masses.

2 Methods

- Original 2012 Renal Cell Carcinoma systematic reviews to be superseded by Updated Maclennan et al. Review
- Update ongoing - data analysis stage.
- Incorporates literature from the recent 4-year hiatus (approx. 30 studies).
- The new RCC update will exhibit originality by interpreting patient outcomes for tumour stage stratification, which previous research has shirked.
- Axioms of the Cochrane method adhered

3 Results

While the RCC update is still in progress, it is clear that nuanced modifications of the traditional approaches are continuously emerging. Interestingly, robotic surgery has proved a viable alternative to robot-less minimally invasive techniques. Moreover, tumour-feeding vessel microdissection could be used in lieu of renal hilum clamping, thus creating zero-ischaemia conditions and avoiding the ramifications of ischaemia time.

4 Conclusion

There is a distinct paucity of QoL outcomes in the literature, which prescribes a need for attention to this area. Studies have suggested that oncological outcomes are the main predicator of choice of surgery modality, and QoL outcomes have marginal impact on decision making. Thus, if holistic decisions regarding surgery are to be made, premises based on QoL and perioperative outcomes must accompany oncological outcomes.

Supervisors: James N'Dow, Steven Maclennan, Thomas Lam

Frequent users of GP out-of-hours services

Sarah Stegink

1 Background

Frequent users (FUs) of GP out-of-hours services (GPOOHS) take up a substantial share of time and resources. By examining the diversity in the reason for contact (RFC) of FUs, we aimed to determine whether they consult regarding a few or multiple problems. The former could imply that specific condition management should be improved while the latter could suggest general susceptibility to experience symptoms or to seek medical care.

2 Methods

We extracted data from an anonymised dataset of all 1,258,038 calls made to NHS24 in 2011, designating patients FUs if they made 5 or more calls. For each FU we extracted age and sex and noted the main reason for each of their contacts. We categorised the 72 different reasons given into 11 groups and excluded calls made by or regarding children and those made within normal GP hours. Finally, we limited the dataset to include only the first call made per time period. We estimated RFC diversity as Shannon Entropy (H), a measure used in information theory and ecology. We compared H between age groups and between patients who had at least one mental health RFC and those who did not.

3 Results

Post exclusions, 13,488 patients (2.7%) qualified as FUs, representing 114,673 contacts (14.8%). Most FUs had multiple RFC, on average calling regarding 3.5 categories. H was similar between older and younger patients (1.03 [1.018:1.039] vs 1.06 [1.048:1.066]) but was higher in patients with at least one mental health RFC (1.19 [1.171:1.214] vs 1.05 [1.036:1.056]).

4 Conclusion

FUs of GPOOHS typically have multiple RFC. While in older patients this could be accounted for by multi-morbidity, similar diversity is seen in younger patients suggesting either generally increased symptom experience or healthcare seeking. This is supported by the association of diversity with mental health RFC.

Supervisor: Christopher Burton

The impact of Chronic Kidney Disease (CKD) on Acute Stroke Outcomes

Iong Man Tung

1 Background

CKD is an independent risk factor for cardiovascular events, including stroke, and stroke patients with CKD has worse prognosis compared to those without CKD. We aimed to assess whether the relation between CKD and outcomes in stroke including mortality and common complications in a large cohort of Asian population.

2 Methods

Data were acquired from Universal Coverage Health Security Insurance Scheme Database in Thailand, with total sample of 594,681. Binary logistic regression was used to assess the relationship between CKD and the outcomes including in-hospital mortality, long length of stay (≥4 days), pneumonia, sepsis, respiratory failure and myocardial infarction. Further analysis was carried out to examine whether the impact CKD on stroke patients' outcome differs in the presence of co-morbidities, including anemia, type 2 DM, hypertension, arrhythmia, heart failure and chronic ischemia heart disease.

3 Results

51.5% of the sample had an ischemic stroke, 32.9% had haemorrhagic stroke and the remaining were undetermined stroke types. Their mean age 63.75 years and 55% were male. 18,994 (3.2%) patients had CKD. Overall CKD was associated with increased odds of in-hospital mortality (OR, 1.32; 95% CI = 1.27-1.38), longer length of stay (OR, 1.03; 95% CI = 1.00-1.06), sepsis (OR, 1.41; 95% CI = 1.33-1.50), respiratory failure (OR, 1.56; 95% CI = 1.49-1.64) and myocardial infarction (OR, 1.65; 95% CI = 1.45-1.89). However, CKD was not associated with increase odds of pneumonia (OR, 0.99; 95% CI = 0.94-1.03). Female (OR, 1.44; 95% CI = 1.35-1.53) has a significantly increased odds of in-hospital mortality compared to male counterparts (OR, 1.25; 95% CI = 1.17-1.33) in those with CKD. Presence of other co-morbidity attenuates the association between CKD and the above outcomes.

4 Conclusion

CKD is associated with increased odds of in-hospital mortality as well as increased odds of developing complications such as sepsis, respiratory failure and myocardial infarction.

Supervisors: Phyo Myint, Raphae Barlas, Priya Vart

A review of Parkinson's disease epidemiology data in information sources for doctors and patients

Julia Thomas

1 Background

Accurate information on Parkinson's disease (PD) epidemiology is essential so that patients and doctors can plan for this chronic degenerative disease. However, the information sources readily accessible to both doctors and patients are of unknown accuracy and varying content.

2 Methods

In this review, the accuracy of patient information leaflets, general review articles and national guidelines were all identified using comparisons with the best evidence in systematic reviews.

3 Results

The prevalence of dementia was 150 per 100,000 in the best systematic review compared to a median of 300 in general reviews, with patient information leaflets quoting figures ranging from 68 to

311. The best figure for incidence in systematic reviews was 16 per 100,000, and figures in doctors' and patients' information gave larger ranges but remained accurate. Males are more likely to get PD and have a poorer prognosis. Patients' and doctors' information stated that incidence rates were generally higher in men, but gave no specific figures. Point prevalence of PD patients with dementia was 31.1% but no-one has systematically reviewed the risk of developing dementia during the course of PD and how long this takes. It is unclear whether a third of patients have dementia soon after PD onset, or whether dementia is inevitable after suffering from PD for a number of years. Two high-quality systematic reviews calculated mortality ratios of 1.5 and 2.2, which agrees with general reviews (1.8-2.3). However, many patient information leaflets stated that life expectancy does not change much with PD, which is misleading. As national guidelines are often concerned with disease management, they gave limited information on PD epidemiology but data given was generally accurate.

4 Conclusion

This research brings PD epidemiology data from systematic reviews together to provide an accurate picture of the disease, which differs from the information patients and doctors receive.

Supervisor: Carl Counsell

Externally Funded Summer Research Scholarships 2016

Comorbidity as a driver of outcome differences in men and women with less advanced CKD?

Theodosios Balaskas

1   Background

More women than men seem to have less advanced (stage 3) Chronic Kidney Disease (CKD), but more men seem to initiate Renal Replacement Therapy (RRT), die and suffer heart attacks. Our aim was to investigate whether differences in comorbidities account for differences in outcomes between men and women with stage 3 CKD.

2   Methods

We used the GLOMMS-II cohort (~18,000 people with stage 3 CKD & ~20,000 people with normal kidney function). Hospital episode, RRT and mortality data were available during 6.5 years follow-up. The prevalence at baseline of ischaemic heart disease, congestive cardiac failure, peripheral vascular disease, stroke and diabetes in stage 3 CKD was described by gender and compared to those with normal kidney function. RRT initiation, mortality and myocardial infarction events were described and compared by gender and presence of comorbidities. Incidence rates and rate ratios for RRT initiation and mortality were calculated.

3   Results

The majority with stage 3 CKD were women (65%). The prevalence of the comorbidities was higher amongst men than women, whether with stage 3 CKD or normal kidney function (i.e. IHD 19.9% & 12.5% or 7.5% & 2.9% respectively). A higher proportion of men with stage 3 CKD initiated RRT (0.8%), died without initiating RRT (41.3%) and had myocardial infarction events (8.5%) compared to women (0.2%, 36.9% & 6.9% respectively). Diabetes (vs no diabetes) increased the RRT initiation rate in both men and women (rate ratios adjusted for age: 3.4 (1.8-6.6) & 5.7 (2.5-13.1) respectively). Having a comorbidity increased the mortality rate in both men and women (i.e. mortality rate ratios adjusted for age for diabetes: 1.9 (1.7-2.2) & 1.8 (1.7-2.0) respectively).

4   Conclusion

The higher prevalence of diabetes amongst men partially explains why a greater proportion of men initiate RRT. The higher prevalence of comorbidity amongst men partially explains why more men die.

Homocysteine and hippocampal size, cognitive performance and survival: a longitudinal study of non-demented elderly people

Yuan Ye Beh

1 Background

Increased blood homocysteine, a non-protein amino acid, is associated with increased risk of Alzheimer's disease (AD) and poorer cognitive performance. Few studies have investigated its relationship with hippocampal atrophy (one of the earliest markers of AD) and survival in an elderly population without cognitive impairment at baseline. This project aims to investigate the effect of blood homocysteine on longitudinal hippocampal volume, longitudinal cognitive ability and survival outcome in a well-characterised sample of people in their 80th year.

2 Methods

Homocysteine was measured at baseline in 149 participants from the Aberdeen Birth Cohort 1936 at 64y. Subsequently, they completed four waves of cognitive tests from 64y – 73y. Hippocampal volume was extracted from the MRI scans taken at 68y and 73y using FreeSurfer software package. Initially, we used linear regression to examine the relationship, then performed multilevel fixed effect model to account for correlation between repeated measures of the same participant and missing values due to dropouts. Finally, we used Cox regression to investigate the effect of homocysteine on survival. Analysis was done using IBM SPSS version 24 and MLwiN 2.36.

3 Results

The multiple regression model of hippocampal volume is significant ($p=0.003$, $R2=0.218$), with the reciprocal of homocysteine and gender contribute independently to the model ($p=0.003$, $p=0.020$). Multilevel fixed effect model shows that age past 60 and homocysteine level predict hippocampal size ($p=0.03$, $p=0.0002$). For each year past 60, hippocampal volume is predicted to reduce by 35.4 mm3; each unit increase (micromol/L) in homocysteine also reduces the hippocampal volume by 35.1 mm3 and increases mortality risk by 5.5% over the follow-up period (64y-80y).

4 Conclusion

Higher blood homocysteine level is associated with smaller hippocampal size in an aging population without cognitive impairment. Blood homocysteine level at 64y influences survival during the follow-up period to 80y after adjusting for gender.

Determinants of falls and fractures after stroke over long term follow up

Emma James Foster

1 Background

The lasting neurological stroke symptoms and associated reduced bone mass lead to increased risk of falls and fractures after stroke. Despite recent advances, fall risk factors which are related to personal characteristics and stroke related factors in stroke survivors are poorly understood. This study, therefore, aimed to investigate such determinants that are linked to increased risk of falls and fractures after stroke.

2 Methods

We analysed data from a prospective stroke register, between 2003-2015. Univariate and multivariate Cox Proportional Hazard models were constructed. The models were adjusted for patient and stroke characteristics and co-morbidities including: previous falls/fractures, stroke/TIA, congestive heart failure, coronary heart disease/myocardial infarction, atrial fibrillation, diabetes, hypertension, peripheral vascular disease, chronic kidney disease, chronic obstructive pulmonary disease, dementia, hyperlipidaemia and cancer.

3 Results

7248 patients discharged after stroke (89.6% ischaemic) were included. The mean age (SD) was 76.3±12.1 years; 50.6% women. 1136 (15.7%) suffered a fall and 666 (9.2%) had a fracture during the 10 year follow up (median follow up 6.94 years). Risk factors for falls and fractures were increasing age [HR 1.04(95%CI:1.03-1.04) for falls and HR 1.03(95%CI:1.02-1.03) for fractures, respectively], history of falls [HR 1.42(95%CI:1.14-1.75), HR 1.82(95% CI:1.39-2.37)] and atrial fibrillation [HR 1.18(95% CI:1.03-1.35), HR 1.21(95% CI:1.02-1.43)]. In addition, previous stroke/TIA and hyperlipidaemia were identified as risk factors for falls HR 1.16(95%CI: 1.01-1.32) and HR 1.36(95%CI: 1.01-1.81), respectively. Female sex [HR 0.77(95%CI:0.68-0.87), HR 0.63(95%CI:0.53-0.75)], Total Anterior Circulation Stroke [HR 0.58(95%CI:0.46-0.72), HR 0.59(95%CI:0.44-0.79)], prestroke disability depicted by prestroke modified Rankin Score of >=3 [HR 0.78(95%CI:0.65-0.95), HR 0.69(95%CI:0.54-0.89] were associated with reduced risk of falls and fractures. Malignancy was associated with reduced fall risk [HR 0.76(95% CI: 0.62-0.93)].

4 Conclusion

In this study we have identified new personal and stroke related risk factors that predict falls and fracture risk after stroke.

Understanding the Impact of Stress on Safety Behaviours in Healthcare: A Simulation Study

Jonathan May

1 Background

It is well established that hospital doctors frequently experience high levels of stress in their working lives and that this can have adverse impacts on their physical and mental health, as well as their performance (e.g. reduced working memory, impaired communication). Our aim was to examine the impact of urgency and cognitive load on stress and performance in medical students undergoing a simulated ECG scenario.

2 Methods

This was accomplished by recording medical students participating in such a simulation under controlled conditions while wearing an ECG monitor, and requesting questionnaires from participants to be completed at various points before and after. Questions included scoring their perceived self-efficacy, anxiety at that moment, and general anxiety levels the simulation. Their performance was also marked against a checklist by a healthcare professional trained in the ECG procedure. A database including all of this information was then created, and different activities involved in the simulation timestamped by use of recordings to allow synchronisation with heart rate date before analysis began.

3 Results

One significant result was that of a positive correlation between a medical student's general anxiety level, and their anxiety level at various points in the simulation.
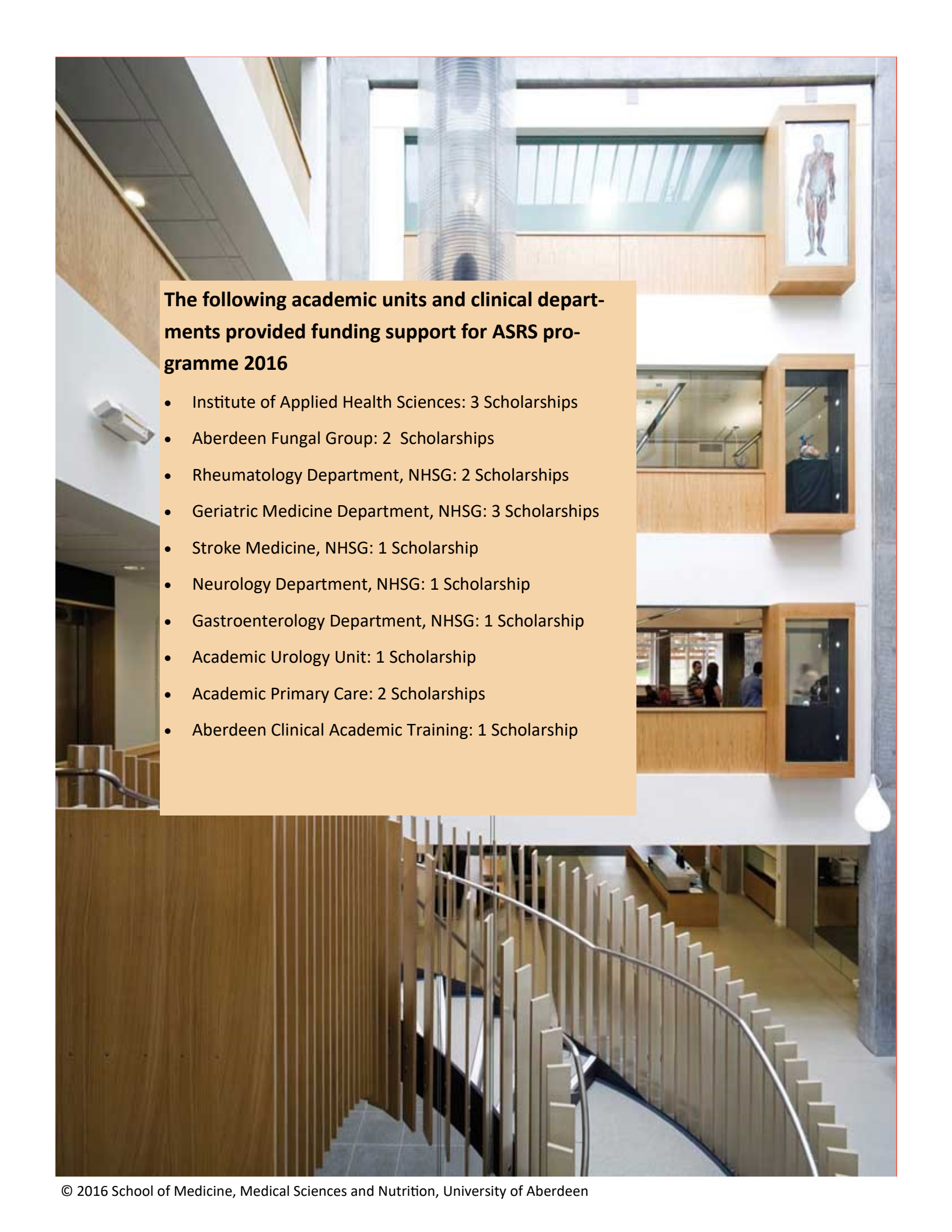
4 Conclusion

While not unexpected, as this data related to participants in the process of medical training (with the vast majority likely to work as doctors), it could be useful finding with respect to patient safety. For example, if trait anxiety is an effective indicator of state anxiety (and therefore potentially an indicator of performance under pressure) this might be used to prioritise additional support to clinicians.

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- Institute of Applied Health Sciences: 3 Scholarships

- Aberdeen Fungal Group: 2 Scholarships

- Rheumatology Department, NHSG: 2 Scholarships

- Geriatric Medicine Department, NHSG: 3 Scholarships

- Stroke Medicine, NHSG: 1 Scholarship

- Neurology Department, NHSG: 1 Scholarship

- Gastroenterology Department, NHSG: 1 Scholarship

- Academic Urology Unit: 1 Scholarship

- Academic Primary Care: 2 Scholarships

- Aberdeen Clinical Academic Training: 1 Scholarship