selective serotonin reuptake inhibitors (SSRIs) are the most frequently cited environmental risk factors.

We sought phenotypic and genetic associations with microscopic colitis in European patients enrolled in the UK Biobank.

Methods We undertook a genome-wide association study of 483 cases of microscopic colitis defined by ICD code K52.8 (other specified noninfective gastroenteritis and colitis) and 4 50 616 controls. We tested 9527357 single nucleotide polymorphisms (SNPs) imputed using the haplotype reference consortium (HRC) reference panel. Association tests were performed using a linear mixed model (BOLT-LMM) including age, gender, study centre and chip as covariates. We also tested for associations with classical HLA alleles that were imputed using HLA*IMP 02.

Results Participants with microscopic colitis were older (61.9 [56.2–65.4] vs. controls 58.6 [50.5–63.8], p=5e-15); more frequently female (65.6% [317/483] vs 54.2% [244531/450616], p=5e-07); more likely to smoke (14.7% [71/483] vs 10.4% [46792/450616], p=0.003) and were more often also diagnosed with coeliac disease (3.3% [16/483] and 0.4% [1991/450616], p=7e-10) than controls. In terms of drug factors, participants with microscopic colitis were more likely to have been exposed to proton-pump inhibitors (20.3% [98/483] cases vs 10.3% [46397/450156] controls, p=9e-11) than controls, but not aspirin/NSAIDs or SSRIs.

We found a genome-wide significant association signal within the HLA region. The lead SNP was rs2596560 (OR 0.64, 95% CI: 0.57, 0.71, p=4e-9). Subsequent HLA imputation demonstrated that the signal was in linkage disequilibrium with the class I and II alleles that comprise the ancestral MHC 8.1 haplotype that has been linked with coeliac disease. Multivariable linear analyses showed that microscopic colitis (p=9e-08) and coeliac disease were independently associated with the rs2596560 SNP. There were no specific genetic associations seen in the subset of participants with microscopic colitis taking aspirin/NSAIDS, PPIs, or SSRIs.

Conclusions We have confirmed a genome-wide significant association for microscopic colitis in the HLA region. Further studies are needed to understand the role of this locus in the pathogenesis of microscopic colitis and larger drug exposed cohorts will need to be identified to explore possible pharmacogenetic associations.

OTU-023 RANDOMISED TRIAL OF EPA AND ASPIRIN FOR COLORECTAL CANCER CHEMOPREVENTION: THE SEAFOOD POLYP PREVENTION TRIAL

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The omega-3 fatty acid eicosapentaenoic acid (EPA) and aspirin are candidate colorectal cancer (CRC) chemoprevention agents, which both have proof-of-concept for anti-CRC activity in man, aligned with an excellent safety profile.

Methods A randomised, placebo-controlled 2 × 2 factorial trial of EPA free fatty acid (FFA) 2 g daily (E; either as the FFA or triglyceride [TG]) and/or aspirin 300 mg daily (A) in 'high risk' patients (≥3 adenomas if one≥10 mm, or ≥5 small adenomas) identified at screening colonoscopy in the English Bowel Cancer Screening Programme (BCSP). The primary endpoint was the adenoma detection rate (ADRa; the% with any adenoma) at one year surveillance colonoscopy. Secondary endpoints included mean number of adenomas per patient (MAP), 'advanced' ADRa, adenoma location (right/left) and type (conventional/serrated). Analysis was on an intention-to-treat basis using an 'at the margins' approach, adjusted for BCSP site and repeat endoscopy at baseline.

We recruited 709 participants (80% male, mean[SD] 65[5] years, 82% BMI >25 Kg/m^2). The four treatment groups (E +A n=177; E n=178; A n=176; placebo n=176) were well-matched at baseline. There were no differences in EPA levels or tolerability between FFA and TG users. Overall, ADRa was 62%, with no evidence of any effect for EPA (risk ratio 0.98 [95% CI 0.87–1.12]) or aspirin (0.99 [0.87–1.12]). Aspirin use was associated with reduced total MAP (incidence rate ratio 0.78 [95%CI 0.68–0.90]), with evidence of an effect on serrated (0.46 [0.25–0.87]) and right-sided (0.73 [0.61–0.88]) lesions. Evidence that EPA reduced MAP was restricted to conventional (0.86 [0.74–0.99]), left-sided (0.75 [0.60–0.94]) adenomas, but not total MAP (0.91 [0.79–1.05]). EPA and aspirin treatment were well tolerated with an excess of mild-moderate GI adverse events (AEs), especially in the E arm. There were 6 bleeding AEs across the treatment arms.

Neither EPA nor aspirin treatment was associated with reduction in the ADRa in 'high risk' patients. Secondary analyses revealed no evidence that EPA was effective in reducing the total number of adenomas, but there was some evidence for efficacy of aspirin. Both agents displayed effects on MAP, which were adenoma type- and site-specific, compatible with known anti-(proximal) CRC activity of aspirin. Best use of EPA and aspirin may need a precision medicine approach to adenoma recurrence. ISRCTN05926847 – This project was funded by the EME Programme, an MRC and NIHR partnership. The views expressed in this publication are those of the author(s) and not necessarily those of the MRC, NHS, NIHR or the DoH.

OTU-024 IMPACT OF GFOBT SCREENING IN ENGLAND ON COLORECTAL CANCER MORTALITY

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Introduction Colorectal cancer (CRC) screening using biennial gFOBT was introduced in England in September 2006[1] and by 2010 was being offered >90% of 60–69 year olds, rising to >95% of 60–74 year olds by 2014. Uptake of screening has shown no substantial change since 2006 and in 2016 was 58% for the whole of England. This study seeks to examine the trends in CRC mortality and ascertain any impact of screening.

Methods Data for the period 2001–2016 was extracted from the ONS website (www.ons.gov.uk) and CRC mortality rates by 5 year age bands from age 45 calculated. CRC was defined

according to the ICD 10th Revision codes C18 (colon) and C19/C20/C21 (rectum, recto-sigmoid and anus). To allow comparisons over time data on anal cancers and from Wales are included. Rates in age groups never offered screening were compared with those potentially screened (age group 65–74 years). Joinpoint analysis was undertaken to look for changes in trends.

Results Comparing 2005 and 2016 CRC mortality rates we found a decline of 28.8% in men and 27.4% in women in the 65–74 year olds, the age group where screening would be expected to have had greatest effect. In comparison in 50–59 year olds there was a 21.3% decline in CRC mortality in men and a 5.5% decline in women. Whilst joinpoint analysis identified no step change in mortality rate over time, closer examination of the data showed that the decline in CRC mortality has been predominantly in the C18 code (colon). For C18 there was a 37.8% decline in men and a 37.7% decline in women. In comparison there were 36.0% and 29.2% declines respectively in the 50–59 year olds. For the C19–21 code there was a mortality decline of 15.4% in men and 6.2% in women in the 65–74 year olds and in the 50–59 year olds a decline of 2.2% in men and an increase of 39.0% in women.

Conclusion Overall CRC mortality has shown a steady decline. Declines have been substantially greater in the screened age groups although no step change was identifiable with joinpoint analysis. At this time-point the mortality reductions are predominantly in colon cancer (C18). Despite concerns that gFOBT screening maybe less effective in women mortality reductions were similar to men.

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OTU-025 GASTROINTESTINAL CONSEQUENCES OF CANCER: AN EVALUATION OF TEN YEARS EXPERIENCE AT A TERTIARY CENTRE

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OTU-026 FEASIBILITY & ECONOMIC EVALUATION – CHROMOENDOSCOPY FOR DETECTING PROXIMAL SERRATED NEOPLASIA: RANDOMISED CONTROLLED TRIAL, CONSCOP

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Introduction Most post-colonoscopy interval colorectal cancers occur in the proximal colon. Serrated lesions are often precursors to these and considered harder to detect. Chromocolonoscopy may improve detection rates, however the safety, feasibility and economic impact of this intervention to detect and resect proximal serrated neoplasia are not known.

Methods We conducted a parallel randomised controlled, open label trial within centres in the Bowel Screening Wales (BSW) programme. Participants testing positive on Faecal Occult Blood Test were randomised to standard white light colonoscopy or chromocolonscopy. Randomisation was performed centrally via an internet based minimisation algorithm. Data from index colonoscopies and associated clearance procedures were analysed. All proximal polyps were centrally reviewed by an expert pathology panel.

Results Between November 2014 and June 2016, 741 people (360 white light, 381 chromocolonoscopy) from all BSW centres consented to participate in the study and all were included in the analysis. For participants in the chromocolonoscopy arm, the procedure took an average of 6.3 (95% CIs: 4.2–8.4) min longer but serious adverse reaction rates, bowel preparation scores, completion rates, endoscopist assessment of procedural difficulties, procedure comfort scores, technical quality indicators, and types of sedation were similar in each arm. The proximal serrated polyp detection rate was significantly higher in the chromocolonoscopy arm (23/360 (6.4%) vs 45/381 (11.8%); univariable OR 1.96, 95% CI: 1.16–3.32, p=0.012; multivariable OR 2.04, 95% CI: 1.18–3.50, p=0.010). A 1% likelihood increase in additional significant serrated lesions retrieval would cost £35.22.

Conclusions A large RCT of index chromocolonoscopy powered for improved significant serrated polyp detection within a screening population is safe and feasible and initial efficacy results are encouraging. ClinicalTrials.gov: NCT01972451.

OTU-027 A STUDY OF POST COLONOSCOPY COLORECTAL CANCER (PCCRC) IN ENGLAND

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Introduction PCCRC is a key quality indicator for the detection and prevention of colorectal adenocarcinoma (CRC). It is not known whether rates of PCCRC are changing over time. There is limited evidence of factors associated with PCCRC that might be amenable to quality improvement interventions.

This study investigated trends in rates of PCCRC in the NHS in England; the extent of variation between NHS trusts; and potential causal associations with PCCRC.

Methods Using linked national Hospital Episode Statistics and National Cancer Registration and Analysis Service data all individuals who had undergone a colonoscopy procedure between 1/1/2006 and 31/12/2012 and who developed a CRC to 31/12/2015 were identified. NHS trust provider status and potential associations with PCCRC were included in the analysis.

International consensus methodology was used to calculate the PCCRC – 3 year rate (PCCRC-3 yr).[1 2] Colonoscopies