Results 168 men, median age 70 (range 34 – 83), 50 women median age 61 (29 – 87), 28 treated for GI, 34 gynaecological & 156 urological cancer were randomised to booklet (n = 68), nurse (n = 80) or gastroenterologist (n = 70). 30 (44%) from the booklet and 4 (5%) from the nurse arm crossed to the gastroenterologist. Groups were well balanced for baseline scores and patient characteristics. 66.5% of patients had a baseline IBDQ-B score indicating moderate/severe symptoms. Intention to treat analysis showed a mean improvement in IBDQ-B score in the booklet arm of 4.9 (95% CIs 1.4–8.4), in the nurse arm 8.8 (6.9–11.2) and 10.3 (7.7–13.1) in the gastroenterologist arm. Improvement in IBDQ-B score was both clinically and statistically significant (compared to booklet) in the nurse (p = 0.04), gastroenterologist (p = 0.014) and combined treatment arms (p = 0.006). Outcomes in the nurse treated arm were not worse than those treated by the gastroenterologist (p = 0.428). Improvements were sustained over time.

Conclusion Targeted intervention following a detailed clinical algorithm can significantly ameliorate radiotherapy-induced GI symptoms. Most patients can be managed by a suitably trained and supported nurse. (Funding RfPB, NIHR)

Disclosure of Interest None Declared

OC-069 CONSTITUTIVE ACTIVATION OF THE DNA DAMAGE RESPONSE PATHWAY IN CANCER REPRESENTS A DEREGULATED PATHWAY

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Introduction The DNA damage response (DDR) is an innate cellular response allowing cells to halt the cell cycle and repair DNA damage sustained by activating various mechanisms. The efficacy of conventional cancer treatment modalities is related in their ability to induce DNA damage. Constitutive activation of the ataxia telangectasia mutated (ATM) dependent DDR and repair pathways have been reported in (pre) malignant human tissues and may undermine the efficacy of current cancer therapies. Inhibition of proteins involved in the DDR cascade is an attractive therapeutic concept that may overcome resistance to current cytotoxics and potentiate the effects of radiotherapy.

Methods A tumour microarray was created using 179 sporadic colorectal cancers; 152 were of the microsatellite stable phenotype. The microarray was interrogated using antibodies against proteins of the DDR signalling cascade. A colorectal cancer cell line model was utilised to asses the functionality of the constitutively activated DNA damage pathway. ATM inhibition in combination with ionising irradiation was analysed in the cell line model using radioactive quantification of DNA synthesis, flow cytometric cell separation, clonogenic survival and immunoblotting.

Results Phosphorylated Chk2 threonine-68, a surrogate marker of the DDR, was present in 22% of microsatellite-stable colorectal tumours and 33% of tumours with the microsatellite instability phenotype. High p53 staining was present in 53% of microsatellite stable cancers and 26% microsatellite instable cancers.

P21-null HCT116 cells display constitutive activation of the ATM DDR but display a defect in the ionising radiation induced S-phase checkpoint, termed radioresistant DNA synthesis. This radioresistant phenotype is associated with increased basal levels of Cdc25A protein, deficient DNA damage-induced degradation of Cdc25A and Chk2 mis-localisation. P21-null HCT116 and SW620 cells, which exhibit basal Chk2 threonine-68 phosphorylation, were unable to abrogate the S-phase checkpoint when treated with an ATM inhibitor, suggesting that the ATM–Chk2 arm is non-functional in these cells: inhibition of ATM did not potentiate the efficacy of ionising irradiation.

Conclusion In a colorectal cancer cell line model constitutive activation of the ATM DDR pathway reflected a non-functional pathway and inhibition of ATM in these circumstances was unable to potentiate the efficacy of ionising irradiation. Basal Chk2 threonine-68 phosphorylation in colorectal cancer may reflect a deregulated ATM DDR pathway and/or checkpoint adaption.

A predictive model is proposed that integrates functionality of the ATM-Chk2 axis, p53 mutation status and defects in DNA repair pathways when considering ATM inhibitor therapy.

Disclosure of Interest None Declared

OC-070 PERCEIVED DELAY AMONG PATIENTS WITH COLORECTAL, STOMACH AND OESOPHAGEAL CANCER: ANALYSIS OF DATA FROM A NATIONAL GP AUDIT

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Introduction The UK has significantly poorer cancer survival rates than comparable countries and diagnostic delay is perceived to be a significant contributory factor to this. The RCGP National Audit of Cancer Diagnosis in Primary Care (2009/10) included data on 3655 patients with colorectal and gastro-oesophageal cancer, including free text comments on avoidable delays in diagnosis, as perceived by the participating GPs. The aim of this study was to identify the principal causes of delay, as perceived by GPs, and how they differ by cancer site.

Methods Avoidable delay was reported for 36% of patients with colorectal cancer, 37% gastric cancer and 35% oesophageal cancer. Free text reports of the nature of the delay were available for 753 (28%) colorectal, 87 (28%) gastric and 164 (27%) oesophageal cancer patients. An extended version of The Model of Pathways to Treatment (Walter *et al* 2011) was developed for use as the analytical framework. Comments were categorised by CD with uncertain cases discussed and resolved with GR. In order to validate GP perceptions of diagnostic delay we compared categorised primary care and referral intervals for patients with and without perceived delay.

Results Primary care and referral intervals were significantly longer for patients with a perceived avoidable diagnostic delay (p = <0.0001), for all three cancer sites. The commonest reasons for delay for colorectal, gastric and oesophageal cancer patients were GP appraisal (29%, 14%, 16% respectively), referral delays (e.g. routine rather than 2 week wait) (13%, 23%, 32% respectively) and investigation delays (28%, 34%, 27% respectively). For colorectal cancer patients, help seeking delay was also a significant cause of delay (8%). Because causes of delay were reported by GPs there was a potential reporting bias, with delays occurring prior to first consultation or in secondary care possibly being under-reported.

Conclusion Diagnostic delay for patients with upper and lower GI cancers is multi-faceted, with GP appraisal and type of referral perceived as substantial contributors. Interventions aimed at reducing the time to diagnosis should be targeted at the key causes and settings of delay for different cancer sites.

Disclosure of Interest None Declared

REFERENCE

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OC-071 COMPARISON OF FAECAL M2-PK AND FIT IN SCREENING FOR COLONIC POLYPS IN AN AVERAGE RISK POPULATION

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Introduction Faecal immunochemical tests (FIT) are acceptable to a large part of the general population but used alone are poor at detecting adenomas. An ELISA which measures faecal M2-pyruvate kinase (M2-PK) has been shown to be useful for detecting colonic pathology.
Aims To prospectively compare M2-PK and FIT in screening for colonic polyps and cancer in the second round of our pilot FIT-based Colorectal cancer screening programme.
Methods The second round of our FIT pilot programme was conducted over a two year period. Patients were sent invites by post to return a FIT sample from each of two days. All participants were aged 50 – 74 and living locally to our hospital. As part of this round, over a six month period all invitations additionally included containers to collect a single M2-PK stool sample. All FIT's returned on time were measured locally. All M2-PK samples received within 48 hours of passing stool were frozen and analysed centrally by ScheBo Biotech AG (Germany).

All FIT positive (>100 ngHb/ml) or M2-PK positive (>4 U/ml) patients were contacted and assessed for colonoscopy. All colonoscopies were conducted in the same way between both groups.
Results Over the six month period 1,800 combined M2-PK and FIT invites have been sent.

879 samples were returned and analysed for faecal M2-PK and FIT; of these 245 were positive for either one or both of these markers. After being contacted 34 (13%) of this group were excluded as they had a colonoscopy within 3 years and were all in polyp surveillance programmes.

Of the remaining patients: 30 (3.4% of 879) were FIT positive M2-PK negative; 160 (18.2%) were positive for M2-PK (> 4U/ml) negative for FIT and 21 (2.3%) were positive for both markers.

In the FIT positive M2-PK negative group there were 10 patients with adenomas (adenoma detection rate 33%). In those who were M2-PK positive but FIT negative there were 34 people with adenomas (ADR 23%). Therefore these adenomas would not have been detected by relying on FIT alone. Of the remaining 21 positive for both, 6 (29%) had adenomas and another 4 (19%) had colitis/proctitis. There have not been any cancers in this group to date.

Interestingly sessile serrated adenomas were detected in 5 (4.4%) of people M2-PK positive but only two (less than 1%) in our entire FIT positive group.
Conclusion Studies have shown FIT has relatively low sensitivity for adenomas. The addition of another stool marker such as faecal M2-PK increases the detection of polyps in a screening population. A single M2-PK sample detects more adenomas than two day FIT alone. Also M2-PK appears to be more sensitive for serrated adenomas than FIT but further studies are needed to confirm this.
Disclosure of Interest None Declared

AYP symposium: surgery in adolescents

OC-072 THE MICROAEROPHILIC MICROBIOTA OF DE-NOVO PAEDIATRIC INFLAMMATORY BOWEL DISEASE: THE BISCUIT STUDY

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Introduction Children presenting for the first time with inflammatory bowel disease (IBD) offer a unique opportunity to study etiological agents before the confounders of treatment. Microaerophilic bacteria can exploit the ecological niche of the intestinal epithelium; *Helicobacter* and *Campylobacter* are previously implicated in IBD pathogenesis. The aim of the study was to assess these and other microaerophilic bacteria in de-novo paediatric IBD.
Methods 100 children undergoing colonoscopy were recruited including 44 treatment naïve de-novo IBD patients and 42 with normal colons. Colonic biopsies were subjected to microaerophilic culture with Gram-negative isolates then identified by sequencing. Biopsies were also PCR screened for the specific microaerophilic bacterial groups: Helicobacteraceae, Campylobacteraceae and *Sutterella wadsworthensis*.
Results 129 Gram-negative microaerophilic bacterial isolates were identified from 10 genera. The most frequently cultured was *S. wadsworthensis* (32 distinct isolates). Unusual *Campylobacter* were isolated from 8 subjects (including 3 *C. concisus*, 1 *C. curvus*, 1 *C. lari*, 1 *C. rectus*, 3 *C. showae*). No *Helicobacter* were cultured. When comparing IBD vs. normal colon control by PCR the prevalence figures were not significantly different (*Helicobacter* 11% vs. 12%, p = 1.00; *Campylobacter* 75% vs. 76%, p = 1.00; *S. wadsworthensis* 82% vs. 71%, p = 0.312).
Conclusion This study offers a comprehensive overview of the microaerophilic microbiota of the paediatric colon including at IBD onset. *Campylobacter* appear to be surprisingly common, are not more strongly associated with IBD and can be isolated from around 8% of paediatric colonic biopsies. *S. wadsworthensis* appears to be a common commensal. *Helicobacter* species are relatively rare in the paediatric colon.
Disclosure of Interest None Declared

OC-073 RISKS OF MAJOR CONGENITAL ANOMALIES IN CHILDREN BORN TO WOMEN WITH INFLAMMATORY BOWEL DISEASE: A UNITED KINGDOM POPULATION-BASED COHORT STUDY

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Introduction Inflammatory bowel disease (IBD) affects women during the most fertile period of life. Previous studies of pregnant women with IBD on the risk of major congenital anomalies have inconsistent results due to diverse study populations and small sample sizes.
Methods We identified all singleton live births to women aged 15–45 between 1990 and 2010 from a large UK primary care database. We grouped children according to whether their mothers had IBD before childbirth or not and whether if so this was Crohn's disease (CD) or ulcerative colitis (UC). For children born to women with IBD, we also extracted records of prescriptions of 5-aminosalicylic acid, steroids and azathioprine in the first trimester of pregnancy. We calculated absolute risks of any major congenital anomaly and system-specific anomalies, and used logistic regression with a generalised estimating equation to compare risks. In women with IBD, we repeated the analyses to estimate the risks in children exposed or not exposed to medication. We adjusted the results for maternal age, year of childbirth, socioeconomic deprivation and maternal smoking.
Results Of 1,703 children born to women with IBD and 384,811 children born to women without IBD, 2.7% and 2.8% had records of any major congenital anomaly respectively. The risks of major congenital anomaly for CD and UC were 3.7% and 1.9% respectively. The adjusted odds ratio (AOR) of IBD with any major congenital anomaly was 0.98 (95% confidence interval [95%CI] 0.73–1.31). In children of women with IBD, 32.4% were exposed to 5-aminosalicylic acid in the first trimester and 12.3% and 8.7% to steroids and azathioprine respectively. There was no statistically significant increase in the risk of major congenital anomaly in children exposed to 5-aminosalicylic acid (AOR = 0.82, 95%CI 0.42–1.61), steroids (AOR = 0.48, 95%CI 0.15–1.50) or azathioprine (AOR = 1.27, 95%CI 0.48–3.39) in the first trimester compared with those unexposed. For system-specific