



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.

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#### 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  $\geq 1$  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  $\geq 3$  adenomas compared to those with  $< 3$  adenomas at baseline (HR 1.47, 95% CI: 1.04 - 2.08) and those with adenomas  $\geq 10$  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.

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#### 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<sup>1</sup>. To exclude other polyposis syndromes, new 2019 BSG guidelines<sup>2</sup> 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<sup>3</sup> 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, BMP1A, 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<sup>1</sup>, 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<sup>2</sup>. 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.

**Abstract 057 Table 1** Characteristics of SPS patients with positive genetic testing

Gene affected	Mutation	WHO SPS type	Age at diagnosis	Clinical outcome
RNF43	c.471 del G <i>Pathogenic variant</i>	II	68	Cascade genetic testing for at-risk relatives
MUTYH APC	c.1187G>A <i>Pathogenic variant</i> c.646-4T>G <i>Uncertain variant</i>	I	70	Cascade genetic testing for at-risk relatives
MUTYH	c.1187G>A <i>Pathogenic variant</i>	II	32	Cascade genetic testing for at-risk relatives
SMAD4	c.455-2A>G <i>Pathogenic variant</i>	I	78	Upper GI endoscopic surveillance, HHT screening and cascade genetic testing for at-risk relatives
POLD1	c.946G>A <i>Pathogenic variant</i>	I	70	Cascade genetic testing for at-risk relatives
CHEK2	c.1427C>T <i>Pathogenic variant</i>	I	34	Annual PSA testing and cascade genetic testing for at-risk relatives
CHEK2	c.1100delC <i>Pathogenic variant</i>	I	68	Moderate risk breast screening and cascade genetic testing for at-risk relatives
MSH6	c.1054G>A <i>Uncertain variant</i>	I	30	No change
MSH6	c.2398G>C <i>Uncertain variant</i>	I	59	No change
MSH6	c.3026A>T <i>Uncertain variant</i>	I	36	No change
MSH2	c.835C>G, <i>Uncertain variant</i>	I	37	No change
APC	c.3479C>A <i>Uncertain variant</i>	II	54	No change
APC	c.2486C>T <i>Uncertain variant</i>	I	38	No change
NTHL1	c.512C>T <i>Uncertain variant</i>	II	52	No change

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## Neurogastroenterology

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## IS THE LOW FODMAP DIET EFFECTIVE IN THE LONG TERM? THE LARGEST MULTICENTRE PROSPECTIVE STUDY

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**Introduction** The low FODMAP diet (LFD) has been demonstrated to be effective in managing the symptoms of irritable bowel syndrome (IBS) in the short term. However, data remains limited on the long-term effects of this dietary therapy. The aim of this study was to assess the long-term effect of the LFD on symptom management and adherence.

**Methods** Patients with IBS who had received LFD advice between 2012–2019 were prospectively recruited at 7 centres in the United Kingdom. Participants were invited to complete dietary questionnaires assessing the LFD at long term follow up (>6 months). Symptoms were assessed using a modified gastrointestinal symptom rating scale (0, none; 1, mild; 2, moderate; 3, severe).

**Results** 589 patients were approached, with 154 participants completing the study (76% female, mean age 51±15 years). The mean duration of follow up following initiation of the LFD was 42±28 months. A statistically significant improvement in abdominal pain (2.3±0.8 vs 1.2±0.9, p<0.001), abdominal bloating/distention (2.3±0.8 vs 1.4±1.0, p<0.001) and bowel urgency (2.0±1.1 vs 1.3±1.0, p<0.001) was noted following the LFD at long term versus baseline. 78% (n=120) of individuals reported following an adapted LFD at long term follow up. 60% (n=92) reported grains (wheat, rye, barley) as a trigger for their symptoms, with 64% (n=98) purchasing gluten or wheat free products in the long term.

**Conclusion** This is the largest study demonstrating the efficacy of the LFD in the long term for individuals with IBS. Adherence to an adapted LFD appears to be good in the long term, with the majority of individuals reporting grains as a trigger and purchasing gluten or wheat free products to manage their symptoms.

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## MRI METHODS TO DEFINE COLONIC FUNCTION IN HEALTH AND CONSTIPATION

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**Background** RECLAIM is a multicentre study examining patients with functional constipation (FC) and IBS with constipation (IBS-C), along with healthy volunteers (HV) to correlate MRI findings with those from colonic manometry, and