Methods We studied 8 patients, identified from our anticoagulation database, who had been previously established on warfarin, and then commenced azathioprine or mercaptopurine for inflammatory bowel disease (2), systemic lupus erythematosus (1), nephritic syndrome (1), Wegener's granulomatosis (1), polyarteritis nodosa (1), dermatomyositis (1) and renal transplant (1). The effect of thiopurine on international normalised ratio (INR), and warfarin dose prior to and following commencement of thiopurine was recorded.

Results In 6/8 patients, following introduction of azathioprine or mercaptopurine, the warfarin dose had to be significantly increased (100% [18–500], Median [range]) in order to maintain a therapeutic INR. Any subsequent reductions in thiopurine dose were mirrored by a rise in INR and lower requirement for warfarin.

In 2 IBD patients, each with a high warfarin requirement, thiopurine metabolites were measured. In both patients MeMP:TGN ratio was >11. Thiopurine dose was reduced to 25% and allopurinol 100 mg added. INR was carefully monitored. In both cases INR increased within a week (to 6.9 and 11.2) and warfarin doses were subsequently reduced by ½ and 2/3 respectively to regain therapeutic INR.

Conclusion It is important for clinicians to be aware of the potential inhibitory action of thiopurines on warfarin's anticoagulant effect. Close INR monitoring is essential when initiating thiopurines and especially when reducing their dose and/or adding allopurinol. Failure to recognise the latter could result in bleeding due to over-anticoagulation. The high MeMP:TGN ratio in 2 of our patients also raises the possibility that thiopurine metabolites may play a role in the interaction between thiopurines and warfarin.

Disclosure of Interest None Declared.

PWE-081 DIAGNOSTIC PERFORMANCE OF FAECAL CALPROTECTIN IN PRIMARY CARE

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Introduction Faecal calprotectin is recommended by NICE¹ for distinguishing between irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) in patients with lower gastrointestinal (GI) symptoms in primary care. If cancer is suspected in these patients and 'red-flag' symptoms such as anaemia or bleeding, they should be referred to Gastroenterology in accordance with the NICE suspected cancer guideline.² We use calprotectin in secondary care and will be extending the service to primary care providers. However, a number of GPs have been requesting faecal calprotectin on an ad-hoc basis for 1 year, giving us valuable insight into how the test performs in primary care.

Methods An audit was carried out of primary care calprotectin data in a 1 year period (Dec 12–Dec 13). This data was compared to an audit of 1 month of secondary care data (Jun 13). Clinical details, such as endoscopy and histology results were extracted from electronic patient records.

Results In total 198 requests for calprotectin came from primary care in 1 year and 40 were unsuitable for analysis (wrong sample type or delayed arrival in lab). Of the remaining 158 calprotectin requests, 76% were considered appropriate, having clinical details including symptoms described by NICE. Worryingly, 17%

of requests had inappropriate clinical details such as bleeding; such patients' referral to Gastroenterology was potentially delayed by requesting calprotectin. In 7% of requests no reason for request was discernable.

Of the primary care requests, 29% results were consistent with intestinal inflammation (>50 µg/g). If GPs use our proposed algorithm which suggests only referring patients with a calprotectin >50 µg/g, and those where strong clinical suspicion remains, there is potential for up to 71% reduction in patients referred to Gastroenterology with 'IBS/IBD' symptoms.

Diagnostic performance of calprotectin compared with endoscopy and histology diagnosis in secondary care is excellent with a sensitivity of 100% and a specificity of 91%. In primary care the corresponding data gives a sensitivity of 93% and a specificity of 79%.

Conclusion We received a large number of unsuitable samples. In addition GPs appear to be inappropriately requesting calprotectin in patients with symptoms such as bleeding, therefore it is critical to offer the service in a controlled way as part of a locally agreed care pathway. We are producing a GP information leaflet to advise on appropriate sample collection, result interpretation and the proposed patient pathway. We will re-audit primary care data once this is introduced to investigate whether a targeted approach leads to improved diagnostic performance of calprotectin in primary care.

REFERENCES

- 1 Faecal Calprotectin diagnostic tests for inflammatory diseases of the bowel, NICE DG11
- 2 Referral for suspected cancer, NICE CG27

Disclosure of Interest None Declared.

PWE-082 THE IMPACT OF NOD2 VARIANTS ON GUT MICROBIOTA IN CROHN'S DISEASE AND HEALTHY CONTROLS

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Introduction Crohn's disease (CD) is now understood to be caused by the interaction between genetic and environmental factors with dysregulation of gut microbiota playing a pivotal role. *NOD2*, the strongest genetic risk factor for CD, encodes a pattern recognition receptor and plays an important role in epithelial defence. Studies of *NOD2*-knockout mice have demonstrated shifts in gut microbiota. Human studies to date have been limited by relatively small numbers of individuals homozygous for *NOD2* mutations without accurate matching of controls.

Methods Individuals with CD of known *NOD2* status were identified from the UK IBD genetics consortium. Patients in clinical remission were selected if they carried 2 of the common *NOD2* variants (homozygotes or compound heterozygotes). Each *NOD2* mutant patient was matched to a *NOD2* wild-type

patient. For all CD patients a household control was approached. Healthy volunteers stratified by *NOD2* genotype were recruited from the Cambridge Bioresource.

Faecal samples were frozen within 24h of collection. DNA was extracted using the FASTDNA Spin Kit for Soil. The V1–3 region of the 16S rRNA gene was amplified and amplicons were sequenced with Illumina MiSeq. Sequence data was processed in Mothur. Calprotectin was measured in all samples by ELISA.

Results 97/107 individuals were included in the primary analysis (40 CD patients [58% *NOD2* mutant], 32 bioresource volunteers [50% *NOD2* mutant], 25 household controls). The minimum reads per sample were 3953, mean 21216.

There was a significant reduction in diversity (inverse Simpson index), *Ruminococcaceae* including *Faecalibacteria* and increase in *Enterobacteriaceae* in samples from CD patients vs. controls (all $p < 0.0001$). There were no differences in diversity or relative abundance of any bacterial families when stratified by *NOD2* status, either within the CD patients or bioresource controls.

Conclusion This study confirms previously identified shifts in gut microbiota in CD patients. However, no significant differences in gut microbiota were seen when analysed by *NOD2* status. This may be a reflection of sample size or of studying gut bacteria in stool as opposed to the mucosally-associated compartment. We are presently recruiting additional cases and controls to increase study power for additional analysis.

Disclosure of Interest None Declared.

PWE-083 DISTINGUISHING BETWEEN POSSIBLE MENTAL HEALTH DISORDERS AND PSYCHOLOGICAL DISTRESS BY SCREENING FOR ACCEPTANCE AND ADJUSTMENT ISSUES

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Introduction A recent study indicated that 30% of IBD patients suffer from psychological distress, and that poor acceptance and adjustment is a predictor of distress (Swart *et al.* 2013). Psychological distress encompasses the symptoms of depression, anxiety, emotional difficulty and poor adjustment, but is not the same as mental illnesses such as Major Depressive Disorder or Generalised Anxiety Disorder. Early indications suggest IBD patients are particularly susceptible to adjustment disorders, which may be the cause of much distress.

Methods As part of a service evaluation, 2400 IBD patients in the Luton and Dunstable catchment area were invited to participate in a web-based psychological and quality of life assessment. The “Acceptance and Action Questionnaire” (AAQ-II) was used for acceptance/adjustment, as well as the “Patient Health Questionnaire” (PHQ-9) for depression, and the “Generalised Anxiety Disorder Questionnaire” (GAD-7) for anxiety.

Results 360 patients completed the assessment (45% male, mean age = 53; SD = 17). 31% of patients scored highly on the PHQ-9; 27% of patients scored highly on the GAD-7; and 27% of patients also scored highly on the AAQ-II. Linear regression, after taking account of relevant clinical factors, showed that poor acceptance was associated with high depression and anxiety. Cross tabulation indicated 20% of patients showed high depression and poor acceptance, and 11% of patients showed

high depression and good acceptance/adjustment. Anxiety sees a similar picture with 18% high anxiety and poor acceptance/adjustment, and 8% high anxiety and good acceptance/adjustment.

Conclusion The self-report prevalence rates of depression and anxiety we found are typical of chronic illness populations, however the cross-tabulation results suggest a more complex picture. While further research is needed, theory suggests those 20% are struggling with depression which stems from their acceptance and adjustment issues. Similarly, those 11% with high depression and good acceptance are likely to have a mental health disorder like Major Depressive Disorder – 11% is a similar prevalence rate found when using diagnostic interviews. These groups of patients would likely benefit most from different treatment paths. Specifically, severe depressive symptoms stemming from acceptance/adjustment issues would likely benefit more from Acceptance and Commitment Therapy than standard procedures for treatment of depression with antidepressants and Cognitive Behavioural Therapy.

REFERENCE

Swart N, Wellsted D, Lithgo K, Price T, Johnson MW. PWE-110 acceptance and adjustment in a district general cohort of inflammatory bowel disease patients: findings and implications. *Gut* 2013;62:A175–A176

Disclosure of Interest None Declared.

PWE-084 NATIONWIDE LINKAGE ANALYSIS IN SCOTLAND – HAS MORTALITY FOR HOSPITAL ADMISSION FOR CROHN’S DISEASE CHANGED IN THE 21ST CENTURY?

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Introduction Data from patients hospitalised with Crohn’s disease (CD) between 1998 and 2000 in Scotland indicate higher 3-year mortality rates than the general population. ⁽¹⁾ We now have the opportunity of comparing these data with contemporary mortality data in patients admitted in Scotland between 2007–2009. We hypothesised key alterations in management of CD over the last decade may have reduced mortality.

Methods The Scottish Morbidity Records and linked datasets were used to assess 3-year crude mortality, standardised mortality ratio (SMR) and multivariate analyses of factors associated with 3-year mortality. The 3-year mortality was determined after four admission types: surgery-elective or emergency; medical-elective or emergency. Age-standardised mortality rates (ASR) were used to compare mortality rates between periods.

Results The number of patients hospitalised for 4 or more days with CD was 1460 [Period 1] to 1565 [Period 2] (15.6 to 14.5 per 100,000 Scottish population per year). There was no change in the crude or adjusted 3-year mortality rate between study periods (crude 9.0% to 9.1%, adjusted OR = 0.87 CI: 0.65–1.17; $p = 0.355$). In subgroup analysis, the adjusted 3-year mortality increased following elective surgery (OR 13.5, CI: 1.66 – 109.99) and decreased following emergency medical admission (OR = 0.68, CI: 0.47–0.97).

The directly age-standardised mortality rates (ASR) per 10,000 person years were unchanged between study periods ([Period 1 ASR 299, CI: 251–348][Period 2 ASR 281, CI: 233–328]).