alteration accrual in adenoma progression. A cost-effective test to more accurately define the cohort of patients that will never progress to CRC would reduce the burden of procedures on both the patient and NHS.

Methods FFPE adenoma tissue resected from patients who subsequently developed CRC (progressors) and matched adenomas from patients who remained cancer-free for 5+ years from the date of polypectomy (non-progressors) from a single-centre hospital archive (2008–2014) were analysed using low pass whole genome sequencing (LP-WGS). All adenomas were sequenced to a depth of >0.1x on an Illumina platform and CNA burden was investigated.

Results In this case-control study, progressors n=12 have a greater CNA burden than non-progressors n=37, with >0.05% of the genome altered in progressors and <0.01% in non-progressors, p=0.292. The number of distinct copy-number segments were analysed to compare the presence of candidate CNAs. Gains were seen in chromosomes 7, 9 and 12 (>25%) and losses in 18 (>10%) in the progressor cohort. In comparison, minimal chromosomal changes were seen in non-progressors.

Conclusions Adenomas from people who subsequent progressor to cancer may have a greater percentage of the genome altered when compared to non-progressors, with the majority of non-progressor adenomas having little or no genomic alterations. Larger sample sizes are required to confirm this. In the future, it is conceivable that patients with high burden of genomic alterations in their adenomas would be offered more intensive follow-up surveillance that low-burden adenoma patients.

054 EVALUATING ORAL AND INTRAVENOUS IRON THERAPY ON BACTERIAL POPULATIONS IN NORMAL MUCOSA AND COLORECTAL TUMOUR

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Introduction Anaemia is prevalent in around 60% of colorectal cancer (CRC) patients, mostly due to iron deficiency anaemia (IDA) and typically treated with oral iron supplements. However, this may increase the availability of luminal iron to gut bacteria leading to bacterial growth. This may potentially promote microbial dysbiosis, favouring the growth of pathogenic bacteria at the expense of commensal bacteria. Many pathogenic bacteria have heightened iron acquisition mechanism which aid their virulence, which can contribute to tumour promoting inflammation. To assess this, we compared bacterial populations and systemic cytokine production in CRC patients with IDA treated with oral or intravenous iron supplements.

Methods Patients with CRC and IDA received oral-ferrous sulphate (OI) (n=20) or intravenous ferric carboxymaltose (IVI) (n=20). Normal and tumour tissues were obtained post-surgery and analysed for mucosal adherent gut microbiota using 16S rRNA profiling. Bacterial richness was assessed using the Chao1 test and α-diversity was assessed using the Phylogenetic and Shannon index tests. Systemic cytokine levels were measured in the serum before and after treatment using a cytokine multiplex assay.

Results Species richness was significantly higher in normal mucosa from the OI treatment group compared to the IVI group (p=0.033). Likewise, species α-diversity in normal mucosa was significantly greater in OI treated patients (Phylogenetic p=0.037, Shannon p=0.036). However, tumours showed no differences in species richness or α-diversity between treatment groups. Following OI treatment, serum levels of the pro-inflammatory cytokines IL-1b and IL-12p40 were significantly increased (p=0.01 and p=0.03), respectively, and the anti-inflammatory cytokine IL-4 levels were significantly reduced (p=0.01). In contrast, no changes in these cytokines were observed in the IVI group.

Conclusion OI therapy increased bacterial richness and α-diversity in normal colonic mucosa and contributed to systemic inflammation in CRC patients. However, the tumour microbiota seems to be protected against increased gut iron, with no difference between OI and IVI therapy. This may be due to pre-existing dysbiosis within the cancer; hence, iron influence may be restricted in the tumours. Ongoing work will assess the abundance and diversity of protective and pathogenic bacteria to determine if these are causative in the systemic inflammation observed with OI therapy.

055 LACTULOSE INCREASES SMALL BOWEL BUT NOT COLONIC WATER CONTENT; QUESTIONING THE OSMOTIC LAXATIVE DOGMA

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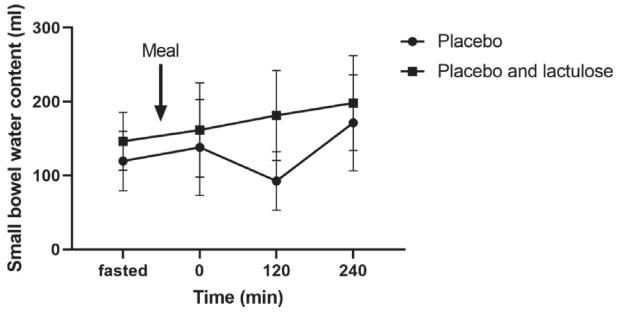
Introduction Lactulose is widely perceived as an osmotic laxative which increases small bowel water content but its impact on large bowel water content is unclear. Ondansetron has been shown to slow left sided colonic transit but whether this is due to reduced secretions, enhanced absorption or solely altered motility is unknown. Our aim was to test the effect of therapeutic doses of lactulose and whether ondansetron altered its laxative effect.

Methods This was a double-blind, randomised, two-treatment crossover study in 16 healthy volunteers who attended for 2 study periods. Participants received the study drug (either 8 mg ondansetron or placebo) and had MRI scans fasted then every 2 hours for 6 hours after a rice pudding meal. They then received lactulose (20 ml [39 mmol]) twice daily and the study drug three times daily for 36 hours. On day 3 they had lactulose and the study drug, and further MRI scans every 2 hours for 4 hours. Measurements included small bowel water content (SBWC), magnetic resonance T1 relaxometry to assess water content in the ascending colon (AC) (T1 has previously shown to be directly proportion to stool% water) and gut transit from the weighted average position of transit markers ingested on Day 2.

Results In the placebo arm, lactulose increased small bowel water content maximally at 120 minutes (figure 1), with an increase of 89 ml (95% CI 32 ml to 145 ml) compared to the test meal without lactulose. Lactulose significantly increased AUC SBWC from 0–240 minutes (43.3 [25.0] l.



Abstract O55 Figure 1

hour *versus* 30.0 [17.0] l.hour with no lactulose, $p=0.0078$) but had no effect on T1AC even after 36 hours treatment (0.74 [0.4]s *versus* 0.64 [0.28]s, $p=0.72$). Ondansetron did not significantly alter SBWC or T1AC, either after a meal alone or when combined with repeated doses of lactulose. Gut transit (median [IQR]), was unchanged by ondansetron compared to placebo (1.7 [0.5–5.8] versus 1.4 [0.5–6], $p=0.63$).

Conclusions Although lactulose increases SBWC by an amount close to that predicted by its osmotic load (130 ml) this did not significantly alter colonic water content. This may be due to its known rapid metabolism and suggests its laxative effect may be due to the stimulatory effects of products of fermentation. Ondansetron did not alter postprandial intestinal water nor reduce the effect of lactulose suggesting that its anti-diarrhoeal effect may be primarily due to altered colonic motility.

O56 RISK FACTORS FOR PROXIMAL COLON CANCER: HOW INFORMATIVE ARE POLYP FINDINGS IN DETERMINING FUTURE RISK?

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Introduction Early detection and removal of premalignant colorectal polyps with a high potential to progress to invasive cancer is important for incidence reduction. However, there is evidence that cancers in the proximal colon tend to be detected later than other subsites resulting in more advanced stage at diagnosis and lower survival. This study examined which polyp characteristics were independently associated with proximal colon cancer incidence.

Methods Data were used from the All Adenomas study, which examined endoscopy and associated pathology data on ~30,000 individuals with at least one adenoma identified. Eligible participants underwent colonoscopy between 1984 and 2010 in one of 17 UK hospitals. Polyp characteristics at baseline colonoscopy, including number, size, histology, grade and location were obtained from the database. Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for incidence of proximal colon adenocarcinoma. Time since baseline colonoscopy was used as the underlying time scale. HRs were mutually adjusted for polyp characteristics in addition to demographic- and colonoscopy-related confounders.

Results Of the 27,812 (42.4% female) participants included in the analysis, 227 (0.82%) developed proximal colon cancer during a median follow-up of 9 years. Cumulative incidence over 15 years was 1.4% (95% CI: 1.2% - 1.6%). Proximal colon cancer incidence was higher among participants with ≥1 adenoma in the proximal colon at baseline, either solely or in addition to distal adenomas, compared to patients with only distal adenomas (HR 1.95, 95% CI: 1.46 – 2.62). The risk was also higher among those with ≥3 adenomas compared to those with <3 adenomas at baseline (HR 1.47, 95% CI: 1.04 – 2.08) and those with adenomas ≥10 mm compared to those with adenomas <10 mm (HR 1.47, 95% CI: 1.07 – 2.01). Neither adenoma histology nor grade were independently associated with the outcome.

Conclusions Adenoma location, number and size are informative of subsequent proximal colon cancer. This study provides evidence needed to identify individuals at high risk for proximal colon cancer who would require post-polypectomy colonoscopy surveillance for the early detection and removal of cancer and precancerous lesions in this subsite.

O57 THE VALUE OF GERMLINE MUTATION TESTING IN SERRATED POLYPOSIS SYNDROME

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Introduction Serrated Polyposis Syndrome (SPS) is now known to be the commonest polyposis syndrome. Previous analyses for germline mutations have shown no consistent positive findings[1]. To exclude other polyposis syndromes, new 2019 BSG guidelines[2] advise gene panel testing if: the patient is under 50 years of age; if there are multiple affected individuals within a family; or if there is dysplasia within any of the polyps.

Methods A database of patients with SPS according to the WHO 2019 criteria[3] was established at the Oxford University Hospitals NHS Trust. Data collection began in 2010 and in total there are 192 SPS patients. The results of any patients sent for genetic testing were analysed.

Results Out of 192 patients, 76 underwent genetic testing. The majority were tested for a hereditary colorectal cancer panel including MUTYH, APC, PTEN, SMAD4, BMPR1A, STK11 and Lynch syndrome mismatch repair genes. Of these, 14 had a positive genetic test result. Table 1 characterises patient with positive results.

Conclusions 7% (14/192) of SPS patients were affected by heterozygous germline mutations, higher than in previous series[1], including previously unreported associations with CHEK2 and POLD1. This led to a change in management for patients or their families in seven cases. Only 57% (8/14) of these patients would have been recommended for gene panel testing in the current BSG guidelines[2]. Detection of germline mutations could have significant impact on risk assessment and clinical management, including advice on extra-colonic surveillance in patients and their family members.