

germline pathogenic/likely pathogenic variants (PV/LPVs) informs decision making regarding CRC risk reduction for the patient, as well as at-risk family members. Utility of genetic testing in MCRA patients remain uncertain, with current guideline recommendations based on limited and low-quality evidence.

Methods We performed a cross-sectional review of the prospectively collected and maintained polyposis registry and family cancer clinic database at our institution. Index (proband) patients with 10-99 cumulative adenomas aged ≥ 18 at time of testing, with no previously identified familial mutation, who underwent constitutional testing of colorectal cancer predisposition genes were included in the analysis. Molecular testing results were interpreted as reported by the responsible genetic testing laboratory and updated if later re-classified. Clinicopathological outcomes of age, adenoma burden, years of testing (1999-2009 vs 2010-present), gender, ethnicity, personal history of CRC, personal history of other malignancy, and first-degree familial history of CRC were extracted for multiple logistic regression analysis.

Results Of a total of 42,998 recorded patients, 886 patients were identified for screening, with a total of 259 patients with MCRA meeting all inclusion criteria and were eligible for study inclusion. Overall diagnostic yields were greater than 10% at any adenoma burden. *APC* and biallelic *MUTYH* mutations constituted the majority of identified PV/LPVs at any adenoma burden. Young age, high adenoma burden, personal history of CRC and first-degree familial history of CRC were significantly associated with higher diagnostic yield. ($p < 0.05$).

Conclusions An overall diagnostic yield of $>10\%$ at any adenoma burden supports current evidence for constitutional genetic testing in MCRA patients in line with current BSG guidelines. Further studies with prospective trial design and larger cohorts undergoing constitutional multi-gene panel testing is required to substantiate guidance on other aspects of management, including surveillance in relatives of those with MCRA.

OFR-7 BREATH TESTING FOR COLORECTAL POLYPS AND CANCER- THE COLORECTAL BREATH ANALYSIS1 STUDY (COBRA1)

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Introduction Colorectal cancer (CRC) is the 2nd commonest cause of cancer death in the UK, making up 11% of new cancer cases. Despite this, 5-year survival rates are 58%, amongst the lowest in Europe. There is need for improvement because CRC survival rates can exceed 90% if detected early. This study aimed to investigate the diagnostic accuracy of breath testing for CRC. If successful, a breath test could provide a highly acceptable non-invasive tool to improve and streamline existing referral CRC pathways. This could lead to earlier and more targeted diagnosis, ultimately saving both lives and resources.

Method COBRA1 was a multicentre cohort study investigating volatile organic compounds (VOCs) in the breath of 1432 patients attending one of seven London hospitals for colonoscopy or for colorectal adenocarcinoma resection. Patient

breath was collected using the ReCIVA breath sampler and thermal desorption tubes. Patients were nil by mouth for at least 6 hours and were sampled immediately prior to their procedure, in a separate area. All colorectal pathologies were diagnosed using the standard reference test (colonoscopy), with histological confirmation for CRC, polyps, or inflammatory bowel disease. Breath was analysed using gas chromatography mass spectrometry (GC-MS), and resulting VOC data processed using the GC-MS data platform MSHub. A machine learning algorithm was used to identify VOC components with the best discriminating ability and to develop a multivariate discriminant analysis model. VOCs were identified using the NIST mass spectral library.

Results The presence of CRC (n=162) could be predicted from positive and negative controls (n=1270) with a sensitivity of 77%, specificity of 87% and an area under the ROC (AUROC) curve of 0.87. 15 of the most predictive VOCs were from organosulphur, alcohol, alkane, ester and phenol chemical groups. VOC abundances also appeared to be related to the T stage of the tumour. Polyps (n=592) could be predicted from positive and negative controls (n=619): sensitivity 66%, specificity 54%, AUROC curve of 0.65. Subgroup analysis of symptomatic patients (n=855), demonstrated a sensitivity of 82%, a specificity of 88% for CRC detection, with an AUROC curve of 0.90.

Conclusions Analysis of exhaled VOCs could discriminate patients with CRC from those without, using the gold-standard diagnostic test and VOC analytical method. Results can be compared favourably to stool-based tests, particularly for polyps and symptomatic patients. These exciting findings pave the way for larger targeted VOC studies to validate results and explore implementation into clinical practice.

Neurogastroenterology

OTH-2 THE SYMPTOM BURDEN OF IRRITABLE BOWEL SYNDROME IN TERTIARY CARE DURING THE COVID-19 PANDEMIC

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Introduction Recent data on the natural history of Irritable Bowel Syndrome (IBS) highlight the prognostic importance of extra-intestinal and psychological symptom profiles. Those with a high psychological burden have been shown to have the worst prognosis, and are consequently most likely to be referred to tertiary care. The Covid-19 pandemic caused significant disruption to tertiary services and affected the mental health of the nation, however there is minimal data on the effects on patients with IBS in tertiary care. We therefore compared the symptom profiles of tertiary referrals with refractory IBS, 12-months before, and 12-months after the onset of Covid-19 restrictions in the UK.

Methods As part of their routine care, all patients with refractory IBS referred to the tertiary service before and after the Covid-19 pandemic prospectively completed a series of questionnaires during their baseline consultation including; IBS symptom severity score (IBS-SSS), non-colonic symptom score, Hospital Anxiety and Depression (HAD), and Quality of Life (QoL). Demographic data and symptom profiles were