

Further work is required to explore why FC concentrations are lower in proximal disease despite presence of active inflammation.

## REFERENCES

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**Disclosure of Interest** None Declared.

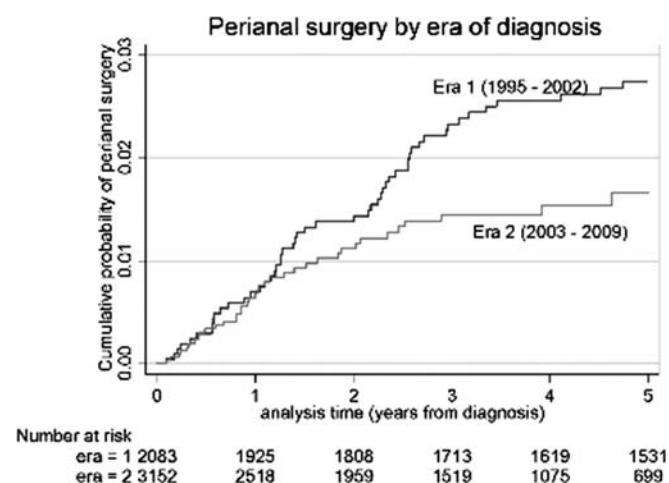
## PWE-117 HAVE PERIANAL SURGERY RATES DECREASED WITH THE RISE IN THIOPURINE USE IN CROHN'S DISEASE?

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10.1136/gutjnl-2014-307263.377

**Introduction** Although thiopurines (TPs) have proven efficacy in the maintenance of remission in Crohn's disease (CD) and may reduce the need for intestinal surgery, their impact on perianal disease is not firmly established since previous trials have not evaluated the efficacy of TPs on perianal disease as a primary endpoint. Our aim was to examine the temporal trends in perianal surgery and TP use using the Clinical Practice Research Datalink (CPRD).

**Methods** Using electronic primary care records, we performed a UK population based study. Incident cases of CD were identified between 1995 and 2009 from the nationally representative CPRD which contains clinical records and prescribing data for 13 million people in the UK and is a validated research database. Patients were included if they had been registered with a practice for greater than 12 months. The primary endpoint was first perianal surgery defined by READ/OXMIS coding. The cohort was divided into two defined historical era; era 1 (1995–2002) and era 2 (2003–2009). We performed Kaplan-Meier survival analysis to establish the 5 year rates of first perianal surgery and trends in TP prescribing by era of diagnosis. Log-rank test for trend was used to compare survival outcomes between groups.



Abstract PWE-117 Figure 1

**Results** 5235 patients met the diagnostic criteria for an incident case of CD. 2083 were diagnosed in era 1 (1995–2002) and 3152 in era 2 (2003–2009). The mean duration of follow up was 4.8 years/person. 56.3% of patients were female and median age at diagnosis was 38.5 years (IQR: 24.8–58.1 years). 124 patients underwent perianal surgery. The overall 5 year rate of perianal surgery was 2.2% (95% CI: 1.8–2.7%). Stratified by era of diagnosis the rate was lower in the more recent era: 2.7% (95% CI: 2.1–3.6%) and 1.7% (95% CI: 1.2–2.3%) in era 1 and era 2 respectively (log-rank test for trend  $p = 0.03$ ). Conversely, during the same period, the 5 year cumulative probability of receiving a TP increased between era 1 and era 2 from 29.1% to 42.2% (log-rank test for trend  $p < 0.001$ ).

**Conclusion** Over the 15 year study period, the risk of perianal surgery fell by one third which coincided with a one third increase in TP use during the same period. Other changes in IBD management are also likely to have contributed to this fall in surgery. Further studies to determine independent risk factors associated with perianal surgery are in progress.

**Disclosure of Interest** None Declared.

## PWE-118 PREDICTORS OF COLECTOMY AND THE IMPACT OF THIOPURINES ON THE RISK OF COLECTOMY IN ULCERATIVE COLITIS – A NATIONAL UK BASED OBSERVATIONAL STUDY

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10.1136/gutjnl-2014-307263.378

**Introduction** Thiopurines (TPs) including azathioprine and mercaptopurine have an established role in maintaining disease remission in ulcerative colitis (UC) but their impact on the risk of colectomy remains unknown. Our aim was to establish predictors of colectomy and determine the effect of TPs on the risk for colectomy using the Clinical Practice Research Datalink (CPRD).

**Methods** We conducted a population based study using electronic primary care records in the UK. We identified incident cases of UC between 1989 and 2009 in the CPRD which contains prescribing and clinical data for 8% of the UK population and is a validated research database. Patients were included if registered with a practice for at least 12 months prior to diagnosis. We compared rates of colectomy between TP users and non-users and examined the impact of treatment duration. We performed survival analysis using the Kaplan-Meier method. Independent risk factors for surgery were determined using a multivariable Cox proportional hazards model.

**Results** Overall, 8673 patient met our inclusion criteria of which 479 (5.5%) went on to have a total colectomy during 21 years of follow up. 51.4% were male and the median age was 46 years (IQR: 32–62 years). Female patients were less likely to undergo colectomy (HR 0.70, 95% CI: 0.58–0.84,  $p < 0.001$ ). There was a threefold increase in the risk of colectomy amongst TP users compared with non-users (HR 3.48, 95% CI: 2.84–4.37,  $p < 0.001$ ). Of the TP users, those receiving greater than 12 months of treatment, were least likely to undergo colectomy compared with users for less than 3 months (HR 0.29, 95% CI: 0.21–0.40,  $p < 0.001$ ). Early steroid users were almost twice as

likely to undergo colectomy (HR 1.94, 95% CI: 1.59–2.37,  $p < 0.001$ ). 5-ASA use was protective, with users 65% less likely to undergo colectomy than non-users (HR 0.35, 95% CI: 0.28–0.44,  $p < 0.001$ ).

**Conclusion** Male sex, TP use and early steroid use within 3 months of diagnosis are predictors of colectomy in UC. Amongst TP users, sustained TP use for greater than 12 months duration, was associated with a reduction in colectomy rates. 5-ASA use was associated with a two thirds reduction in risk of colectomy. Our findings support the role of 5-ASA use and prolonged TP treatment for UC patients with a severe disease phenotype.

**Disclosure of Interest** None Declared.

#### PWE-119 DECREASED FREQUENCY OF PERIPHERAL AND INTESTINAL NKG2A-POSITIVE T CELLS IN ULCERATIVE COLITIS PATIENTS

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10.1136/gutjnl-2014-307263.379

**Introduction** The intestinal tract is home to a numerous immune cellular components that continuously encounter abundant exogenous stimuli, where remain in a state of controlled inflammation normally. Inflammatory bowel disease (IBD) is characterised by chronic and refractory intestinal inflammation comprising ulcerative colitis (UC) and Crohn's disease (CD) in main. Inhibitory natural killer receptors (iNKR) are expressed on NK cells, involved in NK-cell tolerance to self. There is increasing evidence that iNKR like NKG2A expressed on T cells are importantly involved in the regulation of immune responses though no studies have addressed the potential role in the pathogenesis of IBD. We analysed the expression of NKG2A on T cells in dextran sulfate sodium (DSS)-induced colitis model mouse and IBD patients.

**Methods** Male BALB/c mice were administrated 5% DSS in distilled water for 7 days ad libitum for induction of experimental colitis. For controls, age-matched BALB/c mice were given distilled water. NKG2A+ T cells in peripheral blood mononuclear cells (PBMCs) and lamina propria mononuclear cells (LPMCs) were analysed by flow cytometry. For histological analysis of DSS-induced colitis mice, hematoxylin and eosin (H&E) staining and immunohistochemistry were performed. For blocking experiments using antibody (Ab), mice were intraperitoneally injected with 300 µg of anti-NKG2A monoclonal Ab or control IgG after oral administration of 5% DSS. PBMCs samples from 23 healthy controls, 20 UC and 16 CD patients were analysed by flow cytometry. Tissue sections from 7 controls, 6 UC and 5 CD patients were subjected to histological analysis. Data were evaluated using the Student's *t*-test or the Mann-Whitney U-test.

**Results** In the active phase of DSS-induced colitis mouse, the frequency of NKG2A+ T cells was significantly decreased in the peripheral blood and increased in the intestine, suggesting the mobilisation of this T cell subset to the sites of inflammation. Administration of anti-NKG2A Ab increased the number of inflammatory foci in DSS-induced colitis, suggesting the involvement of NKG2A+ T cells in this colitis model. In UC patients, the frequency of NKG2A+ T cells in PBMCs was significantly decreased, compared with CD patients and healthy controls, regardless of clinical conditions. Notably, in sharp contrast to the DSS-induced colitis mouse, the frequency

of NKG2A+ cells in LPMCs was also decreased in UC patients.

**Conclusion** These results suggest that inadequate local infiltration of NKG2A+ T cells may be involved in the pathogenesis of UC. Our study demonstrates the frequency of NKG2A+ T cells is decreased in both PBMCs and LPMCs in UC patients, implicating this T cell subset as a potential therapeutic target for UC.

**Disclosure of Interest** None Declared.

#### PWE-120 WHAT DO HEALTHCARE PROFESSIONALS KNOW ABOUT FATIGUE IN PATIENTS WITH IBD AND HOW DO THEY MANAGE IT?

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10.1136/gutjnl-2014-307263.380

**Introduction** Fatigue is one of the top complaints in inflammatory bowel disease (IBD) with 40% of patients in remission and 86% in active condition reporting fatigue.<sup>1</sup> However patients report that their complaints of fatigue are often not addressed in clinical consultations.<sup>2</sup> This study aimed to gain an understanding of healthcare practitioners' (HCPs) perception of IBD fatigue as experienced by people with IBD.

**Methods** Descriptive phenomenology with purposive sampling was used to identify a range of professionals (gastroenterologists, IBD nurses, general practitioners, dietitians, psychologists and pharmacists). In-depth semi-structured interviews were conducted with 20 HCPs who work with people with IBD (June–Dec 2012). Colazzi's framework was used to analyse the data.<sup>3</sup>

**Results** Three main themes and several sub-themes were identified. The main themes were: the phenomenon of fatigue as perceived by HCPs; the impact of fatigue on patients' lives; and the methods used by HCPs to deal with fatigue. Fatigue was identified as an important, but difficult and often frustrating, symptom to understand. The study participants perceived fatigue as 'a complicated and complex thing'. HCPs reported that fatigue impacts on the emotional, private and public aspects of patients' functioning, however there were very few methods suggested on how to assess and manage the fatigue in a systematic way. Many expressed a desire for better education about fatigue and better multi-disciplinary effort to manage fatigue.

**Conclusion** Despite fatigue being one of the symptoms most frequently reported by IBD patients, it remains poorly understood by HCPs, who find fatigue challenging and frustrating. There is a need for a systematic and structured assessment and management of this distressing symptom and HCPs should communicate with each other about care for each individual patient. There is a need for an assessment framework and for intervention strategies to be tested. It is essential for multidisciplinary team members to be involved in planning and managing coordinated care of patients reporting fatigue in IBD.

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