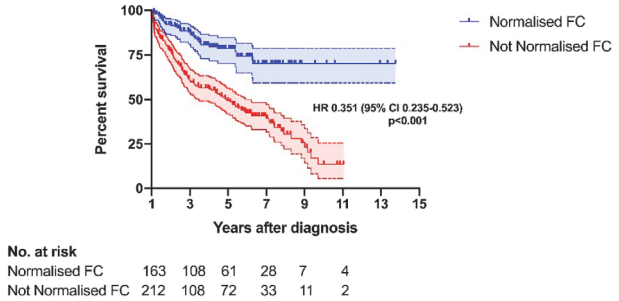

Abstract O10 Figure 1

compared to a strategy based on symptoms alone. The aim of this study was to determine whether normalisation of FC (<250 µg/g) within 12-months of diagnosis is associated with a reduction in disease progression in CD.

Methods This was a retrospective cohort study performed at a tertiary IBD centre. All incident cases of CD diagnosed between 2005–2017 were identified. Patients with a FC measurement of >250 µg/g at diagnosis who also had at least 1 follow up FC measured within the first 12-months of diagnosis and >12 months of follow up were included. The primary endpoint was a composite of progression in Montreal disease behaviour (B1 to B2/3 or B2 to B3 or new perianal disease), surgery or hospitalisation.

Results A total of 375 patients were included with a median follow up of 5.3 years (IQR 3.1–7.4). Normalisation of FC (<250 µg/g) within 12 months of diagnosis was confirmed in 43.5% (n=163/375) of the cohort. On multivariable Cox-proportional hazards regression analysis, individuals who normalised their FC within 12 months of diagnosis had a significantly lower risk of composite disease progression (HR 0.351, 95% CI 0.235–0.523, p<0.001) (figure 1). In addition, normalisation of FC was the only predictor that remained significant for all of the separate progression end-points (progression in Montreal behaviour/new perianal disease: HR 0.250, 95% CI 0.122–0.512, p<0.001; hospitalisation: HR 0.346, 95% CI 0.217–0.553, p<0.001; surgery: HR 0.370. 95% CI 0.181–0.755, p=0.006). Patients initiated on a biologic within 3 months of diagnosis were significantly more likely to normalise their FC within 12 months of diagnosis (OR 4.288, 95% CI 1.585–11.0601, p=0.004).

Conclusions Normalisation of FC by 12-months of diagnosis is associated with a reduced risk of disease progression in CD. The immediate implication for healthcare providers and patients is that by ensuring resolution of mucosal inflammation - using FC as a proxy target - within 1 year of diagnosis has a dramatic effect on disease course.

O11 OUTCOMES OF GP OUTREACH PROGRAMME OFFERING COLONOSCOPIC SURVEILLANCE FOR IBD PATIENTS MANAGED IN PRIMARY CARE

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Introduction Colonoscopic surveillance in IBD patients can reduce the development of colorectal cancer (CRC) and the rate of CRC-associated death. We recently reported that 27% of IBD patients living in East Devon are managed exclusively in primary care of whom about 23% maybe eligible for colonoscopic surveillance. We devised an outreach programme, whereby we invited primary care physicians to enrol these patients in a colonoscopic surveillance programme.

Methods In December 2017 we contacted 37 general practices, where 161 patients with UC who were eligible for surveillance had been identified. Each practice was sent a letter explaining the goals of the project, a link to the National Institute for Healthcare and Clinical Excellence (NICE) guidance for CRC surveillance in IBD patients and patient information booklets. We informed the practices of their eligible patients and asked them to refer patients for secondary care IBD consults if appropriate. We included an outcome form that captured whether the patient was referred, was deemed inappropriate for surveillance, had surveillance elsewhere, had declined surveillance, or was no longer registered at the practice.

Results Sixty-five percent of practices (24/37) responded and we received responses for 57 of 161 (35%) potentially eligible patients. Thirty-five (61%) patients were referred to our IBD service; 7 (12%) patients declined surveillance; 7 (12%) patients were deemed by their GP to be unfit for surveillance and 5 (10%) were no longer registered at the identified GP practice; 2 (4%) had surveillance arranged elsewhere and 1 (2%) patient had died. Amongst the 35 patients referred to secondary care; 22 (63%) underwent surveillance colonoscopy, 12 (34%) declined surveillance after discussion or did not attend their booked appointments and one is awaiting colonoscopy. Half of patients who had a colonoscopy had active inflammation. We diagnosed one CRC He was an elderly man with a locally invasive signet ring caecal tumour, without distant metastases, who went onto to have a curative right hemicolectomy without complication.

Conclusions Patients with longstanding IBD are frequently managed exclusively in primary care and maybe overlooked for colonoscopic CRC surveillance. There is a need to implement processes to facilitate identification and recall of patients eligible for surveillance across primary and secondary care.

O12 REVERSION TO BASELINE MICROBIOME FOLLOWING SUCCESSFUL COURSE OF EXCLUSIVE ENTERAL NUTRITION IN PAEDIATRIC CROHN'S DISEASE

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10.1136/gutjnl-2020-bsgcampus.12

Introduction To characterise the microbiome composition and functionality in paediatric Crohn's disease (CD) patients during a course of exclusive enteral nutrition (EEN) and subsequent food-reintroduction

Methods CD patients were recruited between August 2014-June 2016. Patients were treated with an 8 wk course of EEN. Clinical disease activity was defined using the weighted paediatric Crohn's disease activity index (wPCDAI). Serial faecal samples were collected prior to EEN, at 30d and 56d of EEN, and two further samples were collected post-EEN (17d

and 52d) during food re-introduction (FR). Microbiome was assessed by 16s rRNA gene sequencing of the V4 region performed on the MiSeq (Illumina). Community structure was resolved at 97% similarity operational taxonomic unit (OTU). Short chain fatty acids (SCFA) were quantified with gas chromatography and are expressed in µmol/g. Faecal calprotectin (FC) was measured using the CALPROLAB0170 (ALP) (Lysaker, Norway) ELISA kit. Continuous data are present as mean and standard deviation unless otherwise stated.

Results 66 CD patients were recruited (Female 25; age 13.4 yr). Clinical remission (wPCDAI<12.5) was achieved in 41 (62%). During EEN there was an increase in Shannon diversity (start: 0.3 [0.22] vs 30d EEN: 0.48 [0.2], p<0.001; vs 56d EEN: 0.43 [0.27], p=0.05). During FR these indices did not change.

Based on β-diversity dispersion analysis, estimated using Bray-Curtis distance, EEN induced clear alterations to the microbiome. Permutation ANOVA was used to identify significant changes to the microbiome during EEN. Most of the change that occurred was apparent within the first 4 weeks of treatment with R2: 4.7%, (p=0.001) and by the end of EEN R2: 3.2%, (p=0.001).

In patients to enter remission using EEN, we observed a quick reversion in the microbiome composition to that of pre-treatment (p=0.23).

Assessing the metabolic activity of the microbiome we observed a significant decrease in the concentration of acetate (start: 423.6 [183.6], end: 224.9 [101.5]; p< 0.001), propionate (start: 93.8 [50.6], end: 55.7 [27.3]; p< 0.001) and butyrate (start: 95.0 [64.2], end: 41.0 [50.7]; p< 0.001). During FR, there was a rapid reversion in levels of acetate and propionate (acetate EEN end: 224.9 [101.5] vs 17d FR: 362.4 [179.7]; p=0.003; propionate EEN end: 55.7 [27.3] vs 17d FR: 93.0 [46.9]; p=0.002).

Faecal calprotectin significantly decreased during EEN (start: 1402.4 [586.3]; 4wk EEN: 877.5 [593.1], p<0.001; 8wk EEN: 720 [664], p<0.001) and was quickly reversed during food re-introduction (17d FR: 1025 [603], p=0.025; 52d FR: 1105 [651], p=0.003)

Conclusions EEN induces specific effects on faecal microbiome and markers of functional activity. This is characterised by a reduction in metabolic activity during EEN, with reversion to pre-EEN state during food re-introduction paralleling an elevation of faecal calprotectin

013 REGULATION AND ROLE OF ALPHAE INTEGRIN IN MIGRATION AND RETENTION OF LYMPHOCYTES IN INTESTINAL MUCOSA

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Introduction Targeting integrins that mediate adhesion and migration of lymphocytes to the gastrointestinal (GI) tract is an effective therapy in inflammatory bowel disease (IBD). α4β7 and α4β1 are expressed on circulating lymphocytes that may mediate inflammation, while αEβ7 integrin is expressed primarily on a subset of T cells within the mucosa. Etrolizumab is a humanized monoclonal antibody that selectively binds the β7 subunit of the α4β7 and αEβ7 integrin heterodimers. The relative role of individual integrin heterodimers in lymphocyte migration and retention in the GI tract remains to be characterized.

Methods pSMAD3, MAdCAM, VCAM and ICAM levels were measured in colonic and ileal biopsies. α4β7+ and α4β7- human T cells were induced to express αE integrin by TGF-β 1 stimulation followed by qPCR array gene expression analysis. A murine photo-convertible reporter system was used to determine the effect of blockade of α4β7 and/or αEβ7 integrins on lymphocyte migration and retention. T cell-epithelial cell interactions were evaluated using intravital two-photon microscopy.

Results pSMAD3 was observed in the epithelium and lamina propria in IBD biopsies, suggesting active TGF-β signalling. Adhesion molecule expression was increased in inflamed biopsies. TGF-β1 stimulation induced αE integrin expression on both α4β7+ and α4β7- circulating T cells. αEβ7+ cells derived from α4β7+ and α4β7- progenitors had similar cytokine, chemokine, transcription factors and effector molecule gene expression. In a mouse model of T cell migration, combined blockade of both α4β7 and αEβ7 with anti-β7 (etrolizumab surrogate) led to a greater reduction of T cell accumulation in the intestinal mucosa and epithelium compared to single blockade of either α4β7 or αEβ7. Further intravital two-photon microscopy and photo-specific labelling experiments revealed that blockade of αEβ7 reduces T cell:epithelial cell interactions, increases the migratory speed of activated T cells in the intestinal mucosa, and facilitates effector T cell egress from the intestinal mucosa through lymphatic vessels.

Conclusions αEβ7 is induced by TGF-β1 on both α4β7+ or α4β7- T cells. Co-blockade of α4β7 and αEβ7 together leads to greater inhibition of T cell accumulation in gastrointestinal tissues through a stepwise inhibition of T cell migration and subsequent tissue retention.

014 WHOLE BLOOD PROFILING OF T-CELL DERIVED MIRNA ALLOWS THE DEVELOPMENT OF PROGNOSTIC MODELS IN IBD

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Introduction There is an unmet need for blood-based biomarkers that help predict disease and its course at inception to allow tailoring of treatments, achieve early mucosal healing and improve clinical outcomes. In our study, we explore the clinical utility of miRNAs in Inflammatory bowel disease (IBD).

Methods A 2-stage prospective multi-centre case control study was performed. Small RNA sequencing was performed on a discovery cohort of immunomagnetically separated leucocytes (90 CD4+ & CD8+ T-lymphocytes and CD14+ monocytes)