Abstracts

symptom response (adequate relief), gut microbiome (16S rRNA sequencing), short-chain fatty acids (SCFA, gas liquid chromatography), volatile organic compounds (VOC) (gas chromatography/mass spectrometry) and urine metabolomics (NMR spectroscopy) at baseline (BL) and 4 weeks. Data were analysed by Chi² for dichotomous outcomes and Kruskal-WallisMann-Whitney U tests for continuous variables. Predictive analysis was tested using receiver operator curves (ROC) and orthogonol partial least squared discriminant analysis (OPLS-DA).

Results Response rate (adequate relief) at 4 weeks was greater in the LFD+GOS (67%) and LFD (50%) than the Control group (30%) (p=0.046). The phylum Actinobacteria was lower (p<0.001), specifically *Bifidobacterium* (p=0.002) and *Collin-sella* (p=0.004), in the LFD and LFD+B GOS groups compared to Control at 4 weeks. Prediction of response to the LFD was seen in the LFD group only, with significant separation of BL faecal VOC profiles (AUC=0.854, p=0.045), faecal propionate (AUC=0.848, p=0.009), and urine metabolite profiles (Q²=0.296 vs randomised-0.175). *Roseburia*, *Blautia*, *Lachnospira* and *Faecalibacterium*, were positively but not significantly associated with VOC classes that predicted response when all samples were correlated. Microbiome and VOC showed a significant negative correlation between propionic acid derivatives and *Phascolarctobacterium* (r=-0.85 and-0.81, p<0.05) at BL in the LFD group only although the difference in *Phascolarctobacterium* between responders (1.5%) and non-responders (9.3%) at BL did not reach significance (p=0.055).

Conclusions The LFD +B GOS improves symptoms in IBS compared to Control but the LFD significantly reduces Actinobacteria and addition of 1.4 g/d of prebiotic B-GOS does not overcome this effect. Faecal VOCs and SCFAs and urine metabolomes may predict clinical response to the LFD, and specific bacterial groups correlate with predictive metabolites. Larger studies are required to validate these algorithms to develop personalised nutrition in IBS.

Colon and Anorectum

OTU-021 EFFECT OF THE TWO-WEEK WAIT REFERRAL PATHWAY ON COLORECTAL CANCER DETECTION: SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction In 2000 the two-week-wait (TWW) suspected cancer pathway was launched; national TWW performance data is lacking. This systematic review is the first to comprehensively evaluate the latest evidence on cancer detection through the TWW for suspected lower gastrointestinal malignancy.

Method This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses [PRISMA] 2009 statement. Cochrane, EMBASE, Medline via Pubmed, NHS Evidence, Trip and the British Library Catalogue were searched, plus references were hand-searched. Disagreements were resolved via consensus. Meta-analysis of pooled cancer conversions rates with 95% confidence intervals were calculated using a random effects model in R studio.

Results 95 full papers and 28 conference abstracts were reviewed. 77.5% full papers reported cancer conversion rate, corresponding weighted mean was calculated with a cancer conversion rate of 7.7% (6.9–8.5 C.I.). A forest plot of full-text paper results is shown in figure 1.

Abstract OTU-021 Table 1

Author, Year	Conversion rate [95% CI]
Aljarabah, 2009	0.100 [0.063–0.144]
Allgar, 2006	0.110 [0.082–0.141]
Aslam, 2017	0.069 [0.065–0.073]
Banerjee, 2017	0.068 [0.048–0.091]
Barwick, 2004	0.100 [0.056–0.155]
Beggs, 2011	0.073 [0.047–0.104]
Bhangu, 2010	0.060 [0.049–0.072]
Borowski, 2016	0.058 [0.053–0.063]
Chohan, 2004	0.138 [0.108–0.171]
Courtney, 2013	0.055 [0.050–0.060]
Debnath, 2002	0.089 [0.056–0.129]
Eccersley, 2003	0.150 [0.100–0.207]
Flashman, 2004	0.094 [0.076–0.113]
Hall, 2015, Peacock, 2013	0.064 [0.052–0.078]
John, 2008	0.110 [0.055–0.180]
Khong, 2015	0.055 [0.046–0.065]
Leung, 2010	0.081 [0.066–0.098]
Maruthachalam, 2005	0.081 [0.061–0.104]
Mukherjee, 2010	0.051 [0.035–0.070]
Padwick, 2013	0.053 [0.040–0.069]
Patel, 2014	0.072 [0.054–0.092]
Rai, 2007	0.100 [0.082–0.119]
Rai, 2007	0.060 [0.032–0.096]
Rai, 2008	0.108 [0.082–0.137]
Rao, 2005	0.044 [0.024–0.069]
Shaw, 2009	0.090 [0.078–0.102]
Smith, 2007	0.063 [0.054–0.072]
Sorelli, 2014	0.060 [0.008–0.147]
Spencer, 2004	0.103 [0.068–0.145]
Vaughan–Shaw, 2013	0.078 [0.068–0.088]
RE Model	0.077 [0.069–0.085]

Conclusion The pooled cancer conversion rate via TWW is similar to the cancer detection rate in the asymptomatic Bowel Cancer Screening Population (latest figure 8%) and is not having its intended impact on cancer diagnosis. Re-evaluation of the referral criteria needs consideration, focusing on symptoms with higher PPV in cancer.

OTU-022 GWAS OF MICROSCOPIC COLITIS IN THE UK BIOBANK CONFIRMS ASSOCIATION WITHIN THE HLA REGION

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Introduction The pathogenesis of microscopic colitis is poorly elucidated: it reportedly involves immune responses to luminal factors in genetically predisposed individuals. Previous genetic studies reported associations with HLA risk alleles in collagenous but not lymphocytic colitis. Non-steroidal anti-inflammatory drugs (NSAIDs), proton-pump inhibitors (PPIs) and

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 end-point 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/m²). 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 2006¹ 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