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## DEVELOPMENT OF A TARGETED METABOLOMIC URINE-BASED PANEL FOR INFLAMMATORY BOWEL DISEASE

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Introduction Ulcerative Colitis (UC) and Crohn's Disease (CD), the Inflammatory Bowel diseases (IBD) are characterised by chronic relapsing remitting inflammation of the gastrointestinal tract. Over the past decade, metabolomic research has allowed for the characterisation of UC, CD, inactive and active disease; many biofluids have been analysed. However, findings have been inconsistent and few offer clinically useful quantitative data.

Methods A comprehensive literature review, and expansion of appropriate biochemical pathways, was carried out to identify metabolic targets for development into a fully quantifiable and targeted assay. A selection of these metabolites was validated for use in predicting IBD via a combination of univariate and multivariate techniques in proton nuclear magnetic resonance (<sup>1</sup>H-NMR) spectroscopy acquired urine data (IBD = 215, controls = 101). A finalised panel was taken forward for an ultra-high-performance liquid chromatography-mass spectrometry (UHPLC-MS) urine-based assay development and consequent validation in a clinical cohort.

Results 42 metabolites were identified as discriminatory, for characterising IBD compared to controls: these have been taken forward for urinary assay development and subsequent validation. Prior analysis of urinary data from a heterogenous IBD cohort demonstrated that using a specified panel of metabolites, as opposed to all data acquired, considerably improved the predictive score (Q2), and significance of models generated (from p=1 to p=0.003 respectively). These metabolites were both of human and microbial origin, reiterating the importance of the gut microbiome in IBD. Following development, the panel will be validated on a *de novo* clinical cohort of IBD patients to quantify metabolic perturbations invoked by disease pathogenesis.

Conclusions This work highlights the efficacy of targeted metabolomic methods and the capabilities of these approaches to characterise IBD. The identification of refined metabolic changes with a pathway-driven approach will not only improve knowledge of both host and microbial metabolism in IBD but may also elucidate potential novel therapeutic targets and markers for therapeutic response.

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## MICROSCOPIC COLITIS: LOST OPPORTUNITY FOR DIAGNOSIS AND TREATMENT RESULTS IN HOSPITAL ADMISSIONS

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Background Microscopic colitis (MC) is a histological diagnosis. MC significantly affects patients' quality of life but there is limited data on the length of symptoms prior to diagnosis and the patient journey. We therefore evaluated the largest UK clinical data set on patients with MC.

Methods A UK study from 2 hospitals of retrospectively collected data from case notes between 2007 and 2017 of all patients diagnosed with histologically confirmed MC. Further data was collected on all colonoscopies complete for chronic diarrhoea/Irritable Bowel Type Syndrome (IBS) type symptoms in the same study period.

**Results** A total of 562 patients were diagnosed with MC of which 24.9% collagenous colitis (72.1% female), 70.1% lymphocytic colitis (63.2% female) and 5% undifferentiated MC (75% female). Collagenous colitis was diagnosed later than lymphocytic colitis (67 vs 63 years (p=0.002)

Patients reported symptoms prior to referral of 3 months (IQR 2 month-1 year). However, 15% had symptoms 3–20 years. From primary care 56.0% were referred routinely and 44.0% via two week wait pathways (2ww). Patients under 2ww were seen quicker (12 days vs 24 days, p<0.0005) as were older patients (p<0.005).

Hospital admission was required in 6.4% of patients due to diarrhoea (80.6%), acute kidney injury (27.8%), abdominal pain (16.7%) and collapse (5.6%). 1.4% of patients were admitted for other reasons and MC diagnosed incidentally. Older patients were more likely to be admitted (OR: 1.074, CI: 1.0.4 - 1.1) and no patients were on budesonide prior to admission. The average length of stay was 12 days (IQR:8–21 days). Of patients admitted, 11.1% had had previous colonoscopies.

In the same study period 10,015 lower gastrointestinal endoscopies (84.3% colonoscopies and 15.7% flexible sigmoidoscopies) were performed (59.3% female, 57 years, IQR 43–69 years). Colonoscopies were performed for investigation of chronic diarrhoea, IBS-diarrhoea (IBS-D), IBS-mixed (IBS-M), or suspected IBD (22.4%, 59.0%, 14.6% and 3.9%). In total, 19.5% of colonoscopies conformed to biopsy guidelines. In the other cases biopsies were taken from incorrect sites: only left or right sides of the colon, the rectum and randomly (15.8%, 10.7%, 24.2%, and 58.7%, respectively). In 8.6% of colonoscopies, no biopsies were taken. The highest adherence to guidelines (48%) occurred in a subgroup of IBD where the indication was to rule out MC.

Conclusion This is the largest international study to report MC findings. Our data demonstrates lost opportunities for diagnosis and treatment of MC both in primary and secondary care which may ultimately result in hospital admission. This may suggest a limited understanding to MC from both primary and secondary care.

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## HETEROGENEITY IN OUTCOME ASSESSMENT FOR IBD IN ROUTINE PRACTICE: A MIXED-METHODS STUDY OF ENGLISH HOSPITALS

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Introduction Global initiatives have sought to standardise outcome assessment for inflammatory bowel disease (IBD) for clinical trials (Core Outcome Sets) and routine practice (ICHOM). Our aims were to investigate variability in the assessment and recording of outcomes elicited by clinicians from patients in hospital-based IBD outpatient services and to

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