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. 77.3% full papers reported cancer conversion rate, corresponding weighted mean was calculated with a cancer conversion rate of 7.7% (6.9–8.5 CI). A forest plot of full-text paper results is shown in figure 1.

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.

Abstract OTU-021 Table 1

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Conversion rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aljarabah, 2019 Allgar, 2006 Aslam, 2017</td>
<td>0.100 [0.063–0.144] 0.110 [0.082–0.141]</td>
</tr>
<tr>
<td>Banerjee, 2017 Banwir, 2004 Beggs, 2011</td>
<td>0.069 [0.065–0.073] 0.068 [0.048–0.091]</td>
</tr>
<tr>
<td>Bhangu, 2010 Borowsk, 2016 Chohan, 2004</td>
<td>0.100 [0.056–0.155] 0.073 [0.047–0.104]</td>
</tr>
<tr>
<td>Courtney, 2013 Debnath, 2002 Eccersley, 2003 Flashman, 2004 Hall, 2015, Peacock, 2013 John, 2008 Khong, 2015 Leung, 2010</td>
<td>0.060 [0.049–0.072] 0.058 [0.053–0.063]</td>
</tr>
<tr>
<td>2013 John, 2008 Khong, 2015 Leung, 2010</td>
<td>0.089 [0.056–0.129] 0.150 [0.100–0.207]</td>
</tr>
<tr>
<td>Manandharalam, 2005 Mahneyre, 2010</td>
<td>0.094 [0.076–0.113] 0.064 [0.052–0.078]</td>
</tr>
<tr>
<td>Padwick, 2013 Patel, 2014 Rai, 2007 Rai, 2007 Rai, 2008 Rao, 2005 Shaw, 2009</td>
<td>0.081 [0.066–0.098] 0.081 [0.061–0.104]</td>
</tr>
<tr>
<td>Smith, 2007 Sorell, 2014 Spencer, 2004</td>
<td>0.051 [0.035–0.070] 0.053 [0.040–0.069]</td>
</tr>
<tr>
<td>Vaughan - Shaw, 2013</td>
<td>0.072 [0.054–0.092] 0.100 [0.082–0.119]</td>
</tr>
<tr>
<td>Vaughan - Shaw, 2013</td>
<td>0.060 [0.032–0.096] 0.108 [0.082–0.137]</td>
</tr>
<tr>
<td>0.044 [0.024–0.069] 0.090 [0.078–0.102]</td>
<td>0.063 [0.054–0.072] 0.060 [0.008–0.147]</td>
</tr>
<tr>
<td>0.103 [0.068–0.145] 0.078 [0.068–0.088]</td>
<td>0.077 [0.069–0.085]</td>
</tr>
</tbody>
</table>

Conclusion 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 4,501,617 controls. We tested 95,273,577 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 ‘imp0 2.0.’

Results Participants with microscopic colitis were older (61.9 [56.2–65.4] vs. controls 58.6 [50.5–63.8], p<5e-13); more frequent female (65.6% [317/483] vs 54.2% [24453/4505616], p=5e-07), more likely to smoke (14.7% [71/483] vs 10.4% [46792/4505616], p=0.003) and were more often also diagnosed with coeliac disease (3.3% [16/483] and 0.4% [1991/4505616], 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% [46397/4505616] 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 65.4, 95% CI 0.64, 0.69; p=5e-15); more frequent female (63.6% [317/483] vs 54.2% [24453/4505616], p=5e-07); more likely to smoke (14.7% [71/483] vs 10.4% [46792/4505616], p=0.003) and were more often also diagnosed with coeliac disease (3.3% [16/483] and 0.4% [1991/4505616], 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% [46397/4505616] controls, p=9e-11) than controls, but not aspirin/NSAIDs or SSRIs.

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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/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]) adenomas. 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 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.

## Abstract OTU-024 Table 1

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>–18.0%</td>
<td>–10.6%</td>
<td>–23.1%</td>
<td>–16.1%</td>
<td>–22.7%</td>
<td>–32.5%</td>
<td>–19.5%</td>
<td>–14.3%</td>
<td>–8.8%</td>
</tr>
<tr>
<td>Women</td>
<td>+14.7%</td>
<td>–5.9%</td>
<td>–0.7%</td>
<td>–5.2%</td>
<td>–24.1%</td>
<td>–28.6%</td>
<td>–10.9%</td>
<td>–11.6%</td>
<td>–2.9%</td>
</tr>
</tbody>
</table>
Feasibility and economic evaluation of chromoendoscopy for detecting proximal serrated neoplasia: a randomised controlled trial – CONSCOP

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 chromocolonoscopy. 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.

Conclusion 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.
Abstract OWE-034 Figure 1 AED/ACC constipation pathway

**Methods**

216 of the 301 patients admitted were admitted to the Accident and Emergency Department (AED). The average length of stay was calculated as 3.3 days, totalling 713 bed days. This equates to £2 85 120 per annum, based on a local tariff of approximately £400 per day.

To reduce admissions/costs related to constipation within our Trust, a pathway was proposed by the specialist physiotherapy clinicians. These patients would be managed and treated in the ACC.

Clinicians led a bid to an in-hospital initiative, resulting in funding of £16 000 for a 12 month study. This secured a staff member for 14.25 hours per week to develop, implement, organise and audit the pathway.

The pathway was formalised, see below, including the development of information leaflets for patients. Changes to practice and patient flow were introduced within AED for patients presenting with primary constipation. Administration staff were trained to liaise between AED and the ACC. Data was collected prospectively.

**Results**

Over the year, 70 patients were referred to the ACC using the new pathway, thereby avoiding hospital admission. This equates to a saving of 231 bed days per annum at the estimated cost of £92 400. Data showed that a number of patients were regular attenders at AED, 9 patients had more than 5 previous admissions with constipation.

**Conclusions**

The study has confirmed the benefits of introducing a patient care pathway for patients presenting to the AED with primary constipation.

The introduction of this pathway provides AED staff with a safe, suitable and efficient treatment pathway for patients with constipation, reducing hospital admissions and bed stays.

The pathway allows patients to manage their symptoms in their own home with support from specialist clinicians, enhancing patient dignity. Although the majority of patients were discharged after this acute episode, the information gathered in the ACC identified patients requiring referral to the functional bowel clinic for ongoing, long-term management. Further audit of this patient group will hopefully demonstrate a reduction in future AED attendances and admissions due to constipation.

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**ADTU-07 5-AMINOSALICYLIC ACID TARGETS COLORECTAL CANCER STEMNESS IN VITRO**

1,2Steven Dixon*, 1Eleanor Mortensson, 2Tom Creed, 1Ann C Williams. 1University Of Bristol, Bristol, UK; 2UH Bristol NHS Foundation Trust, Bristol, UK

10.1136/gutjnl-2018-BSGAbstracts.364

**Introduction**

The mechanism by which 5-aminosalicylic acid (5-ASA) reduces colorectal cancer risk in ulcerative colitis is not fully understood and appears to involve multiple targets. Although previously reported to target Wnt signalling, the functional consequence of inhibition is not fully understood. Using a 3-dimensional (3D) organoid model we report that 5-ASA can prevent the formation of adenoma and carcinoma derived spheroids and propose that it does so through targeting the cancer stem cells.

**Methods**

Human colorectal cancer (CRC) and adenoma (CA) cell lines were seeded into Matrigel (Corning, USA), treated with 5-ASA (Sigma Life Sciences, UK) in culture medium and imaged at multiple timepoints. Z-stacks through the Matrigel hemispheres were analysed using an in-house MatLab (Mathworks, USA) programme to estimate organoid area. In parallel, cells were also grown in T25 flasks and treated with 5-ASA and expression of β-catenin targets assessed by western blotting. Wnt/β-catenin activity was assayed using a TOPflash TCF-luciferase construct in 24-well plates.

**Results**

All cell lines tested formed organoids in Matrigel. 5-ASA slowed the growth of CRC and CA cell organoids in all lines tested at physiologically relevant concentrations (5 and 10 mm) when treatment was initiated 7 days after seeding into Matrigel. Importantly, treatment with 5-ASA within 24 hours of seeding at low doses (2 mM) prevented any organoid growth (figure 1). In these cultures, Wnt/β-catenin signalling, active in the intestinal crypt stem compartment and constitutively active in the majority of CRC, was reduced in CRC cells by 24% (10 mM) – 38% (20 mM) and CA cells by 22% (10 mM) – 44% (20 mM) by treatment with 5-ASA. Furthermore expression of the colonic stem cell marker leucine-rich G-coupled receptor-5 (LGR5) and Wnt-targets c-Myc, Axin-2 and dephosphorylated β-catenin was suppressed in both CRC and CA cell lines by treatment with 5-ASA.
Conclusions Here we demonstrate that 5-ASA impairs growth of CRC and CA in a 3D model. That 5-ASA arrests the growth of organoid if treated at the time of seeding suggests that 5-ASA may be affecting cell stemness. This is likely to be due to at least in-part reduced Wnt/β-catenin activity. Further work is being undertaken to elucidate the mechanism by which of 5-ASA could target cancer stemness to inform on potential clinical trials of 5-ASA as a prophylactic agent for patients at high risk of CRC.

ADTU-08 INCIDENCE AND MANAGEMENT OF IMMUNOTHERAPY-INDUCED COLITIS IN A TERTIARY IBD CENTRE – CLINICAL PRACTICE DATA


Introduction Checkpoint inhibitors are a novel anti-cancer therapy that are standard of care in metastatic melanoma, non-small cell lung and renal cancer. CTLA-4 inhibitors (e.g Ipilimumab) and PD-1 inhibitors (Nivolumab, Pembrolizumab) can be used separately or in combination for melanoma, whereas singlet therapy is currently the norm for others. Their work is being undertaken to elucidate the mechanism by which of 5-ASA could target cancer stemness to inform on potential clinical trials of 5-ASA as a prophylactic agent for patients at high risk of CRC.

REFERENCE

PTU-030 RNA SEQUENCING OF COLORECTAL CANCER BIOSPECIMENS CHARACTERISES DIFFERENTIAL GENE EXPRESSION IN OLD AND YOUNG PATIENTS

Joanna Anderson*, Lennard Lee. Wellcome Trust Centre for Human Genetics, Oxford, UK

Introduction Incidence of colorectal cancer (CRC) increases with age, with older patients having a worse prognosis than younger patients. The underlying molecular features which lead to these age-related differences are unclear, but possible reasons include immune senescence or cellular senescence. Characterisation of differences in gene expression in cancers of older and younger patients, particularly genes driving the immune response to cancer, will contribute to our understanding of the differences between early- and late-presenting tumours and inform treatment strategies.

Methods RNA was extracted from tumour cells and lymph nodes from three cohorts of patients with rectal cancer (n=47), stage 2 CRC (n=72) and stage 3 CRC (n=69). For the stage 3 CRC cohort, RNA was extracted from the primary tumour. After RNA-Sequencing, differential gene expression data was generated between older and younger patients in the Stage 3 cohort, with ‘old’ patients being one standard deviation (SD) above the median, and ‘young’ patients one SD
below the median (median=72 years). Results were validated with a second cohort of Stage 3 CRC samples (n=78).

**Results** In primary tumour samples from the stage 3 cohort, there were 581 genes differentially expressed between older and younger patients at p-adj <0.05, and 159 genes differentially expressed in metastatic lymph nodes between the two groups. In older patients, we found downregulation of the Oxidative Phosphorylation, MYC V1 and MYC V2 gene sets and, interestingly, downregulation of Unfolded Protein Response (UPR) genes. Under normal conditions, the UPR promotes apoptosis in conditions of prolonged cellular stress; downregulation of UPR genes may therefore enhance tumour survival by abrogating this response. Although downregulation of UPR genes may be a natural part of cellular senescence, this change might be exploited by late-presenting tumours.

**Conclusions** Our results have shown that there are detectable differences in tumour and lymph node gene expression between older and younger patients; such findings may further enhance age-dependent personalised therapy. We have chosen to focus on age-related differential gene expression, but differences between other tumour phenotypes may also be investigated and likely to further enhance our biological understanding of cancer biology.

**Abstracts**

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**PTU-031 THE WORLD ENDOSCOPY ORGANISATION CONSENSUS STATEMENTS ON POST-COLONOSCOPY AND POST-IMAGING COLORECTAL CANCER**

Jill Tinmouth, Graeme P Young, Silvia Sanduleanu, Miriam Cuatrecasas, Evelien Dekker, Anna Forsberg, Jola Gore-Booth, Ulrike Haug, Iosif Beintaris, Matthew D Rutter, Roland Valori, Han Mo Chiu, Douglas A Corley, A Plumb, Linda Rabeneck, Douglas J Robertson, Robert E Schoen, Harminder Singh, Jill Timouth, Graeme P Young, Silvia Sanduleanu, University Hospital of North Tees, Stockton-on-Tees, UK; Newcastle University, Newcastle, UK; Durham University, Durham, UK; Gloucestershire Hospitals NHS Foundation Trust, Gloucestershire, UK; National Taiwan University Hospital, Taipei, Taiwan; San Francisco Medical Center, Kaiser Permanente Division of Research, San Francisco, USA; Hospital Clinic and Tumour Bank-Biobank, IDIBAPS, University of Barcelona, Barcelona, Spain; Academic Medical Center, Amsterdam, The Netherlands; Institute of Medicine Salwa Karolinska Institutet, Stockholm, Sweden; Europa Colon, UK; Department of Clinical Epidemiology, Leibniz Institute for Prevention Research and Epidemiology – BIPS, Bremer, Germany; The Maria Skłodowska-Curie Institute – Oncology Center, Warsaw, Poland; Cancer Screening Center, National Cancer Center Hospital, Tokyo, Japan; Netherlands Cancer Institute, Amsterdam, The Netherlands; Institute of Cancer and Pathology, University of Leeds; St James’s Institute of Oncology, St James’s University Hospital, Leeds, UK; University College London, London, UK; Cancer Care Ontario, University of Toronto, Toronto, Canada; VA Medical Center, White River Junction, Vermont and Geisel School of Medicine at Dartmouth, Hanover, Hanover, USA; University of Pittsburgh, Pittsburgh, USA; University of Manitoba, Canada; Sunnybrook Health Sciences Centre, Toronto, Canada; Maastricht University Medical Center, Maastricht, The Netherlands

10.1136/gutjnl-2018-BSGAbstracts.367

**Introduction** Colonoscopy is an imperfect tool. The term ‘interval’ cancer refers to cancers diagnosed after a colorectal screening examination or test in which no cancer was detected, and before the date of the next recommended examination. From a colorectal screening perspective, the term is too restrictive, hence the term Post Colonoscopy Colorectal Cancer (PCCRC) was developed, to incorporate non-screening settings.

**Methods** Our goal was to provide a framework on terminology, identification, analysis and reporting of cancers appearing after a negative colonoscopy (PCCRCs) or computed tomographic colonography (Post-Imaging Colorectal Cancers/ PICRCs). We based our methodology on the AGREE II tool. A team of gastroenterologists, pathologists, epidemiologists, radiologists and patient representatives, formed a panel of 20 members. Following literature review, 402 articles provided background for statements, which were then subjected to anonymous voting (modified Delphi approach). The GRADE system was utilised to rate evidence.

**Results** The final output consists of 21 statements, providing guidance on key aspects of PCCRC/PICRC, namely:

1. Definitions/terminology (2 statements) (table 1)
2. Qualitative review of cases/aetiology attribution (8 statements) (figure 1)
3. Quantitative assessment/calculation of PCCRC rate (7 statements)
4. Non-colonoscopy imaging of the colon (4 statements)

The PCCRC rate is calculated as the number of PCCRCs divided by the total of the PCCRCs plus the number of detected cancers, expressed as a percentage.

A Root-Cause-Analysis checklist, as well as a checklist to assist Peer Review of PCCRC manuscripts have also been developed.

**Conclusions** This is the first consensus aiming to standardise terminology around PCCRC/PICRC, presenting a methodology for analysis of causation of PCCRC/PICRC and defining its potential role as a key quality indicator.

**Abstract PTU-031 Table 1**

<table>
<thead>
<tr>
<th>PCCRC subcategories</th>
<th>Type A</th>
<th>Type B</th>
<th>Type C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval type</td>
<td>Detected prior to recommended screening</td>
<td>Detected after recommended screening</td>
<td>Detected after recommended screening</td>
</tr>
<tr>
<td>Non-interval type</td>
<td>surveillance</td>
<td>surveillance</td>
<td>surveillance</td>
</tr>
<tr>
<td>Where non-screening</td>
<td>surveillance</td>
<td>surveillance</td>
<td>internal had been recommended</td>
</tr>
</tbody>
</table>

**Examples**

- **Patient with 2 small adenomas is advised to return for surveillance in 5 years; 4 years later develops anaemia; colonoscopy reveals CRC**: Patient investigated for change in bowel habit – colonoscopy normal. No further investigation recommended. 5 years later patient develops symptoms and a colonoscopy reveals CRC.

---
Introduction Colorectal cancer (CRC) is diagnosed in over 46 000 people in the UK annually, and is the second most common cause of cancer death. NICE guideline DG27 recommends universal testing for Lynch Syndrome (LS) at diagnosis of colorectal cancer, by testing the CRC for mismatch repair (MMR) status, a hallmark of the disease.

Methods We collected data prospectively from November 2016 to December 2017 of consecutively diagnosed CRC patients at West Midlands University Hospital (WMUH) in London. CRCs were universally screened for tumour features suggestive of LS (Defective MMR, or dMMR) with immunohistochemistry. We also collected clinicopathological data including age at diagnosis, stage, tumour site, histological findings and MMR tumour-status. Statistical analysis was performed using chi-square test and 2 tailed T test for binary and continuous variables respectively.

Results A cohort of 123 consecutive CRC patients were universally tested for dMMR. Twelve patients (9.8%) were MMR-deficient of which only 6 (50%) were predicated by the Bethesda Criteria. 11/12 dMMR CRCs were early stage tumours (Dukes’ A or B, p=0.002), and in 20 Dukes’ B CRCs in patient under 70 years of age, the result was directly relevant to personalised treatment with 5-FU based chemotherapy. The median age in patients with normal or abnormal MMR IHC was 64.6 years and 68.3 years respectively (p 0.41). With regard to histological features; mucinous tumours were more frequently manifest dMMR (p 0.0052), with the presence of this, signet ring cells or a lymphocytic response predictive of dMMR CRC (p 0.023). In all 12 patients with dMMR the cancer was located in the right colon (p 0.00001), MMR germline mutations were found in a total of 4 patients of which 2 (50%) had mutation of MLH1, in 1 case (25%) of MSH2 and in 1 case (25%) of MSH6.

Conclusions Our results demonstrate that universal testing is feasible and effective in the UK. There were significant differences with regard to dMMR CRC site, stage and histological features compared to proficient MMR CRCs. Our data also indicates the importance of genetic testing and personalised oncological care as we were able to identify patients that may have not be selected for MMR testing by the Bethesda criteria.
**PTU-034** GETTING THE BEST OUT OF FAECAL IMMUNOCHEMICAL TESTS AND FAECAL CALPROTECTIN

Charlotte Chuter, James Turville. York Teaching Hospitals NHS Foundation Trust, York, UK

10.1136/gutjnl-2018-BSGAbstracts.370

Introduction NICE DG30 recommends the use of quantitative faecal immunochromatographic tests (FIT) in patients at ‘low risk’ for colorectal cancer (CRC). No lower age limit is advised. Colorectal cancer (CRC) is rare under the age of 50 years representing 6% of all cases, whilst inflammatory bowel disease (IBD), is much more prevalent. In support of NICE DG11 we have successfully introduced a pathway for the use of faecal calprotectin (FC) to support the diagnosis of IBD. It is not known what the relative roles of FIT and FC are in this ‘low risk’ for CRC population.

Methods We analysed pre-existing clinical outcome data on FC from diagnostic accuracy studies and pathway evaluations performed at York Hospital. We identified those that did not fulfil criteria for the ‘two week wait’ referral (NICE NG12 recommendations 1.3.1 to 1.3.3) and stratified them based on age and symptomatology. We calculated sensitivity and specificity of FC in each cohort and compared it with a published FIT comparator (Mowat et al 2015).

Results 2917 patient outcomes were reviewed. 1229 presented with a change in bowel habit under the age of 60 years, so fulfilling DG30 criteria. The prevalence of CRC was 0.5%. The sensitivity and specificity of FC as used in the York Faecal Calprotectin Care Pathway (≤100 mcg/g) is presented below both for CRC and for CRC, high risk adenomatous polyps and IBD combined, aged stratified. This is compared with FIT ≥10 mcg/g outcomes.

<table>
<thead>
<tr>
<th>Abstract PTU-034 Table 1</th>
<th>Age range (yrs)</th>
<th>Sensitivity (CI)</th>
<th>Specificity (CI)</th>
<th>NPV (CI)</th>
<th>PPV (CI)</th>
</tr>
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<tbody>
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<td>CRC</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>FIT≥10 mcg/g*</td>
<td>50–59</td>
<td>66.2 (56–76)</td>
<td>80.0 (74–85)</td>
<td>92 (88–95)</td>
<td>34 (24–46)</td>
</tr>
<tr>
<td>FC≤100 mcg/g</td>
<td>50–59</td>
<td>66.2 (56–76)</td>
<td>80.0 (74–85)</td>
<td>92 (88–95)</td>
<td>34 (24–46)</td>
</tr>
<tr>
<td>CRC, polyps and IBD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIT&lt;10 mcg/g*</td>
<td>50–59</td>
<td>66.2 (56–76)</td>
<td>80.0 (74–85)</td>
<td>92 (88–95)</td>
<td>34 (24–46)</td>
</tr>
<tr>
<td>FC≤100 mcg/g</td>
<td>50–59</td>
<td>66.2 (56–76)</td>
<td>80.0 (74–85)</td>
<td>92 (88–95)</td>
<td>34 (24–46)</td>
</tr>
</tbody>
</table>


Similar outcomes were obtained when combining all patients fulfilling DG30 criteria (that is including those with unexplained weight loss, abdominal pain and iron deficiency anaemia).

Conclusion Despite the large numbers evaluated, the small numbers of patients with CRC make it difficult to draw any conclusions for a lower age limit upon which to apply DG30 and use FIT instead of FC. However when looking at combined CRC, high risk adenomatous polyps and IBD in this ‘low risk’ cohort, FC behaves similarly or better than FIT in those <50 years. As FIT is introduced in support of DG30 its performance should be benchmarked against existing FC pathways.
PTU-036 THE IMPACT OF THE WELSH BOWEL SCREENING PROGRAMME ON EMERGENCY PRESENTATION FOR COLORECTAL CANCER

Sunil Dolwani, Shubhangi Govil, Kate Lifford, Ceri White, Hayley Heard, Dyfed Huws. Division of Population Medicine, Cardiff University, Cardiff, UK; 2School of Medicine, Cardiff University, Cardiff, UK; 3Wales Cancer Intelligence and Surveillance Unit, Public Health Wales, Cardiff, UK; 4Bowel Screening Wales, Llantrisant, UK

Introduction Colorectal cancer (CRC) screening using faecal occult blood testing (FOBT) is effective in reducing mortality. However, more than 20% of all CRC cases present as an emergency due to bowel obstruction which is associated with poorer outcomes. The Welsh bowel screening programme, using biennial FOBT, has been running since October 2008 for people aged 60–69 years, since extended to 74 years. Previous data from an English site showed a decrease in mortality and emergency presentations of CRC. The impact of the Welsh bowel screening programme on emergency presentations for CRC is not known.

Methods Welsh participants diagnosed with CRC aged 60–74 years between 1999 and 2015 were identified from the Welsh Cancer Intelligence and Surveillance Unit register. Data was extracted from the Patient Episode Database for Wales and Bowel Screening Wales to determine route to presentation and screening uptake. Other individual, geographical and cancer-related variables were also examined for their association with emergency presentation. The primary analysis compared emergency presentation for CRC prior to and after the implementation of screening.

Results Preliminary analyses showed that 15 059 people were diagnosed with CRC, with data available for route to diagnosis on 13 022 (62% male, 38% female; mean age at diagnosis 67.7 years). The proportion of those presenting with CRC as an emergency prior to the screening programme implementation was greater than those presenting as emergencies after implementation. However, this needs to be interpreted in the context of 1) screening uptake differences over time, 2) stage differences at diagnosis over time, and 3) overall absolute numbers of cancers detected.

Conclusions Preliminary analyses suggest that the implementation of screening has reduced the proportion of emergency presentations for CRC, but further interrogation of the data is needed to aid interpretation. The impact of demographic and clinical factors on emergency presentation will be discussed.

PTU-037 OUTCOMES IN PATIENTS WHO DECLINE BOWEL CANCER SCREENING COLONOSCOPY AFTER POSITIVE FAECAL OCCULT BLOOD TESTING

Justin Alexander Fegredo, Bansii Patani, Andrew Frank Muller. Kent and Canterbury Hospital, Canterbury, UK

Introduction The Bowel Cancer Screening Programme (BCSP) uses the faecal occult blood test (FOBT) to identify patients who may benefit from colonoscopy to rule out potentially serious usually asymptomatic pathology. Screening of asymptomatic FOBT positive patients enables early identification and removal of premalignant adenomatous polyps thereby significantly reducing risk of progression to colon cancer.

Methods A retrospective cohort study design was employed in order to ascertain the final outcome in patients with a positive FOBT that had subsequently declined colonoscopy within the East Kent Hospitals screening programme. The records of all patients with screening appointments from January 2010 to December 2016 were reviewed in order to identify which further investigations had taken place up to 27 July 2017. Data were obtained from electronic patient records (endoscopy reports, patient letters, pathology viewer and PACS system) and included: results of subsequent colonoscopy or gastroscopy, CT, ultrasound and MRI scans, as well as histology obtained by any means. Data were collated using Microsoft Excel 2016 and analysed with SPSS v15.0.

Results The present study included 376 patients that had declined colonoscopy. The median age was 66.6 y (range 59.8–91.4). Subsequent investigations were performed in 215 (57.2%) patients and identified possible explanatory abnormalities (table 1). The follow-up period for subsequent investigations ranged from 6 months to 7 years depending on whether patients were identified at the end or the beginning of the study period, respectively. Two of four upper gastrointestinal (UGI) cancers and 8 of 24 lower gastrointestinal (LGI) cancers were diagnosed in those with the longest follow-up (i.e. the 2010/11 cohort). Of the 161 patients (42.8%) without follow-up data, 21 (13.0%) had prior diagnoses that may have accounted for a positive FOBT (e.g. gastritis, polyps, telangiectasia etc.).

Abstract PTU-037 Table 1 Outcomes in 376 dissenters from BCSP colonoscopy

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGI inflammation (e.g. gastritis, oesophagitis)</td>
<td>32 (8.5%)</td>
</tr>
<tr>
<td>Portal hypertensive features (e.g. varices)</td>
<td>7 (1.9%)</td>
</tr>
<tr>
<td>Adenomatous polyps</td>
<td>36 (9.6%)</td>
</tr>
<tr>
<td>IBD</td>
<td>13 (3.5%)</td>
</tr>
<tr>
<td>Definite UGI malignancy</td>
<td>4 (1.1%)</td>
</tr>
<tr>
<td>Possible UGI malignancy*</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Definite LGI malignancy</td>
<td>24 (6.4%)</td>
</tr>
<tr>
<td>Possible LGI malignancy*</td>
<td>4 (1.1%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Microscopic colitis</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Melanosis coli</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Radiation colitis/proctis</td>
<td>1 (0.3%)</td>
</tr>
</tbody>
</table>

*Radiological confirmation of malignancy but no histology obtained

Conclusions This study confirms that dissenters with positive FOBT should be encouraged to undergo colonoscopy as in this cohort, a significant proportion subsequently investigated outside of the BCSP will have or develop cancer. Many of the cancers identified were in those with the longest period of follow up, suggesting that the overall risk of potentially serious pathology in this study is likely to be significantly underestimated.
OUTCOMES OF COLONOSCOPIC SCREENING FOR MODERATE RISK FAMILIAL COLORECTAL CANCER

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Abstract PTU-038

Introduction Although national guidelines recommend screening colonoscopy in individuals with familial colorectal cancer, its value is uncertain in the case of moderate-risk subjects. Furthermore, BSG and SIGN guidelines were revised in 2010 and 2011 respectively and it is unclear what impact this has had on the outcomes of screening. In the updated guideline, the moderate risk category has been subdivided into high and low moderate risk groups based on family history. High-moderate subjects are eligible for a screening colonoscopy at age 50 and a further scope every 5 years until the age of 75. The low moderate group should get a colonoscopy age 55 and no further scopes if normal. This contrasts with the previous advice to scope all moderate risk patients at the age of 35–40 and again aged 55.

Methods Retrospective audit of moderate risk subjects referred by the regional genetics service for screening colonoscopy between January 2000 and October 2017. Data collected included demographics, prevalence of adenomas, and high risk adenomas (>1 cm in size, villous histology or showing high grade dysplasia) on the initial screening colonoscopy. The number of referrals before and after local implementation of the guidelines in January 2012 was determined. Exclusion criteria included symptomatic patients, a personal history of CRC and those who did not attend for colonoscopy.

Results A total of 641 moderate risk subjects were referred for colonoscopy of which 179 were excluded. Of the remaining 462 subjects, 418 (90.5%) underwent complete colonoscopy up to the caecum, the rest had completion barium enema or CT colonography. There number of patients referred before and after the guideline update was 360 (mean age of 45.2 years, 53% female) and 102 (mean age 55.6 years, 50% female), respectively. The mean number of referrals per year reduced from 30 to 17 (p=0.002).

Detection of any adenoma increased from 10% (36 patients) to 18.6% (19 patients) after the guideline update (p=0.024) and detection of high-risk adenomas increased from 1.94% (7 patients) to 3.92% (4 patients) after the guideline update (p=ns). No cases of malignancy were detected.

Conclusions Implementation of the revised BSG/SIGN guidelines for screening patients at moderate risk for familial colorectal cancer has resulted in a reduction in referrals for colonoscopy together with an increased yield of neoplasia.

IDENTIFYING FACTORS THAT INFLUENCE COLORECTAL CANCER MISS RATE ON COLONOSCOPY

Andreas Hadjilociaou, Rawen Kader, Gareth Corbett. Cambridge University Hospitals NHS Trust, Cambridge, UK

Abstract PTU-039

Introduction Colorectal cancer (CRC) is the 3rd most common cause of cancer death. Colonoscopy is the ‘gold standard’ for CRC screening and early diagnosis but still sometimes misses lesions. Our aim was to identify potential factors that might influence CRC miss rates on colonoscopy.

Methods Data on all new CRC diagnoses during a 3 year period (1st September 2014 – 31st August 2017) were collected retrospectively from the electronic records of a UK teaching hospital. A CRC miss was defined as a case where CRC was missed on ‘initial’ colonoscopy and identified within 3 years upon subsequent ‘diagnostic’ colonoscopy. We analysed demographic data, and features of the ‘initial’ and ‘diagnostic’ colonoscopies.

Results 691 new CRC cases were identified during the 3 year period. 12 of these were CRC misses (1.74%). Missed CRC cases had an average age of 65.23 years (29–80) and M:F ratio of 1:3. All 12 cases were adenocarcinomas with various histopathological and endoscopic features (table 1). ‘Initial’ colonoscopy identified polyps in 8 cases. In 4/8 (50%) cases the polyp location was identical to the cancer later identified on ‘diagnostic’ colonoscopy.

Interestingly, adjusting for volume of colonoscopies performed by each endoscopist type, trainees and surgeons were 2.5 and 5 times respectively, more likely to miss CRC than physician endoscopists (table 2). Finally, 4 out of 12 (33.33%) cases had the ‘initial’ colonoscopy that missed CRC on a Saturday morning. This translates to a 4-fold increased risk of missing CRC on a Saturday service list compared to any weekday morning (n=4) or afternoon (n=4) session.

Conclusions Despite a small missed CRC cohort, our results suggest that risk of missing CRC on colonoscopy might be higher in female patients and the miss rate might be linked to scope operator with trainee and surgical endoscopists perhaps more likely to miss CRC than physician endoscopists. It was identified later. The risk of colonoscopy missing CRC was higher on a Saturday service list than a normal working day session. Overall, our findings suggest discrepancies that warrant further investigation in larger more cohorts with more statistical power in order to improve CRC screening.

Abstract PTU-039 Table 1 Diagnostic colonoscopy histopathological and endoscopic characteristics in missed CRC cohort

<table>
<thead>
<tr>
<th>Anatomical site in colorectum (% total)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sigmoid</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Splenic flexure</td>
<td>1 (8.33%)</td>
</tr>
<tr>
<td>Transverse</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Hepatic flexure</td>
<td>2 (16.67%)</td>
</tr>
<tr>
<td>Ascending</td>
<td>2 (16.67%)</td>
</tr>
<tr>
<td>Caecum</td>
<td>1 (8.33%)</td>
</tr>
</tbody>
</table>

| Dysplasia (% total)                   |   |
| Low grade                             | 11 (91.67%) |
| High grade                            | 1 (8.33%) |
Abstracts

PTU-040 HMGB1 IN THE PATHOGENESIS OF COLORECTAL CANCER
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10.1136/gutjnl-2018-BSGAbstracts.376

Introduction High Mobility Group Box-1 (HMGB1) is a ubiquitous nuclear protein that regulates gene expression. When phosphorylated, it translocates to the cytoplasm and extracellular space to impact immune responses and epithelial cell behaviour. Our previous data revealed that dynamic subcellular localisation of HMGB1 is associated with colorectal neoplastic progression, with cytoplasmic HMGB1 expression a feature of early carcinogenesis. The leading edge of cancer invasion in polyp cancers (CaP) had strong expression in both nuclear and cytoplasmic compartments. Our aim was to define the biological impact of this expression profile.

Methods CD4+ helper T cells, CD8+ cytotoxic T cells, FOXP3+ regulatory T cells, CD20+ B cells and CD68+ macrophages were assessed by immunohistochemistry on endoscopically retrieved paraffin embedded CaP lesions sourced from the Grampian Tissue Biorepository (n=25). Ethical approval was granted by the Grampian Biorepository Scientific Ethics Committee. The immune cell infiltrate was scopically retrieved paraffin embedded CaP lesions sourced from the Grampian Tissue Biorepository (n=25). Ethical approval was granted by the Grampian Biorepository Scientific Ethics Committee. The immune cell infiltrate was scored by the Livak method.

Results A robust inflammatory infiltrate was identified adjacent to the invasive cancer margin with a preponderance of CD4+ T cells and CD68+ macrophages. The subcellular localisation of HMGB1 (nuclear versus cytoplasmic) did not result in phenotypically distinct populations. There was no difference in epithelial restitution in response to HMGB1 over 48 hours, although high concentration at 72 hours was associated with reduced wound healing (p<0.01) and reduced proliferation rate (p<0.01). HMGB1 stimulation significantly decreased the expression of CLDN4 (p<0.008).

Conclusions Cytoplasmic HMGB1 expression did not impact the phenotype of adjacent immune cell infiltrate at the cancer margin. HMGB1 influences growth dynamics of colonic epithelial cells and reduces the expression of the pore closing tight junction gene, CLDN4. Understanding HMGB1 driven biology in CaP could identify an important mechanism for early carcinogenesis.

PTU-041 METHANOGENESIS IN THE GI TRACT – IMPLICATIONS FOR UK BREATH TESTING
Jordan Haworth, Jennifer Haynes, Charlotte Pitcher, Sam Treadway, Anthony Hobson. The Functional Gut Clinic, Manchester, UK
10.1136/gutjnl-2018-BSGAbstracts.377

Introduction Methane production from gut microbes has been implicated in clinical constipation and manipulation of the microbiome represents an attractive and alternate therapeutic target. Methane production is not routinely measured during breath testing but the recent North American Consensus (NAC) document has recommended this as standard. To assess prevalence of methanogenesis in patients presenting with bloating symptoms we performed a retrospective analysis of our breath test database from the preceding 6 months.

Methods In total 736 subjects were analysed. The presence of methane levels≥10 ppm was considered methane-positive. Breath tests for Carbohydrate Malabsorption and Small Intestinal Bacterial Overgrowth (SIBO) were included. Baseline and intra-study bloating was scored on a scale 0–10 with 0 being absent and 10 being extreme. Results were analysed statistically using independent t-tests.

Results 136 subjects (18.5%) had a positive result for excessive methane. Within this group, 129 subjects had a SIBO breath test with 64.3% having a negative result. The remaining 35.7% had excessive methane and SIBO (determined by a rise in hydrogen >10 ppm above baseline within 60 min after ingestion of substrate). There was an overall increase in bloating symptoms for methane-positive compared to methane-negative patients (p=0.035) in the absence of SIBO.

Discussion Changes in the microbiome to a methane predominant environment occurs in about 20% of patients presenting with bloating symptoms. This supports the NAC statement that methane should be measured routinely during breath testing to avoid false negative results. Manipulation of the microbiome to a more hydrogen predominant profile represents an attractive alternative therapeutic objective to conventional laxative therapy.

PTU-042 AN AUDIT TOOL TO EVALUATE POST-COLONOSCOPY COLORECTAL CANCER (PCCRC) RATES IN ENDOSCOPY UNITS
Rawan Kader, Andreas Hadjinicolau, Gareth Corbett. Department of Gastroenterology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
10.1136/gutjnl-2018-BSGAbstracts.378

Introduction Colorectal cancer (CRC) is the third most common cancer globally and the third most common cause of cancer death. Early diagnosis at stages where disease can be treated, significantly improves survival rates justifying the need for CRC screening programs by ‘gold standard’ colonoscopy. Given the concern for significant numbers of missed lesions, the new JAG Global Rating Scale (GRS) requires all
endoscopy units to develop an audit for post-colonoscopy colorectal cancer (PCCRC). Our aim was to provide a template for performing this audit at a major teaching hospital.

Methods We retrospectively reviewed our electronic patient records and collected data on all new CRC diagnoses made over a three-year period (1 st September 2014 – 31 st August 2017). We looked for evidence of colonscopy performed in the three years prior to diagnosis and applied the following exclusion criteria:

- 1. No colonoscopy within the 3 years prior to diagnosis
- 2. Diagnosis of CRC made at different hospital hindering access to patient records
- 3. Previous flexible sigmoidoscopy only and subsequent CRC diagnosis in transverse/ascending colon
- 4. Unsatisfactory bowel preparation necessitating repeat endoscopy
- 5. Alternative investigation/referral arranged by endoscopist (e. g. due to technical difficulty leading to incomplete endoscopy procedure).

PCCRC rate was defined as the proportion of PCCRC diagnoses amongst all CRC cases. For CRC cases, we also analysed patient demographics, timeframe between colonoscopies and individual endoscopist PCCRC rate.

Results Out of a total 944 CRC cases, 691 were eligible for analysis (Figure 1). There were a total of 12 cases of PCCRC, giving our hospital a PCCRC of 1.74%. The average age of patients with a PCCRC diagnosis was 65.25 years (29–80). The average time between initial and diagnostic colonoscopies in PCCRC cases was 14.33% months (range, 1–24 months in 5 cases (41.67%), 12–24 months in 5 cases (41.47%) and >24 months in 2 cases (16.67%). Physician endoscopist miss rate ranged from 0.11%–0.21%.

Conclusions Results from our audit show our hospital is within the BSG, JAG and the Association of Coloproctology of Great Britain and Ireland (ACPGBI) quality assurance target of <5% PCCRC at 3 years. Ideally, endoscopy units will use similar methods for the mandatory JAG GRS audit, allowing comparison between different endoscopy units to improve quality of CRC screening. Our work provides a guidance tool on performing the audit in the hope of achieving this aim.

Abstract PTU042 Figure 1. Flow chart summarising identification of cases included for analysis.

PTU-043 INTESTINAL DYSBIOSIS OCCURS IN IRON DEFICIENCY AS WELL AS ACTIVE IBD
1Awad Mahalhal, 1,2Sreedhar Subramanian, 1,2DM Pritchard, 1,2CS Probert. 1University Of Liverpool, Liverpool, UK, 2The Royal Liverpool University Hospital, Liverpool, UK
10.1136/gutjnl-2018-BSGAbstracts.379

Introduction We have previously shown that decreases or increases in dietary iron exacerbate murine models of inflammatory bowel disease (IBD). Active IBD is associated with a dysbiosis typified by a reduction in Bacteroidetes and an increase in Firmicutes. We have investigated the human intestinal microbiome in relation to luminal iron, by studying patients with iron deficiency anaemia (IDA) and inactive/active IBD. We report results of changes at the phylum level.

Methods Bacterial gDNA was extracted from faeces of patients with IDA (10), Crohn’s disease (CD 6 active, 24 inactive), ulcerative colitis (UC 7 active, 13 inactive) and healthy controls (24). Faecal iron and calprotectin were assayed by ELISA. Microbiota composition was determined from the sequence of V4 region of 16S rDNA on the Illumina MiSeq platform. Statistical inferences were made using Welch’s t-test with post-hoc analysis (Bioinformatics 2010; 26:715–21). Shannon Diversity Index (SDI) and Principal Component Analysis (PCA) were employed to compare population and phylum-level changes among study groups.

Results Faecal iron concentrations were least in IDA (ANOVA, p=0.001) and significantly lower in IDA than each other group (post hoc p<0.05 for all comparisons). Calprotectin concentrations were increased in association with IBD disease activity.

Faecal phyla changes were seen in IDA as well as in IBD: Proteobacteria were markedly reduced in IDA (1.4%) compared to active IBD (15.5%); IDA and IBD were associated with increased proportions of Firmicutes (p=0.01 and p=0.05 respectively).

Conclusion Dysbiosis occurred in IDA as well as in active IBD. *Proteobacteria* are clearly iron-responsive: the increase in luminal iron associated with active IBD appears to promote their growth and might contribute to the excess of this phylum during relapse. The changes in *Bacteroidetes* appear independent of luminal iron, unlike *Firmicutes*. The influence of iron deficiency and supplementation upon the colonic microbiome warrants further investigation.

PTU-044 TO STENT OR NOT TO STENT IN MALIGNANT LARGE BOWEL OBSTRUCTION
10.1136/gutjnl-2018-BSGAbstracts.380

Introduction Self expanding metallic stents (SEMS) can resolve obstruction due to colorectal cancer (CRC), enabling subsequent elective rather than emergency surgery. This study compared the outcomes after stenting and subsequent elective surgery versus emergency surgery (ES) for obstructing CRC.

Methods Prospectively collected data from a consecutive series of 153 patients with large bowel obstruction secondary to CRC, presenting to a single NHS Trust from April 2010 to March 2017, were retrospectively analysed. Of these, 41 (26.8%) had stenting as a bridge to surgery (SBTS) followed by elective surgery and 112 (73.2%) had ES. Primary outcomes were mortality rates after surgery at 30 days, 90 days and 1 year. Secondary outcomes were the rates of stoma formation and anastomotic leak (both clinical and radiological).

Results Thirty-day mortality was 7.3% with SBTS and 12.5% with ES. Ninety-day mortality was 7.3% with SBTS and 17.9% with ES. One-year mortality was 19.5% with SBTS and 32.1% with ES. The anastomotic leak rate was 7.1% with SBTS and 14.0% with ES. The rate of stoma formation was 39.0% with SBTS and 33.0% with ES. With cancers proximal to the splenic flexure excluded, stoma rates were 38.5% with SBTS and 54.2% with ES.
Conclusions Without adjustment for confounding variables superiority of SBTS over ES cannot be inferred. But these results suggest SBTS can be a safe alternative to ES and may offer advantages in respect of stoma and leak rates.

PTU-045 URINARY VOC AND FAECAL MICROBIOME CHARACTERISATION OF COLORECTAL CANCER PATIENTS, THEIR FIRST-DEGREE RELATIVES AND SPOUSES

1Michael Mcfarlane, 2Andrew Millard, 3Richard Savage, 1Ramesh Arasaradnam, 1Chuka Nwokolo, 1Uhcw, Coventry, UK; 2University of Leicester, Leicester, UK; 3University of Warwick, Coventry, UK

Introduction Colorectal cancer (CRC) is one of the commonest causes of cancer worldwide, and, subsequently, there has been a drive in recent years to identify a non-invasive CRC biomarker. Volatile organic compounds (VOC) detection in various bodily substances, by means such as mass spectrometry and electronic nose, have gained particular interest. CRC patients have been shown to be distinguishable from healthy controls using urinary VOC detection in several studies, including two published by the research group at UHCW and the University of Warwick.1 2 There has also been significant research into the role that the intestinal microbiome plays in health and disease in humans.

The aim of this study was to characterise the urinary VOC and stool microbiome profiles of CRC patients, their spouses and first degree relatives with the goal of determining whether environmental and genetic controls could be distinguished from the CRC subjects using urinary VOC and faecal microbiome profiling.

Methods 56 CRC subjects, 45 spouses and 37 relatives were recruited. Sample analysis was performed using an LC-FAIMS-MS apparatus to detect urinary VOCs, whilst an Illumina Miseq platform was used for 16 s RNA sequencing. Urinary data was processed and analysed using a 5-fold cross-validation with sparse logistics regression and random Forrest statistical classifiers. Microbiome data was analysed using standardised uPARSE and QIIME pathways. Comparisons were also made between pre-treatment and post-treatment CRC samples (n=23) to determine if there was any change in VOC or microbiome profiles after treatment.

Results The urinary VOC profiles of CRC subjects could be distinguished from both sets of healthy controls using both classifiers. Achieved sensitivities were 63%–69%, specificities 64%–69% and AUC 0.71–0.72. No statistically significant differences could be found in the urinary VOC profiles of pre-operative and post-operative samples.

Microbiome analysis revealed over 1300 operational taxonomic units (OTUs), with a similarity of >93% between CRC samples and control groups, with significantly different bacterial abundances identified in 82 OTUs, mainly Clostridiales. Pre-treatment and post-treatment sample analysis revealed differences of 17 (3%) and 22 (4%) OTUs at 3 and 6 months respectively, again principally Clostridiales.

Conclusions This study provides further validity of the use of urinary VOCs as a non-invasive biomarker for CRC detection, demonstrated here against genetic and environmental controls. The LC-FAIMS-MS technology is a variant of the previously utilised FAIMS, although exact chemical identification is not possible due to a lack of a validated database. Microbiome analysis showed broadly similar bacterial profiles between the various groups, will subtle differences in some families, such as clostridiales, and a restricted CRC profile, compared to the healthy controls.

REFERENCE

PTU-046 NOVEL LACTOFERRIN-LOADED ALGINATE MICROGELS DISPLAY ANTI-CLOSTIDIUM DIFFICILE DEFENCE PROPERTIES IN VITRO

1Tanya Monaghan*, 2Shwana Braim, 3Klaudyna Spiewak, 3Malgorzata Brindell, 2Cameron Alexander. 1NHRI Nottingham Biomedical Research Centre, Nottingham University Teaching Hospitals NHS Trust, University Of Nottingham, Nottingham, UK; 2School of Pharmacy, University of Nottingham, Nottingham, UK; 3Faculty of Chemistry, Jagiellonian University, Krakow, Poland

Introduction We previously reported that some forms of bovine lactoferrin (bLf) are effective in substantially delaying C. difficile growth and preventing production of toxins in a human in vitro gut model of C. difficile infection (CDI). The aim of the present study was to develop lactoferrin-loaded alginate microparticles coated with high molecular weight chitosan for enhanced protein stability, and to subsequently evaluate their anti-C. difficile defence properties in vitro.

Methods Different forms of bLf (iron-depleted; apo-bLf; iron-saturated; holo-bLf, and manganese-saturated; Mn-bLf) and BSA-FITC were encapsulated in calcium-alginate and chitosan-coated alginate particles. Micropel particles were fabricated using the emulsification/internal gelation method. Protein encapsulation efficiency was confirmed by fluorescence microscopy imaging of BSA-FITC-loaded hydrogel particles. In vitro release studies conducted in pH-simulated gastrointestinal conditions were employed to investigate protein-loading efficiency and release rate of encapsulated protein. The various encapsulated bLf forms were evaluated for their influence on intestinal epithelial barrier function and cell viability alone, and in combination with purified whole C. difficile toxins A and B or bacterial supernatant samples of the epidemic 027 C. difficile strain. Enterocyte viability and epithelial permeability were assessed using trypan blue exclusion, MTT cytotoxicity assay and changes in trans-epithelial electrical resistance (TEER) in Caco-2 cells, respectively.

Results Alginate microparticles are suitable for encapsulation and pH-triggered release of metal-bound bLf proteins. The application of bLf (5 mg/mL) delivered from alginate microparticles to human intestinal epithelial cells (hIECs) significantly reduced the cytotoxic effect of toxin A and bacterial supernatant samples on Caco-2 cells, as illustrated by increased TEER values and enhanced Caco-2 cell viability. Pre-treatment of Vero cell monolayers with all forms of encapsulated bLf followed by exposure to toxin B or bacterial supernatant induced a fall in mitochondrial enzyme activity.

Conclusions Our results are the first to suggest that alginate-bLf microparticles show protective effects against C. difficile toxin-mediated mucosal damage and impairment of barrier
function in hIECs. The future potential of lactoferrin-loaded alginate microparticles in the treatment and prevention of CDI deserves further investigation in preclinical studies.
Abstracts

**Introduction** Colorectal cancer (CRC) screening using biennial gFOBT was introduced in England in September 2006, and by 2010 was being offered >90% of 60–69 year olds, rising to >95% of 60–74 year olds by 2014. Overdiagnosis of cancer is a major concern of cancer screening programmes; in breast cancer it has been estimated that around 50% of screen detected cancers might be due to overdiagnosis. This study seeks to examine the trends in CRC incidence and ascertain what impact screening has had on incidence.

**Methods** Data for the period 2001–16 was extracted from the ONS website (www.ons.gov.uk) and CRC incidence 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). Changes in incidence rates in age groups never offered screening were compared with those offered screening (age group 60–74 years).

**Results** As shown in table 1 CRC incidence in the 60–64 age band has increased, peaking at 22% (M) and 17% higher(F) in 2009/10 coinciding with the completion of screening roll-out before reducing somewhat. In the 65–69 age band there were similar peaks (21% M and 17% F) in 2008–10 before a decline to below pre-screening rates. In the 70–74 age band for whom screening started in 2010 there were peaks in 2011/12 (17% M and 19% F) before declining below pre-screening rates. These patterns were similar for both colon (C18) and for rectal (C19–21) cancers.

**Conclusion** At this point we could find no evidence of over diagnosis of CRC. While there has been a 13% increase in CRC incidence in the 60–64 age band, consistent with the first (prevalent) screening round there has been no sustained increase in the older age bands offered screening. In contrast there has been an increase in incidence of rectal cancer in women under age 60.

Abstract PTU-049 Table 1 Relative changes in colorectal cancer incidence (C18–21) by 5 year age-band in England & Wales from 2005 to 2015

<table>
<thead>
<tr>
<th>45–49</th>
<th>50–54</th>
<th>55–59</th>
<th>60–64</th>
<th>65–69</th>
<th>70–74</th>
<th>75–79</th>
<th>80–84</th>
<th>85+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>+1%</td>
<td>−5%</td>
<td>+1%</td>
<td>−6%</td>
<td>−11%</td>
<td>−10%</td>
<td>−3%</td>
<td>+3%</td>
</tr>
<tr>
<td>Women</td>
<td>+15%</td>
<td>+20%</td>
<td>+18%</td>
<td>+14%</td>
<td>−4%</td>
<td>−4%</td>
<td>−4%</td>
<td>+5%</td>
</tr>
</tbody>
</table>

**Reference**

**PTU-050** THE SUCCESSFUL IMPLEMENTATION OF FAST-TRACK ROUTINE TESTING FOR MICROSATELLITE INSTABILITY IN A COLORECTAL CANCER PATHWAY

**Introduction** The National Institute for Health and Care guidelines (DG27, Feb 2017) recommend that all patients with colorectal cancer (CRC) should undergo testing for deficient deoxyribonucleic acid (DNA) mismatch repair activity, whose by-product is microsatellite instability (MSI) in DNA. Historically in our trust, MSI testing was done infrequently, in selected high-risk patients, on preserved pathology specimens and with a long wait for results. A new patient care pathway incorporating MSI testing on fresh biopsy tissue with a rapid turnaround time was introduced in January 2017. This service evaluation reviewed performance in the first year of this new pathway.

**Methods** Endoscopists were asked to send an additional fresh biopsy for MSI assay at endoscopic diagnosis of significant neoplasia from January 2017. Data for all patients newly diagnosed with CRC between 1st Jan 2017 to 31st December 2017 were exported from a prospectively populated database.

**Results** A total of 374 patients were identified, median age 72 (range 30–96) of whom 226 (60.4%) patients were diagnosed at endoscopy. One hundred and ninety-one (51.1%) of all patients had MSI assays performed, 142 (62.8%) of those endoscopically diagnosed. Twelve (6.3%) of the patients tested were MSI-high. Median time from submission of sample to result was 13 days (range 3–32).

**Conclusions** Compliance with MSI testing at endoscopic diagnosis is not yet 100%, but this study illustrates that the MSI test can be integrated into the patient care pathway in an NHS setting and used to personalise patient care as turnaround times are sufficiently short for the results to be integrated into pre and post-operative multidisciplinary team meeting discussions.

**PTU-051** SHOULD FOBT POSITIVE PATIENTS WITH PREVIOUS LOW RISK IN SCREENING PROGRAM COLONOSCOPY HAVE FURTHER COLONOSCOPY?

**Introduction and Aim** Current British Society of Gastroenterology guidelines suggest patients who are deemed low risk after adenoma removal at colonoscopy (LRNC) should have no surveillance or colonoscopy interval of 5 years. However patients in the Bowel Screening Program (BCSP) who have LRNC are enrolled for subsequent faecal occult blood testing (FOBt) every 2 years. If test is positive, they are offered a further colonoscopy. Thus, it is possible that a BCSP patient who has LRNC can have up to 2 additional colonoscopies within the BCSP before the surveillance colonoscopy of a similar patient with LRNC, not in the BCSP who chose 5 year interval. AIM: To determine if or not surveillance colonoscopy <5 years from index LRNC led to intermediate or high risk neoplasia findings.

**Methods** We identified all patients with previous LRNC in the North of Tyne screening centre from 2008–2010 who had attended for subsequent colonoscopy (episodes 2 and 3) because they had further positive FOBT. 2 authors (EC and HD) reviewed all endoscopy and histology reports to obtain patient details and identify presence of neoplasia and other pathologies. Colon neoplasia was deemed as low, intermediate or high risk according to BSG surveillance guidelines.

**Results** 81 patients had colonoscopy (episode 2) for positive FOBt after LRNC. Full dataset was obtained for 78 (58%) male. 10 of these had a 3rd colonoscopy (episode 3). Interval between episodes 1 and 2 was 2 years (yrs) in 86% and
4 years in 12%. Interval between episodes 2 and 3 was 2 years in 78%, 3 years in 11% and 4 years in 11%.

The table below shows colonoscopy findings:

<table>
<thead>
<tr>
<th>Episode</th>
<th>No neoplasia</th>
<th>Low risk benign neoplasia</th>
<th>Intermediate risk benign neoplasia</th>
<th>High risk neoplasia</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>57</td>
<td>13</td>
<td>6</td>
<td>1</td>
<td>** **</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

** T3 (Dukes C) rectosigmoid cancer

Conclusions

- 1. Majority (90%) of patients who have positive FOBT after initial LRNC will not require further surveillance colonoscopy
- 2. 29% of patients who have 2nd colonoscopy as FOBT pos. after LRNC will have neoplasia requiring further surveillance (i.e. become intermediate or high risk)
- 3. In our cohort, colonoscopy in 1 patient with positive FOBT after previous LRNC identified a cancer

Our data would support a recommendation that patients with positive FOBT with 2 previous LRNC’s within the BCSP should not be offered further colonoscopy within 5 years of their second procedure.

REFERENCE

**PTU-052 MANAGEMENT OF LARGE SESSILE COLONIC POLYPS BY INTRAOPERATIVE COLONOSCOPY WITH LAPAROSCOPIC SUPPORT**


10.1136/gutjnl-2018-BSGAbstracts.388

Introduction Endoscopic management of large colonic polyps can be challenging, and may lead to incomplete resection/reurrence. Laparoscopic control can facilitate the endoscopic observation and approach to the lesions, and also to recognise and treat complications. Our aim was to study the feasibility and safety of intraoperative colonoscopy (IOC) in facilitating definitive treatment for complex colonic polyps otherwise deemed unsuitable for endoscopic resection.

Methods Patients discussed at the MDT with complex colonic polyps (large and sessile, recurrent, non-lifting but with no evidence of malignancy), deemed unsuitable for conventional endoscopic resection, were scheduled for IOC. Procedures were performed under GA with surgical support available. Depending on endoscopist’s and surgeon’s preference and after discussion, colonoscopy was performed initially without surgical access, or with laparoscopic control, that could be conventional or with single incision (SILS). A PCF-260 JL was utilised, with a soft distal attachment, ERBE 300D diathermy unit and CO2 for insufflation. Resection techniques included Endoscopic Mucosal resection (EMR), Hybrid Endoscopic Submucosal Dissection (ESD), and conventional ESD. Data on all patients undergoing IOC was collected prospectively and analysed from the hospital computer records.

Results Thirty patients underwent IOC (median age 60, IQR 59.5–75 years). Median size was 5 cm (IQR 4.5–6.7 cm). Macroscopic type was sessile with/without flat portion in 12/13 cases. Ten cases underwent endoscopic resection with laparoscopic control, 2 exclusively endoscopic resection, and one only surgical treatment. Laparoscopic interventions included SILS (2), SILS + Right hemicoectomy (1), laparoscopic control (6), laparoscopy+suture of resection site (1), laparoscopy+right hemicoectomy (2). Endoscopic interventions included EMRp (4), Hybrid ESD (8), all in more than one fragment, and without any significant complications. Median procedure time (including endoscopy and surgery) was 235 min (IQR 150–250). Histology revealed: TVA+LGD (10), TVA+HGD (2), T1 cancer (1)(0.5 mm, R0). Nine patients have undergone endoscopic follow up (median 5 months, IQR 4.25–7.5 months). There were two adenoma recurrences on follow up, managed endoscopically.

Conclusion Large/complex colonic polyps can be safely resected by combined endoscopic and laparoscopic approach. In this series colectomy was avoided in 10/13 (77%) cases, with no significant complications. This combined approach should be considered in the armamentarium for the management of large/complex colonic polyps.

**PTU-053 PROGNOSTIC SIGNIFICANCE OF TUMOUR REGRESSION GRADE IN RECTAL CARCINOMA – A 5 YEAR STUDY**

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10.1136/gutjnl-2018-BSGAbstracts.389

Introduction Multimodal therapy is the current recommended treatment of choice for rectal cancer. The effects of the neo-adjuvant therapy/tumour regression can be assessed histologically in the resection specimen.

Methods This is a 5 year retrospective study at a tertiary centre in South India to assess the prognostic significance of the pathological grading of tumour regression in rectal cancer pre-treated with long course neoadjuvant therapy. 137 patients with rectal adenocarcinoma who recieved long course neo-adjuvant chemoradiation followed by surgery were analysed and categorised based on the Tumour Regression Grade(TRG) into 2 groups- Group 1(Good response, TRG 0,1) and Group 2 (Poor response, TRG 2,3). Other factors (clinical and pathological features like lymphovascular/perineural invasion, discontinuous extramural tumour deposits, resection margin status and pTNM stage of tumour) were also evaluated and all variables along with TRG were correlated with disease progression and 5 year survival. Statistical analysis used: IBM SPSS version 20.0 software. Categorical variables expressed using frequency and percentage and the continuous variables presented using mean and standard deviation. The chi-square test was used for finding prognostic factors. Univariate analyses of survival were carried out by Kaplan-Meier method and the evaluations of differences were performed with Log Rank test.

Results Group 1 showed reduced risk for disease progression (p 0.01) and better mean disease free period and overall survival. Poor tumour regression was associated with lymphovascular and perineural invasion and regional lymph node metastases (p<0.001).
Conclusions Pathological assessment of tumour regression serves as a good predictor for disease outcome and should be assessed in all neoadjuvant treated rectal resection specimens.

PTU-054 MICROSATELITE INSTABILITY IN STAGE II COLORECTAL CARCINOMA

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10.1136/gutjnl-2018-BSGAbstracts.390

Introduction 10%–15% of colorectal cancer (CRC) is due to Microsatellite Instability (MSI). The aim of the study was to determine the prognostic significance of detecting MSI in Stage II CRC and to understand the demographic and pathological characteristics of the disease in the Indian scenario.

Methods This was an 8 year retrospective study (2010 to 2017) of 195 patients with Stage II colorectal adenocarcinoma who were categorised into Microsatellite stable (MSS) or MSI based on immunohistochemical expression of the DNA Mismatch Repair (dMMR) proteins. Various clinical and pathological factors as per the Revised Bethesda criteria were compared and analysed between the MSI and MSS groups by Chi-square test and T Test. Kaplan-Meier method was used to calculate the Disease Free Survival (DFS) and Overall-survival (OS) for the 2 groups. Log Rank test was applied to know the strength of association between the DFS and OS with each of the parameters. The data was analysed using IBM SPSS version 20 software.

Results There were 53 (27%) patients in the MSI group. Younger age, and presence of synchronous or metachronous malignancies, right sided location of tumour, poorly differentiated adenocarcinoma, mucin production and presence of peritumoral Crohn’s like lymphocytic response showed statistically significant association with MSI. A definite relationship of MSI status with family history could not be established. The mean DFS in MSI group was 74.7±3.496 months as compared to 69.2±3.631 months in MSS group. Disease related death was seen in 2.8% and 15.7% of patients in MSI and MSS group respectively, p=0.042. Overall survival among the MSI patients was significantly higher (76.6±4.149 months) than the MSS patients (65.0±3.55) p=0.04. MSI patients did not show improved survival with adjuvant therapy.

Conclusions Early stage MSI related CRC has good prognosis even without adjuvant chemotherapy. Knowledge of the MSI status in CRC is useful in management decisions and prognosis. In addition it can help to detect those with Lynch Syndrome who may not fulfil the Revised Bethesda criteria.

PTU-055 FLEXIBLE SIGMOIDOSCOPY-BASED ASSESSMENT FOR SUSPECTED CRC – A SERVICE REVIEW OF THE RAPID ACCESS CLINIC

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10.1136/gutjnl-2018-BSGAbstracts.391

Introduction The colorectal rapid access clinic (RA) was established in our district general hospital in 2001 to provide a streamlined diagnostic service for patients with suspected colorectal cancer (CRC). It offers direct clinician-led flexible sigmoidoscopy (FS) when appropriate clinical criteria are met (i.e. distal colonic symptoms) as indicated on the GP referral form. Video FS is carried out in JAG-approved facilities in the OP clinic. For many patients this acts as a ‘one-stop’ clinic and reduces the need for further attendance. The aim of this study was to provide a descriptive review and evaluate patient outcomes over a 4 year period.

Methods A retrospective analysis of electronic records was carried out for all patients undergoing FS as first investigation during the 12 month period of January-December 2013. Demographics, clinical indications, FS diagnosis, further investigations and final diagnosis were recorded and analysed. A subgroup analysis was carried out according to clinical presentation and cancer outcomes were validated with the Somerset CRC database.

Results 1021 patients underwent FS in the RA clinic. Mean age was 72.5 years, 1.1 F:M ratio. The main referral criteria were: rectal bleeding (41.8%), diarrhea (37.0%), unspecified altered bowel habit (13.8%), constipation (7.4%), abdominal pain (5.1%) and weight loss (2.6%). Diagnosis at examination was: normal (24.8%), diverticulosis (32.9%), polyps (17.5%), haemorrhoids (26.8%), malignancy (5.2%). Further investigations done after FS included barium enema (30%), colonoscopy (21%), contrast abdominal CT (35%) or CT colonogram (0.5%). A further 16 cases (1.5%) were diagnosed with CRC after full colonic assessment. Discharge rate was 12.9% after FS and 76.2% following further investigations. Follow up of patients discharged after RA assessment revealed that four new cases of CRC (0.4%) were diagnosed within 3 years of discharge.

Conclusions This unique RA pathway, with FS followed by selective referral for further colonic assessment, offers a quick and reliable service for the exclusion of suspected CRC with excellent diagnostic accuracy. The incidence of interval CRC is within acceptable limits as compared with other colonic imaging.

PTU-056 LOSS OF CATHELICIDIN (LL-37) IS ASSOCIATED WITH COLORECTAL CANCER PROGRESSION

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10.1136/gutjnl-2018-BSGAbstracts.392

Introduction Cathelicidin (LL-37) is an innate anti-microbial peptide. Previous in vitro studies suggest a protective role in colorectal carcinogenesis. Our recent pre-clinical data revealed that genetic knock out of cathelicidin led to increased size and number of colorectal tumours in the azoxymethane mediated murine model of colorectal cancer (CRC). Cathelicidin expression has not been characterised in human colorectal cancer.

Methods Intensity of epithelial cytoplasmic LL-37 was assessed immunohistochemically in a tissue microarray representing 650 colorectal cancers and 50 paired normal colorectal mucosa samples. Tissue was obtained from chemotherapy and radiotherapy naïve patients obtained at time of surgery for primary colorectal cancer, sourced from the Grampian Tissue Biorepository. Ethical approval was granted by the Grampian
Biorepository Scientific Access Group. Clinico-pathological data were available for each case, including survival up to 18.2 years post-resection. Expression intensity of LL-37 was independently assessed by two observers, blind to clinico-pathological data, as absent, weak, moderate or strong. Descriptive analysis, chi-square test, Fisher’s exact test and log-rank survival analysis was performed using IBM SPSS Statistics (Version 24.0.0.0).

Results The expression of cytoplasmic LL-37 was weaker in colorectal cancer compared to normal colonic epithelium (p<0.001). Increased intensity of LL-37 expression was present in patients staged Dukes A compared to Dukes B (p=0.004) or Dukes C (p=0.003). There was no correlation of LL-37 expression to tumour site, differentiation, extramural venous invasion or mismatch repair protein status. Normal colonic mucosa from patients with Dukes A CRC expressed stronger cytoplasmic LL-37 compared to normal colonic mucosa from patients with Dukes C CRC (p=0.031). There was no relationship between LL-37 expression and overall survival.

Conclusions Loss of epithelial cytoplasmic LL-37 is associated with progression of colorectal cancer, confirming translation of pre-clinical data to human disease. There may be a global field change in LL-37 expression in distant non-malignant cells as CRC progresses. The functional impact of this warrants further investigation and may reveal new insight into the pathogenesis of colorectal cancer.

Abstract PTU057 Figure 2 Investigations performed for detected colorectal cancers

Conclusions CTC was more common in the later cohort, likely related to increasing availability of this imaging modality. This may also explain the increase in flexible sigmoidoscopy, as left sided lesions on CTC require flexible sigmoidoscopy only, rather than full colonoscopy.

Expansion of the referral criteria has not significantly impacted on the number of new CRCs, but has increased the number of non-CRCs. In those presenting with symptoms such as anaemia, abdominal pain and weight loss, with an absence of specific lower gastrointestinal symptoms, CT would be a more appropriate initial investigation than luminal investigations. This will aid in the diagnosis of other significant pathologies, including the many non-CRCs detected via this referral pathway, whilst minimising exposure to invasive luminal investigations with their associated morbidity.
cohort with most lesions being distal, 0–1 s and <40 mm. Table 2 summarises the histology (Group A and Group B) lesions according to site and Paris classification. Additionally, 69 (34%) lesions showed polyp characteristics associated with an increased risk of covert SMIC in previously published data (IIC or 0-Ia, Is +1la with distal location).2

Conclusion High-risk lesions (HGD/cancer) comprised 30% of the total cohort and those potentially associated with covert SMIC (IIC and distal Is/Is+1la lesions) formed 34% of the cohort. From our data, up to 32 lesions per year may necessitate en bloc resection.1 2 This audit has identified the need to plan for service provision in a DGH for large colorectal polyps including potential referral pathways to achieve en bloc resection of lesions with a higher potential for SMIC.

REFERENCE

Abstract PTU-059 NOVEL URINARY AND BLOOD PEPTIDE MARKERS FOR DETECTION OF COLORECTAL CANCER – EARLY RESULTS

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10.1136/gutjnl-2018-BSGAbstracts.395

Introduction The establishment of screening programmes and the two week wait pathway (2WW) to detect CRC is still largely dependent on invasive and expensive endoscopic/radiological methods. There remains a quest for early detection of colorectal cancer (CRC) using non-invasive methods which are well tolerated and patient acceptable. The aim is to identify putative peptide markers for CRC in urine and plasma.

Methods Urine samples from 12 CRC, 6 colorectal adenomas and 6 controls were evaluated in respect to their peptide profiles by capillary electrophoresis-mass spectrometry (CE-MS). The urinary peptide profiles were compared to those of plasma from another cohort of CRC patients (n=16) and controls (n=17) to search for CRC peptide markers differentially expressed both in blood and urine. This was followed by in silico protease prediction for those CRC peptide markers in plasma for which the amino acid sequence could be resolved.

Results From the 392 plasma and 158 urinary CRC peptide marker candidates, ten were found identical and 16 showed sequence overlap demonstrating their origin from the same protein and protein region. Combining these 26 peptides to a support vector machine classifier resulted in the differentiation of the 12 CRC from the 6 colorectal adenomas and 6 controls with a sensitivity of 1.0 (CI:0.84–1.00) and a specificity of 0.92 (CI: 0.84–1.00) after total cross validation.

Conclusions Peptide identification in urine and plasma shows promise as non-invasive markers for CRC. Further work is underway to validate the specific proteases predicted to be responsible for peptide marker generation at tissue level.
PTU-061 Efficacy and acceptability of a renew anal insert in patients who have undergone restorative proctocolectomy

1,2Jonathan Segal, 1,2Cosimo Leo, 1,2Jonathan Hodgkinson, 1Emanuel Cavazzoni, 1,2Carolynne Vaizey, 1Elissa Bradshaw, 1,2Omar Faiz, 1,2Ailsa Hart, 1,2Susan Clark.

1St Mark’s Hospital, Harrow, UK; 2Department of Surgery and Cancer Imperial College, London, UK

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Introduction Restorative proctocolectomy (RPC) has gained acceptance in the surgical management of medically refractive...
Abstracts

Systematic Review

**PTU-062 THE MANAGEMENT OF EARLY POUCH-RELATED SEPTIC COMPLICATIONS IN ULCERATIVE COLITIS**

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Introduction It is well reported that ileoanal pouch-related septic complications (PRSC) increase the chance of pouch failure. There are a number of publications that describe the management of early PRSC in ulcerative colitis (UC) in small series. This article aims to systematically review and summarise the relevant contemporary data on this subject and provide an algorithm for the management of early PRSC.

Method A systematic review was undertaken in accordance with PRISMA guidelines. Studies published between 2000 and 2017 describing the clinical management of PRSC in patients with UC within 30 days of primary ileoanal pouch surgery were included. A qualitative analysis was undertaken due to the heterogeneity and quality of studies included.

Results 1157 abstracts and 266 full text articles were screened. Twelve studies were included for analysis involving a total of 207 patients. The studies described a range of techniques including image-guided, endoscopic, surgical and endocavitational vacuum methods. Based on the evidence from these studies, an algorithm was created to guide the management of early PRSC.

Conclusion Although the rate of successful salvage following early PRSC has improved over time there is a paucity of research correlating the method used with functional outcome. Short course Endo-SPONGE therapy with early surgical closure seems to offer increased chance of salvage. We present an algorithm for the management of early PRSC.

**PTU-063 MISS RATES FOR COLORECTAL CANCER INVESTIGATED WITH COMPUTER TOMOGRAPHY SCANS**

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Introduction Computer tomography (CT) scans are often the initial investigation for patients suspected of colorectal cancer (CRC) because they are better tolerated than colonoscopy. This study aims to evaluate the CRC false negative results (or miss rates) for CT investigations of the colon.

Methods This is a retrospective review of 773 consecutive CRC cases encountered at Royal Berkshire Hospital between 2014 and 2016. Evidence of CT investigations in the previous 3 years was obtained from computerised health records. Only CT scans with the indication suggestive that it was done for suspected bowel malignancy were labelled as ‘missed cancer’. CT scans done to investigate other abdominal organs were not

ulcerative colitis and cancer prevention in familial adenomatous polyposis (FAP).

Incontinence following RPC has not been widely researched. In one study at 10 year follow-up, continence to stool and flatus was present in 79.3% of patients, with 74.4% fully continent overnight. Incontinence following RPC can be multifactorial and be related to pouchitis, cuffitis, impaired pouch emptying and pelvic floor and sphincter weakness. Despite attempting to treat the underlying cause, incontinence may still remain a problem and symptomatic control may be necessary.

Methods This was a single centre prospective study exploring the acceptability and efficacy of the Renew anal insert in controlling and improving incontinence in patients with a ileal pouch. Patients were included if they had undergone RPC for any reason that had self-reported passive incontinence for >2 weeks and were 18 years old at time of enrolment.

Patients with incontinence were asked to use the Renew anal insert for 14 days. The International Consultation on Incontinence Questionnaire-Bowels (ICIQ-B) was recorded before the trial of the Renew anal insert and at the end of the 14 days.

Results 15 patients were included in the study. There were 10 males and 5 females. The median age of the patients was 57 (range 24–74). All 15 patients had RPC for ulcerative colitis. One patient was lost to follow up.

A comparison of the pre and post-intervention scores were made, with the results summarised in table 1.

Abstract PTU-061 Table 1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre Mean±SD</th>
<th>Post Mean±SD</th>
<th>Change *) (Mean (95% CI))</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel pattern</td>
<td>44.1±3.2</td>
<td>42.8±2.6</td>
<td>-1.3 (-6.0, 3.3)</td>
<td>0.55</td>
</tr>
<tr>
<td>Bowel control</td>
<td>58.3±15.6</td>
<td>53.8±20.2</td>
<td>-4.5 (-12.6, 3.5)</td>
<td>0.25</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>36.3±16.4</td>
<td>36.7±14.8</td>
<td>0.5 (5.7, 6.0)</td>
<td>0.88</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>30.5±14.2</td>
<td>31.8±12.9</td>
<td>1.3 (-1.1, 0.8)</td>
<td>0.61</td>
</tr>
<tr>
<td>Day seepage</td>
<td>1.0±0.9</td>
<td>0.7±0.8</td>
<td>-0.3 (-0.7, 0.2)</td>
<td>0.22</td>
</tr>
<tr>
<td>Night seepage</td>
<td>1.8±7.1</td>
<td>0.9±0.9</td>
<td>-0.9 (-1.6, -0.1)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

8/15 patients were satisfied with the device and 6/15 found the device efficacious. Five patients were totally dissatisfied with the device and 6 reported no efficacy.

Conclusions The Renew anal insert may be a treatment that can help patients who have undergone restorative proctocolectomy with faecal incontinence. The Renew anal insert in the correct selected patients is both acceptable and efficacious and is associated with significant reduction in night time seepage.
Immune checkpoint inhibitors (CPIs) are novel agents that work by boosting the body's immune system to fight tumour cells and are transforming cancer therapy. They are generally well tolerated but can cause side effects that mimic various autoimmune diseases. With its rising use across many tumour types, the prevalence of immune related adverse events such as colitis is fast becoming an issue encountered by many gastroenterologists. This review aims to characterise the current trends in management of CPI-induced colitis.

Methods An electronic database search was conducted on Pubmed and Embase. A total of 48 papers were identified for final analysis. This included 29 case reports and 19 case series describing the management of patients with CPI-induced colitis.

Results 48 papers containing 294 patients were included in the review. Of these, 264 were treated with CTLA-4 inhibitors, 18 with PD-1 inhibitors, 1 with PDL-1 inhibitors and 10 with combination therapy. Majority of patients (196) received treatment for melanoma. Other malignancy types included mostly iron deficiency anaemia, change in bowel habit, weight loss, abdominal pain and rectal bleeding. Patients being missed were significantly older than the rest of CRC patients (78.2 years vs. 69.5 years, p=0.000003). A higher proportion of right sided cancers were missed as compared to left sided cancers (7.3% vs. 4.8%) but this was not statistically significant (p=0.36). Average time from scan to diagnosis was 512.9 days (1.4 years). Most CT studies (33 of 42, 79%) were after administration of oral contrast. Two were CT colonoographies that missed one caecal cancer and one rectal cancer at 1.2 and 1.8 years before diagnosis.

Concerning the entire cohort of CRC cases, mean age was 70, male:female ratio was 1:1.16, left sided lesions accounted for 60% and right sided lesions 34%. All of these values are comparable to national statistics.

Conclusions Approximately 1 in 20 patients diagnosed with colorectal cancer had at least one CT scan with no evidence of bowel malignancy in the previous 3 years. Bowel cancer should not be easily excluded by an unremarkable CT scan if there is a high clinical suspicion, especially in a patient older than 70, regardless of the type of scan.
**PTU-066** THE GUT MICROBIOTA INFLUENCES INTESTINAL EPITHELIAL PROLIFERATIVE POTENTIAL

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10.1136/gutjnl-2018-BSGAbstracts.402

Introduction The intestinal epithelium is comprised of a single layer of cells which serves a number of critical functions including the formation of a physical barrier to environmental pathogens and chemical substances, and the absorption of essential nutrients, electrolytes and water. It is also the site of the gut microbiota, a complex and diverse community of bacteria, viruses and fungi, which exists in a mutually beneficial relationship with the human host. The epithelial barrier is maintained through tightly regulated processes of stem cell renewal, epithelial maturation, cell migration and cell death. Failure to finely coordinate these processes can lead to disease states such as cancer. In this study, we aimed to investigate and characterise the role of the intestinal microbiota on epithelial cell proliferation.

Methods We determined the rates of epithelial proliferation in the intestines of Specific-Pathogen-Free (SPF) mice and Germ-Free (GF) mice. We utilised a previously described method which integrates cell tracking using the thymidine analogue Bromodeoxyuridine (BrdU) in crypt-villus units, with a tailored mathematical model, to assess the spatiotemporal dynamics of epithelial cell behaviour in SPF and GF conditions.

Results The rate of epithelial cell production in GF conditions was significantly slower in the colon, ileum and jejunum in comparison to SPF conditions. In the duodenum, there were no significant differences in proliferation rates in GF and SPF conditions. Cell production rates progressively decreased towards the distal part of the intestine, which inversely correlate with the concentration of organisms constituting the intestinal microbiota.

Conclusions These findings indicate that the gut microbiota plays an important role in determining intestinal epithelial cell proliferation rates. This relationship may have important implications in conditions such as colorectal cancer and inflammatory bowel disease, where differences in microbial signatures are known to exist. In turn, it may be possible to harness this knowledge to alter disease progression by modifying the host microbiota.

**PTU-067** THE POSITIVE IMPACT OF THE BOWEL CANCER SCREENING PROGRAMME ON COLORECTAL CANCER DIAGNOSES AND OUTCOMES

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10.1136/gutjnl-2018-BSGAbstracts.403

Introduction The impact of bowel cancer screening programmes (BCSP) on down-staging colorectal cancer (CRC) at presentation is well established and national screening is largely thought to be a success. Uptake of screening remains less than 60%, screening age has been expanded to ages 60–75 and Bowel Scope screening is being rolled out.

Despite BCSP, the number of UK CRC cases has increased by approximately 5% in the last decade. We aim to evaluate the impact of BCSP on the stage of colorectal cancer cases at presentation.

Methods Between 2013 & 2016, approximately 700 new cases of CRC were discussed at the colorectal cancer multi-disciplinary team (MDT) meeting at Kettering General Hospital. The BCSP screening practitioners have collated demographic data, CRC stage, engagement with BCSP (at any time including prior FOBT negative return), emergency presentation, and whether surgery was performed open or laparoscopically. 681 cases have had a full dataset collated and analysed, we report on this data. It is noted that elderly patients over 70 may not have received BCSP invite (though are able to opt in), patients under 55 are not eligible for BCSP (a small number of cases).

### Results

<table>
<thead>
<tr>
<th>Dukes’ stage</th>
<th>BCSP</th>
<th>non-BCSP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>86 (28.1%)</td>
<td>47 (12.5%)</td>
<td>133</td>
</tr>
<tr>
<td>B</td>
<td>91 (29.7%)</td>
<td>120 (32.0%)</td>
<td>211</td>
</tr>
<tr>
<td>C</td>
<td>116 (37.9%)</td>
<td>173 (46.1%)</td>
<td>289</td>
</tr>
<tr>
<td>D</td>
<td>13 (4.3%)</td>
<td>35 (9.3%)</td>
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<td>All cases</td>
<td>105</td>
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In 681 analysed cases, 306 patients (44.9%) had engaged with a BCSP invite (previously and/or at time of diagnosis), 375 had not (55.1%), \( p=0.001 \). CRC is known to be more common in males and in the BCSP engaged cohort the male to female ratio is 1.9:1. In the non-BCSP engaged cohort, the ratio is 1.2:1, \( p=0.0001 \).

In the BCSP cohort, 57.8% of CRC cases were staged as Dukes’ A or B (hence likely to be cured from CRC), in the non-BCSP cohort 55.5% of CRC cases were Dukes’ C or D (likely non-curable/palliative), \( p=0.05 \).

In the BCSP cohort, there were 20 CRC presentations via an emergency admission (6.5% of cases), 81 (21.6%) in non-BCSP cohort, \( p=0.001 \). Of the surgeries undertaken, 173 (56.5% of CRC cases) were performed laparoscopically in the BCSP cohort, 167 (44.5%) in the non-BCSP cohort, \( p=0.05 \).

Conclusions This data illustrates the protection engagement with BCSP (at any time – even previous FOBT negative returns) confers to the profile of CRC case presentation. CRC cases were significantly fewer from the screened cohort – which were significantly less likely to present as an emergency, significantly more likely to undergo laparoscopic surgery, and significantly more likely to be cured.

BCSP appears to protect female patients more than males with a significantly higher proportion of females diagnosed with CRC in the non-screened cohort when compared to the BCSP cohort.
PTU-068 LONG-TERM FOLLOW-UP DATA FOR A SERIES OF POLYP CANCERS RESECTED DURING BOWEL CANCER SCREENING COLONOSCOPY

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Introduction Since commencement of national bowel cancer screening programme (BCSP), malignant colorectal polyps (AKA polyp cancers) – adenomas resected with a focus of cancer – represent 9.8% of detected colorectal cancers (CRC). Optimal management remains unclear.

We previously presented a case series of 48 patients who had a polyp cancer managed by polypectomy alone, suggesting that those staged Haggitt 1 and 2 without adverse prognostic features are safe to be managed non-surgically, as can those with Haggitt 3 if confident of adequate resection margin. We revisit this cohort to assess long-term outcomes.

Methods 48 patients with polyp cancers resected by polypectomy alone (04/2008 – 11/2011) in Leicestershire and Northamptonshire BCSP have had their outcomes reviewed (12/2017).

Results Demographic data

- Median age=66
- Male/Female=33 (68.75%)/15

Location Rectum=5 (10.4%)/Sigmoid=41 (85.4%)/Descending colon=2 (4.2%)

Haggitt 1 Two patients with sigmoid Haggitt 1 polyc cancers have died. One with right sided CRC after 2 years 2 months, the other with sigmoid CRC after 7 years 10 months – both metachronous lesions. Another patient died of lung cancer after 6 years 3 months.

Haggitt 2 A patient died of dementia after 5 years 8 months, another died of Mesothelioma after 2 years 4 months.

Haggitt 3 A patient died of metachronous sigmoid CRC after 5 years, another died of pneumonia after 7 years 8 months.

Other polyp cancers Of 13 other polyp cancers, 5 were pedunculated but not assigned Haggitt stage due to incomplete excision of some cases and invasive cancer – one patient has died with liver metastases (recurrent CRC). There were 8 sessile polyp cancers with 1 recurrent sigmoid CRC and 1 COPD death – too small a group to draw meaningful conclusions.

Conclusion There were 26 patients with Haggitt 1 or 2 polyp cancers without adverse prognostic features managed by polypectomy alone. Mean follow-up of 7 years 3 months has not identified recurrence (by way of metastases), however two patients developed metachronous CRC. This suggests that endoscopic polypectomy is curative.

9 patients with Haggitt 3 polyp cancers have 7 years 9 months mean follow-up (one developed metachronous CRC). Patients staged Haggitt 3 – where there is confidence of adequate resection margin – need to have a discussion around the option of surgery (with its associated risks) versus conservative management.

There are increased risks of adverse outcomes (lymph node metastasis/recurrence) from Haggitt 4 and sessile Kikuchi polyp cancers due to invasion into submucosa, surgery needs to be considered to reduce risk of recurrence.

PTU-069 INCIDENCE OF AND SURVIVAL FOLLOWING PERFORATED DIVERTICULAR DISEASE: A POPULATION-BASED COHORT STUDY FROM ENGLAND

1,2Joe West, 1,2,3Colin Crooks, 4Harmony Otete, 1,2,3David Humes. 1Division of Epidemiology and Public Health, University Of Nottingham, Nottingham, UK; 2NIHR Nottingham Biomedical Research Centre, Nottingham, UK; 3Nottingham Digestive Diseases Centre, Nottingham, UK; 4School of Pharmacy, University of Nottingham, Nottingham, UK

Background Previous studies suggesting the incidence of perforated diverticular disease is increasing are no longer contemporary and were unable to describe trends by age, sex and calendar year. We aimed to provide population based estimates of the incidence of perforated diverticular disease and assess variation by age, calendar time, treatment and sex.

Methods We undertook a historical cohort study using linked primary and secondary care data from 2000–2013 from England. We identified cases of perforated diverticular disease older than 18 years, calculated incidence rates, and modelled variation using Poisson regression along with estimating one year survival with life tables.

Results We identified 2347 cases with an overall incidence of 6.98 per 1 00 000 person years (pyrs) (interquartile range (IQR) 6.70–7.27 per 1 00 000 pyrs). There was an interaction between calendar time, age and treatment (Likelihood Ratio Test p<0.0001). Stratum specific estimates of the increase in incidence for each age group from 2000 to 2013 showed the greatest increase, 49%, in those aged under 45 years who were treated conservatively without surgery (Incidence Rate Ratio 1.49, 95% CI 1.36–1.61) adjusting for sex and region. This increase was seen in conjunction with an increased use of diagnostic imaging especially in the younger age groups. One year survival was highest in those under the age of 65 years who were treated conservatively (96.4%). In those over 65 years one year survival was lower and varied as to whether patients were treated operatively or not (71.4% vs. 50.7%).

Conclusions The incidence of perforated diverticular disease has increased from 2000 to 2013 with the greatest increase in younger age groups who also had the best survival. The increase in incidence in younger groups in part may be due to the identification of patients with localised perforations more frequently identified due to an increase in the use of CT scans.
INCIDENCE OF AND SURVIVAL FOLLOWING RISK STRATIFICATION OF SYMPTOMATIC PATIENTS BREATH TESTING FOR COLORECTAL POLYPS AND DIVERTICULAR ABSCESS: A POPULATION-BASED COHORT STUDY FROM ENGLAND

Background Diverticular abscess represents a significant complication of diverticular disease. We aimed to provide population based estimates of the incidence of diverticular abscess and assess variation by age, calendar time, treatment and sex.

Methods We undertook a historical cohort study using linked primary and secondary care data from 2000–2013 from England. We identified cases of diverticular abscess older than 18 years, calculated incidence rates, and modelled variation using Poisson regression along with estimating one year survival with life tables.

Results We identified 622 cases with an overall incidence of 1.9 per 100 000 person years (pyrs) (interquartile range (IQR) 1.7–2.0 per 100 000 pyrs). Over the time period of the study there was a 1.5 fold increase in the incidence of diverticular abscess (adjusted IRR 1.5, 95% CI 1.0–2.5). This increase was seen in conjunction with an increased use of diagnostic imaging with 92.2% having a CT in 2013 compared to 60% in 2007 (p=0.003). One year survival was 80.1% (95% CI, 76.7%–83.1%) overall and was lowest in those undergoing surgery 68.7% (95% CI 60.3%–75.7%).

Conclusions There has been a 1.5 fold increase in the incidence of diverticular abscess from 2000 to 2013. The condition is associated with a poor one year survival especially following surgery. This increase in incidence may in part be due to improved identification of cases due to an increased use of imaging.

RISK STRATIFICATION OF SYMPTOMATIC PATIENTS USING FAECAL BIOMARKERS AND URINARY VOLATILE ORGANIC COMPOUNDS

Introduction There remains an urgent need for non-invasive, low cost methods for diagnosis of colorectal cancer (CRC). We undertook a diagnostic accuracy study using faecal haemoglobin (F-Hb), faecal calprotectin (FCP) and urinary volatile organic compounds (VOCs) in patients presenting with lower gastrointestinal symptoms referred via Two Week Wait colorectal pathway.

Methods Of 1850 patients approached, 1016 were recruited prospectively. Of these, 562 with complete colonic investigations returned matched urine and stool samples and were included in the final statistical analysis.

Results The sensitivity and specificity for CRC using F-Hb were 0.80 (95% confidence interval (CI): 0.66–0.93) and 0.93 (CI: 0.91–0.95) respectively. The negative predictive value (NPV) was 0.99 (CI: 0.98–1.0). Using urinary VOCs the sensitivity and specificity were 0.63 (CI: 0.46–0.79) and 0.63 (CI: 0.59–0.67) respectively and the NPV was 0.96 (CI: 0.94–0.98). For those with F-Hb negative CRC (false negatives), adding urinary VOCs revealed the sensitivity of 0.97 (CI: 0.90–1.0) and specificity of 0.72 (CI: 0.68–0.76) with the NPV of 1.0 (CI: 0.99–1.0).

Conclusions Urinary VOCs applied to a F-Hb negative group excludes CRC with the NPV of 1.0. Thus, the addition of urinary VOCs shows promise as a second stage test in investigating symptomatic population.

BREATH TESTING FOR COLORECTAL POLYPS AND CANCER: A LOAD OF HOT AIR?

Introduction Colorectal cancer (CRC) is the 2nd most common UK cause of cancer death. The bowel cancer screening programme (BCSP) targets those aged 60–74, but is dependent upon uptake. Some colonoscopies may be unnecessary and are not without risk. A breath test could be a useful tool for triaging for colonoscopy those without red-flag symptoms, or possibly for screening for advanced polyps and cancer. Prior studies have shown promising results of a breath test using exhaled propanal for detecting CRC (96% sensitivity/76% specificity). The Colorectal BReath Analysis (COBRA) study aims to determine the diagnostic accuracy of breath VOCs for detecting CRC and adenomatous polyps.

Methods COBRA is an ongoing prospective cohort study of 2000 patients attending for colonoscopies across 4 London BCSP centres. Exhaled breath (500 mls) is collected using the ReCIVA breath sampling device, onto 4 thermal desorption (TD) tubes. Analysis by gas chromatography mass spectrometry (GCMS) and proton transfer reaction mass spectrometry (PTRMS) identifies and quantifies breath compounds, at St Mary’s Hospital VOC laboratory. Polyp risk classification is determined using the BSG 2010 polyp surveillance guidelines and latest evidence.

Results 406 patients were recruited from July to December 2017. 7 cancer and 126 polyp patients were BCSP colonoscopy diagnosed, giving an incidence of 4% and 63% respectively for London BCSP patients. Clinical data for the PTR-MS analysis using the H3O+ and NO+ precursor ions are presented in table 1. PTR data analysis so far indicates that
there are discriminatory breath compounds between pathology groups, but analysis of possible influences of the bowel preparation regimen is ongoing.

<table>
<thead>
<tr>
<th>Abstract PTU-072 Table 1</th>
<th>H3O+ ionisation (PTR MS)</th>
<th>NO+ ionisation (PTR MS)</th>
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<tbody>
<tr>
<td>Total samples excluded</td>
<td>62</td>
<td>87</td>
</tr>
<tr>
<td>Instrument fault, inadequate colonoscopy, missing clinical data</td>
<td>42</td>
<td>49</td>
</tr>
<tr>
<td>Failure to reach quality control standards</td>
<td>20</td>
<td>38</td>
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<tr>
<td>Total samples included</td>
<td>344</td>
<td>319</td>
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<tr>
<td>Male</td>
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<td>178</td>
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<td>IBSIP patient</td>
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<td>Median age</td>
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<td>Colonoscopy findings:</td>
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<td>Normal</td>
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<td>83</td>
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<tr>
<td>Diverticular disease or haemorrhoids</td>
<td>40</td>
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<tr>
<td>Inflammatory bowel disease</td>
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<td>29</td>
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<tr>
<td>Low risk polyps</td>
<td>87</td>
<td>85</td>
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<tr>
<td>Intermediate risk polyps</td>
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<td>18</td>
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<td>High risk polyps</td>
<td>60</td>
<td>51</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Inherited polyposis (FAP, Lynch, Juvenile polyposis)</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>

Conclusions: Findings suggest that large scale breath testing is feasible within clinical practice. Whilst analysis of this preliminary dataset suggests the presence of discriminatory compounds between disease groups, analysis is ongoing. The true diagnostic accuracy of breath testing in this setting is expected to be revealed once all patients have been recruited to this study.

**Abstract OWE-026**

**CONDITIONED PAIN MODULATION IN FUNCTIONAL GASTROINTESTINAL DISORDERS: SYSTEMATIC REVIEW & META-ANALYSIS**

1Ahmed Albuwadi*, 2Katherine Freis, 3Max Gysen, 1James Ruffle, 1Qasim Azy, 1,2 Adam Farman. 1Centre for Neuroscience and Trauma, Blizard Institute, Wingate Institute of Neurogastronomy, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK; 2Faculty of Health Sciences, Aarhus University, Aarhus, Denmark; 3School of Medicine, Heidelberg University, Heidelberg, Germany; 4Department of Gastroenterology, University Hospitals Midlands NHS Trust, Stoke on Trent, UK; 5Institute of Applied Clinical Science, University of Keele, Keele, UK

Background: Functional gastrointestinal disorders (FGID) are common and characterised by chronic unexplained visceral pain. Conditioned pain modulation (CPM), a bulbar reflex permitting “pain to inhibit pain” by descending inhibition, is a validated measure that interrogates the brain-gut axis. Previous studies variably implicate diminished CPM in the pathophysiology of FGID. We aimed to clarify this relationship by meta-analysis.

Methods: PubMed and Web of Science databases were searched until April 2017. Studies that were included comprised of randomised controlled studies investigating CPM in FGID patients with abdominal pain, defined according any iteration of the Rome criteria. We excluded studies if patients had a concomitant pain condition, other than FGIDs. The methodological quality of included studies was evaluated following an adapted scoring system for controlled trials.

Results: We identified 645 studies, of which 14 were relevant and met the inclusion criteria; 12 included patients with irritable bowel syndrome (IBS), 1 with functional dyspepsia and 1 with functional abdominal pain. CPM was reduced in FGID patients versus healthy controls, odds ratio 3.95 (95% confidence interval 2.06–7.58) (Figure 1). There was significant heterogeneity in effect sizes (Q-test $\chi^2=59.4$, $p<0.001$, $I^2 \geq 78.1\%$) in the absence of publication bias. When including only studies with IBS, the odds ratio increased to 4.83 (Q-test $\chi^2=52$, $p<0.001$, $I^2 = 78.8\%$).

Conclusion: CPM is significantly reduced in patients with FGID when compared to healthy controls. These data provide evidence that deficiencies in visceral pain bulbar-mediated descending inhibitory pathways is an important pathophysiological facet which could represent a novel treatment target.

Introduction: Diabetic gastroparesis (DG) affects up to 20% patients with type 1 Diabetes Mellitus (DM). Impaired gastric function is thought to be the cause of nausea, vomiting, abdominal pain and impaired glycaemic control. DG does not respond reliably to intensive insulin regimes or prokinetic medications. Jejunal nutrition (JN) is an option in patients that cannot maintain weight. The benefits are thought to be improved nutrition and glycaemia; however, we have observed that some DG patients can eat normally during JN.

We propose that DG represents a failure of oral nutrition to ‘switch’ the stomach from the fasted to the fed state with a need for delivery of nutrients directly to the jejunum triggering neuro-hormonal mechanisms that induces normal gastric function. This study tests the hypothesis that JN prior to a meal improves postprandial symptoms and gastric function.

Methods: Diabetic patients with severe symptoms (GCSI >27), diabetic controls (GCSI <14) and healthy controls (HC) entered a randomised, double blind, controlled trial. Glycemia was controlled. NJ feeding tube was placed. Liquid nutrient (2 kcal/min) or water was infused for 60 min. The validated Nottingham Test Meal was then ingested (NTM liquid: 400 mL; 300 kcal; solid: 12 non–nutrient agar beads). Symptoms were documented (VAS), gastric function by MRI and the GI-peptide response was monitored. Mixed model analysis compared response to intervention and between groups.

Results: 9 DG patients, 9 diabetic and 12 HC were recruited. There was no difference in demographic features between...