PWE-170 A DEDICATED COLORECTAL CANCER GENETICS SERVICE IMPROVES ADHERENCE WITH MOLECULAR TESTING FOR LYNCH SYNDROME

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[1,*]S Stevens, [1]L Sergot, [1]F Turkes, [1]J Smith, [1]K Monahan. [1]*Family History of Bowel Cancer Clinic, West Middlesex University Hospital and Imperial College, NHS, London, UK*

Introduction Lynch Syndrome (LS) accounts for 2–3% of colorectal cancer (CRC); ~1000 cases of CRC in the United Kingdom annually. It occurs as a result of mutations in DNA repair genes; limiting DNA repair and causing Microsatellite Instability (MSI). Previous studies have demonstrated that in current practise less than 10% of these cases are identified as LS due to a lack of appropriate testing with immunohistochemistry or MSI analysis. The international Revised Bethesda Criteria were devised in 2004 to help identify such cases; these criteria include all individuals diagnosed < 50 years of age, those with synchronous or metachronous CRC or LS-related cancer, those with significant family history of CRC or a LS-related cancer, or individuals diagnosed < 60 years of age with MSI-type histology.
Methods We identified all new cases of colorectal cancer over a 1 year period prior to and subsequent to the establishment of a dedicated 'Family History of Bowel Cancer Service'. Adherence to the Revised Bethesda Criteria was determined by examination of medical records and UK National Bowel Cancer Audit Programme (NBOCAP) data. Pathology reports were studied in patients aged under 60 years of age at diagnosis looking for features consistent with MSI-H histology. We used Chi-squared testing to calculate significance for binary variables.
Results Over the two year period 198 cases of colorectal cancer were discussed at the CRC multidisciplinary meeting. 41 patients fulfilled the Revised Bethesda Criteria for screening for Lynch Syndrome; 12 individuals were diagnosed under the age of 50 years (~6%); 4 patients were diagnosed under 60 years of age and had MSI-H type histology and 25 patients had a significant family history of CRC or a LS-related cancer. In the year prior to the introduction of the clinic, we identified 18 cases meeting the Revised Bethesda Criteria for screening for LS; however, only 1 patient had been tested (5.6%). In contrast following the introduction of the clinic 19 of 23 identified cases (82.6%) were tested. Chi-squared testing demonstrated clinical significance when comparing the screening prior to and subsequent to the introduction of the clinic, p value = 9.7x 10–7 (Chi = 23.9956). 6 of the screened cases demonstrated molecular features with MSI and abnormal Immunohistochemistry, and are undergoing further germline genetic testing.
Conclusion The establishment of a dedicated 'Family History of Bowel Cancer Service' resulted in a significant improvement in the screening for Lynch Syndrome in accordance with the Revised Bethesda Criteria, 2004. We would recommend that this service should be extended throughout the United Kingdom to help aid early diagnoses and improve long-term outcomes.
Disclosure of Interest None Declared.

PWE-171 BONE MORPHOGENETIC PROTEIN (BMP) PATHWAY DYSREGULATION SUBVERTS ONCOGENE INDUCED SENESCENCE MECHANISMS IN THE SERRATED PATHWAY OF TUMOURIGENESIS

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[1,2,*]T Boitsova, [1]H Rafferty, [1]H Davis, [1]C Bardella, [3]P Gill, [4]J East, [1]I Tomlinson, [3]R Chetty, [2]A Silver, [1,4]S Leedham. [1]*Molecular and Population Genetics, Wellcome Trust Centre for Human Genetics, Oxford;* [2]*Colorectal Cancer Genetics, Barts and the London Hospital Medical School, London;* [3]*Histopathology;* [4]*Translational Gastroenterology Unit, Oxford University Hospitals, Oxford, UK*

Introduction The serrated colorectal carcinogenesis pathway is increasingly recognised as a distinct and important route to CpG island methylated phenotype (CIMP) carcinomas, yet comparatively little is known about the molecular pathogenesis of these lesions. The precursor lesions - hyperplastic and serrated polyps, are initiated by *BRAF* or *KRAS* mutations which initially induce proliferation but are followed by activation of oncogene-induced senescence (OIS) pathways resulting in telomere independent cell-cycle arrest. Subversion of OIS mechanisms is thus necessary for progression of serrated lesions. We assessed (epi)genetic mutation burden and morphogen expression in different colorectal polyps and investigated the effect of disrupted morphogen balance on OIS systems
Methods Colonoscopic samples of hyperplastic, serrated, conventional adenomas and neighbouring normal tissue were used. Individual crypt gene expression was measured, DNA extracted and (epi)mutation burden assessed. Epigenetic silencing of the BMP antagonist *GREM2* was assessed in serrated polyps and a methylated cell-line. *K-rasV12* transfection of mouse embryonic fibroblasts (MEF) was used to induce OIS and assess dynamic morphogen changes in senescing cells. *shRNA* knockdown of *BMP4* in a cancer (HCT116) and primary immortalised (HCEC) cell-line was used to reverse the changes seen in human polyps.
Results Marked BMP component changes were seen in both serrated and traditional adenomas, with fewer changes in rectal hyperplastic polyps. Only serrated polyps showed aberrant gene methylation, including epigenetic transcriptional silencing of the BMP antagonist *GREM2*. Differential BMP ligand expression (*BMP2* downregulated, *BMP4* upregulated) was noted in adenomas and confirmed with *in situ* hybridisation. *KrasV12* OIS induction in MEF's caused the reversed expression pattern of BMP ligands to that seen in polyps, a change not seen in replicative senescence of the same cells. *BMP4* shRNA knockdown impeded anchorage-dependent growth of HCT116 cells and provoked a rapid cell senescence response in HCEC cells with growth arrest and up-regulation of both *p21*and *p16.*
Conclusion We hypothesise that BMP ligands are involved in mediating (*BMP2*), or subverting (*BMP4*) oncogene-induced senescence, and that epigenetic silencing of specific BMP pathway constituents is selected early during serrated tumourigenesis. By demonstrating the mechanistic involvement of the BMP pathway in OIS we have identified an important early tumour promoting role of morphogen dysregulation which may inform future drug development.
Disclosure of Interest None Declared.

PWE-172 MICRONUTRIENT-ANTIOXIDANT SUPPLEMENTATION HAS NO IMPACT ON GASTRIC ATROPHY IN ZAMBIAN ADULTS: A RANDOMISED CONTROLLED TRIAL

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[1,*]V Kayamba, [2]M S Chomba, [3]P Kelly. [1]*Dept Medicine, University Teaching Hospital, Lusaka, Zambia;* [2]*Dept Medicine, UTH, Lusaka, Zambia;* [3]*Blizard Institute, Barts & The London, London, UK*

Introduction With the increasing number of gastric cancer cases in young patients in Zambia, we set out to investigate the possibility of reversing gastric atrophy, a precancerous lesion, using micronutrient-antioxidant supplementation in a retrospective analysis of a published randomised controlled trial. We recently reported that low antioxidant levels were associated with gastric cancer in Zambia. In an earlier study, we had demonstrated that people with the HIV infection tend to have higher gastric pH than those without HIV.
Methods Archival samples from a randomised controlled trial, (Kelly *et al Trans R Soc Trop Med Hyg.* 2008; 102:194–9) were used in this study. These were collected from healthy volunteers in Misisi, a densely populated and impoverished township in Lusaka, and carefully stored at –80°C in a secure laboratory at the University Teaching Hospital, the largest referral hospital in Zambia. In this controlled trial, 500 volunteers were randomly allocated to either a micronutrient-antioxidant supplementation or placebo. The

supplements contained vitamins, A, B1, B2, B6, B12, C, D_3, E, niacin, folic acid, iron, zinc, copper and selenium. We analysed 215 samples collected in 2005, from subjects who had taken either supplementation or placebo for a median of 19 (range 14 to 27) months. Gastric atrophy was determined using pepsinogen 1 to 2 ratio of less than 3.0 using BIOHIT ELISA kits, Helsinki, Finland, according to the manufacturer's instructions. Fasting gastric pH was available on 121 participants. The presence of atrophy was compared between the intervention and the placebo groups. Other factors analysed included the effect of HIV infection, age, body mass index (BMI), smoking, alcohol intake and gastric pH.

Results Gastric atrophy was found in 8 (7.8%) of 103 subjects on supplementation, and 7 (6.3%) of 112 on placebo (RR 1.24; 95%CI 0.47–3.3; $P = 0.22$). HIV infection was diagnosed in 5 participants with atrophy and 61 without (RR 1.07; 95%CI 0.37–3.2; $P = 1.0$). The lack of effect of supplementation on atrophy was not changed after stratification for HIV status (M-H OR 2.0; $P = 09.20$). Gastric atrophy was found to be more prevalent in those above the age of 40 years. In univariate and multivariate analysis, BMI, smoking, alcohol intake showed no impact on gastric atrophy. Gastric pH and pepsinogen 1:2 ratio were inversely correlated (Spearman's r = –0.34; $P = 0.0001$).

Conclusion An average of nine months of micronutrient-antioxidant supplementation has no impact on gastric atrophy in Zambian healthy adults. The high gastric pH seen in HIV patients can not be attributed to gastric atrophy.

Disclosure of Interest None Declared.

Nutrition

PWE-173 ELIGIBILITY FOR BARIATRIC SURGERY IN ENGLAND ACCORDING TO NICE GUIDELINES

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[1,*]A Ahmad, [1]A Laverty, [1]E Aasheim, [1]A Majeed, [1]C Millett, [1]S Saxena. *[1]Imperial College London, London, UK*

Introduction The number of people in England who are potentially eligible for bariatric surgery according to criteria set out in UK national guidance is not known. We used data from Health Survey for England (HSE) 2006, representative of the non-institutionalised English population, to determine the number of people eligible for bariatric surgery and their socio-demographic characteristics.

The National Institute for Health and Clinical Excellence (NICE) criteria for eligibility are those with body mass index (BMI) 3540 kg/m^2 with at least one comorbidity that could be improved by losing weight, or a BMI > 40 kg/m^2. The comorbidities examined were hypertension, type 2 diabetes, stroke, coronary heart disease, and osteoarthritis.

Methods Of 13,742 adult respondents in HSE 2006, we excluded participants with invalid data for BMI (N = 2103), comorbidities (N = 2187) or socio-demographic variables (N = 27), for a final study sample of 9,425 participants.

Results 374 (4.0%) had BMI 3540 kg/m^2 with at least one comorbid condition and 179 (1.9%) had BMI > 40 kg/m^2. 5.9% of the general adult population therefore fulfilled criteria for bariatric surgery in England. Those eligible were more likely than the general population to be women (60.1% vs 39.9% P < 0.01), retired (22.4% vs 12.8% P < 0.01), and have no educational qualifications (35.7% vs 21.3% P < 0.01).

Conclusion The number of adults potentially eligible for bariatric surgery in England (2,346,542 people based on census data) far exceeds provision. Greater investment may be required to ensure the National Health Service (NHS) and other health services internationally have the capacity to meet the needs of all those eligible for bariatric surgery under national guidance. In doing so, monitoring of implementation is essential to ensure access based on need.

Disclosure of Interest None Declared.

PWE-174 EVALUATION OF A COMMUNITY-BASED NUTRITIONAL SCREENING AND INTERVENTION SERVICE FOR NEWCASTLE ELDERLY CARE HOME RESIDENTS: THE EFFECT ON NUTRITIONAL AND CLINICAL OUTCOMES

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[1]C G Mountford, [2,*]A Okonkwo, [3]L Sweeney, [1]N P Thompson. *[1]Dept of Gastroenterology, Newcastle Upon Tyne Hospitals NHS Foundation Trust; [2]Medical School, Newcastle University; [3]Dept of Dietetics, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK*

Introduction Malnutrition affects more than 3 million people in the United Kingdom. Elderly care home residents are at particular risk. This study aimed to establish the prevalence of malnutrition in Newcastle elderly care home residents and investigate whether a community nutritional screening and intervention programme could be successfully delivered and could improve nutritional and clinical outcomes in residents who were malnourished or at risk of malnutrition.

Methods This was a multi-centre community-based cohort study in five care homes in Newcastle. 205 participants entered the study; 66 males and 139 females (mean age 84.2 ± 8.5 years). Residents were excluded if they were receiving end of life or respite care, were in hospital or were uncooperative with measurements. Follow-up data was available on 175 residents. Residents already taking an oral nutritional supplement (ONS) were excluded from the interventions. Those with a 'Malnutrition Universal Screening Score' ('MUST') of 0 were followed up at 12 weeks, but received no active intervention. Those with a score of 1 received dietetic advice to increase oral intake and those with a score of 2 or more received dietetic advice and were prescribed an ONS (220ml, 1.5kCal/ml) twice daily for 12 weeks.

Body mass index (BMI), 'MUST' score, mini nutritional assessment score® and mid upper arm muscle circumference (MAMC) were recorded at baseline and 12 weeks. Feeling of wellbeing was assessed using the Geriatric Depression Scale (GDS). Hospital admission data for the study period were compared to data for the previous year for each home.

Results Prevalence of malnutrition or risk of malnutrition was 36.6% (95% CI 30.0 to 43.2). Mortality during the study period for residents with a 'MUST' score of 0 or 1 was 7.9% and rose to 50.0% in those with a score of 4 (P = 0.004). Nutritional status did not deteriorate in the majority (86%) of residents during the study. However, there were no clinically significant improvements in anthropometric measures, including BMI (P = 0.445) and MAMC (P = 0.256) following any study intervention. There were no significant changes in GDS (P = 0.385) or hospital admission rates (P = 0.537) following any intervention.

Conclusion Malnutrition is common in care home residents and associated with increased mortality. Nutritional interventions, including ONS, given over a 3-month period in those with a MUST score of 2 or more, did not appear to improve nutritional status, reduce mortality or decrease hospital admission rates.

Disclosure of Interest None Declared.

PWE-175 SIMPLE INTERVENTION IMPROVES OUTCOME IN DELIVERY OF PARENTERAL NUTRTION

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[1]P Davies, [1]J Bowness, [2]C Whittingham, [3,*]A Bassi. *[1]Surgery; [2]Dietetics; [3]Gastroenterology, St Helens and Knowsley NHS Trust, Prescot, UK*

Introduction Recent report by NCEPOD into hospital care of patients receiving parenteral nutrition (PN) suggested that only 19% adult patients had PN care that was considered to represent good practise. An initial audit (retrospective audit over six months) in our hospital suggested lack of quality control at the point of