Anti-drug antibodies can affect biopharmaceutical pharmacokinetics by increasing or decreasing drug clearance. Drug-tolerant (total), unlike drug-sensitive (free), antibody assays permit antibodies to be measured in the presence of drug.

We aimed to confirm the positivity threshold of our total anti-tumour necrosis factor (TNF) antibody ELISA assays in healthy volunteers and to use this threshold to report the prevalence of clearing and transient antibodies in patients treated with infliximab and adalimumab.

Methods Serum was obtained from 498 anti-TNF-naïve healthy adults recruited to the Exeter 10,000 study and tested for total anti-drug antibodies to infliximab and adalimumab. We used bootstrapping to calculate the 80% one-sided lower confidence interval [CI] of the 99th centile recommended by the FDA to define assay thresholds.

We used paired drug and anti-drug antibody levels derived from our national therapeutic drug monitoring service to report the distribution of clearing (antibody positive, drug negative) vs non-clearing (antibody positive, drug positive) antibodies. In patients with at least two test results, antibodies were classified as transient (single positive test with subsequent negative test) or persistent (at least two positive tests).

Results The 80% one-sided lower CI of the 99th centile titre for total anti-drug antibody to infliximab and adalimumab were 8.7 AU/mL and 5.9 AU/mL, respectively.

Using these thresholds, at the time of last testing, of 7,428 and 4,043 patients treated with infliximab and adalimumab; 21.1% and 8.3% had clearing antibodies and 27.9% and 20.0% had non-clearing antibodies, to infliximab and adalimumab, respectively.

Amongst patients with at least two tests, most developed persistent antibodies. Irrespective of anti-TNF drug, or threshold used, less than 10% patients developed transient antibodies.

Across both our national TDM cohort and the PANTS study, there were significant associations between anti-drug antibody and drug levels (figure 1). In PANTS, higher anti-drug antibody levels were associated with poorer outcomes at weeks 14 and 54.

Conclusions We report lower positivity thresholds for the IDK-monitor® total anti-TNF antibody ELISA assays than the manufacturer, in particular, for adalimumab. Transient antibody formation is uncommon: most patients develop persistent anti-drug antibodies that lead to drug clearance.
p=0.023) as did less deprived quintiles and those who had index RH on an elective admission (0.69 (0.62–0.77), p<0.001). A comorbidity score of >5 was associated with 40% increased further surgery risk (1.41 (1.05–1.89), p=0.023).

51% subjects had a colonoscopy within 2 years of index RH. Recommended 6–12 month colonoscopy assessment increased from 14% in 2007 to 29% in 2016. Overall, unadjusted 6–12 month colonoscopy was 22% however this varied 4-fold between providers. Adjusting for further surgery, illness that might prevent or delay colonoscopy or subject death, 42% of subjects did not undergo a 6–12 month colonoscopy. This fell to 26% if colonoscopy was included.

Figure 1 shows a funnel plot of 6–12 month colonoscopy following right hemicolecction (RH) for Crohn’s disease by provider. Dots represent providers and lines indicate 1, 2 and 3 standard deviations from the mean.

Conclusions Despite novel therapeutics and better understanding of the natural history of CD there remains a high risk of recurrent surgery. Colonoscopy assessment after RH has been increasing over time but there remain large unexplained variations in colonoscopy practice between providers.

### P121 RISK OF INFLAMMATORY BOWEL DISEASE IN SUBJECTS PRESENTING WITH EYE-DISORDERS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

1Dominic King*, 2Johnt Chandan, 2Tom Thomas, 2Nij Bhala, 2Krish Nanarathan,
2Nicola Adderley, 2Raoul Reulen, 1Nigel Trudgill, 1Sandwell and West Birmingham Hospitals NHS Trust, UK; 2University of Birmingham, UK

10.1136/gutjnl-2020-bsgcampus.196

Introduction A number of eye diseases including uveitis and episcleritis/scleritis may occur in association with inflammatory bowel disease (IBD). We have examined the risk of later developing IBD in such eye conditions and the time to diagnosis.

Methods The Health Improvement Network, a large UK primary care database was examined. Cases of eye disorders associated with IBD were matched to controls on age, sex and GP registration. Subjects were followed until a diagnosis of ulcerative colitis (UC) or Crohn’s disease (CD) and incident rate ratio (IRR) modelled, adjusting for age, sex, body mass index, comorbidity, deprivation level and smoking status. The time to a later diagnosis of IBD in cases and controls was compared using the Mann-Whitney U test.

Results 5,349 EN cases (median age 36 (IQR 23–51), 78% female) were matched to 21,100 controls. Median time to UC diagnosis was reduced in EN compared to control subjects (224 and 1,856 days respectively p<0.001). The rate of UC was not significantly increased in EN subjects compared to controls (IRR 1.67 (95%CI 0.87–3.24) p=0.13). Median time to CD diagnosis in EN cases was 114 days compared to 1,136 in controls p<0.001. The rate of CD in EN was 12-fold that of controls (12.76 (7.62–21.38) p<0.001). EN subjects had a 1.2% excess risk of IBD compared to controls.

863 PG cases (age 57 (39–73), 40% male) were matched to 3,404 controls. Few IBD diagnoses were made during the study period (16 in PG cases and 6 in controls). Time to IBD diagnosis in PG cases was reduced compared to controls p=0.047. The rate of IBD in PG was 13-fold that of controls (13.21 (5.07–34.41) p<0.001). PG subjects had a 1.8% excess risk of IBD.

When skin disorders combined (EN, PG, SS and AS) were examined, 7,340 cases (median age 36 (23–50), female 74%) were matched to 21,764 controls. 133 cases of IBD were observed in the skin disorder group compared to 53 in controls. The rate of UC was more than 3-fold higher in the skin disorder group (3.63 (2.17–6.08) p<0.001). The rate of CD was 11-fold higher in the skin disorder group (11.21 (7.30–17.20) p<0.001). Skin disorder subjects had a 1.6% excess risk of IBD. When those with anaemia, weight loss, lower gastrointestinal bleeding, diarrhoea or loperamide use within 6-months of diagnosis were examined an 8.3% excess risk was seen.

Conclusions Skin disorders associated with IBD are not unique to IBD and clinicians who diagnose these conditions may not consider IBD leading to a delayed diagnosis. The relative risk of IBD is high in such skin disorders and symptoms suggestive of IBD should be sought, and screening investigations and gastroenterology referral considered.