trends in surgery for abdominal CD at a tertiary referral during the 13 last years.

Methods: All patients who underwent surgery for abdominal CD between January 2004 and December 2016 were included. Demographic, CD, and perioperative characteristics were compared in two consecutive periods (2004–2010 and 2011–2016).

Results: During the study period, 908 procedures were performed (48% male, mean age 43 ± 16 years). Demographic and CD characteristics changed significantly over time: during the second time period, comorbidities were more frequent (46 vs. 35%, $p < 0.0001$), and pre-operative steroids (36 vs. 28%, $p < 0.01$) and anti-TNF (40 vs. 20%, $p < 0.0001$) treatments were more frequently used. Smoking (8 vs. 14%, $p < 0.0001$) and use of immunosuppressors (22 vs. 32%, $p < 0.001$) decreased. In addition, more penetrating disease and more complex cases were operated on (56 vs. 63%, $p = 0.03$) in the second period. Laparoscopic approach (57 vs. 49%, $p < 0.04$) was more frequently performed during the second period, whereas diverting stoma rate (10 vs. 17%, $p < 0.002$) and mean blood loss (167 ± 222 vs. 123 ± 243 ml, $p < 0.01$) decreased significantly. Overall, surgical, medical, and major (Dindo ≥ 3) morbidity rates and mean length of stay did not change between the two periods.

Conclusions: This study reports that post-operative course remained stable in spite of changes in the severity of abdominal CD cases operated on. Refinement of surgical technique offsets increased severity of Crohn's disease and co-morbidities to maintain low post-operative morbidity.

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Is liver steatosis a risk factor for hepatotoxicity in patients with inflammatory bowel disease on thiopruines?

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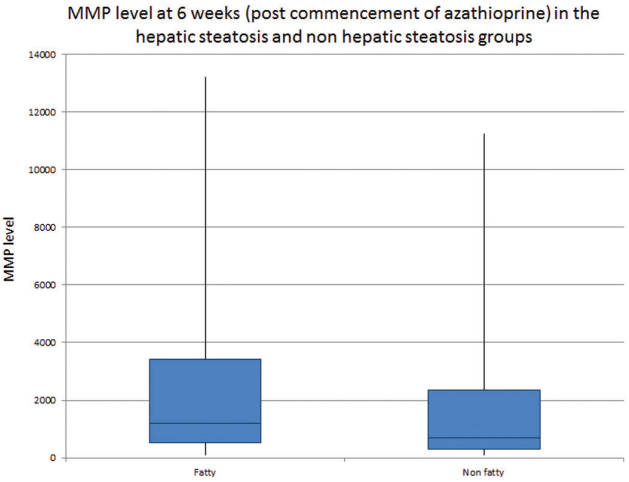
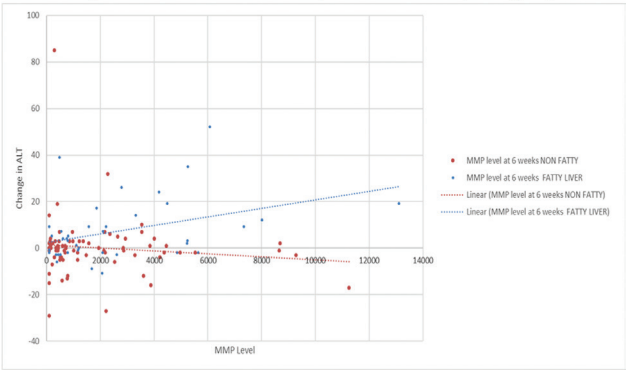
Background: The literature shows that inflammatory bowel disease (IBD) patients with hepatic steatosis do not tolerate the immunosuppression used in IBD.[1] We hypothesised that hepatic steatosis may be a risk factor for hepatoxicity in patients with IBD on azathioprine, and specifically whether MMP had a role in this process.

Methods: To investigate this, we performed a retrospective review of patients started on azathioprine treatment at the Bristol Royal Infirmary between 2014 and 2017. There were 600 patients in total. One hundred and twenty-one patients met our inclusion criteria which were at least one ultrasound scan commenting on the appearance of the liver, liver function tests (LFTs) at commencement of azathioprine and liver function tests and an MMP level around 6 weeks after starting treatment.

Results: Of 121 patients included in our study we identified 40 patients (33%) with radiological hepatic steatosis and 81 patients with no evidence of steatosis. We found (using a Wilcoxon rank-sum test) strong evidence to indicate that patients with hepatic steatosis had higher than expected MMP levels at 6 weeks ($p = 0.03$). Our results also found that there is a positive association between MMP levels and change in ALT in patients with fatty liver ($p < 0.001$). However, we found no association between either fatty liver status and ALT, or MMP and change in ALT alone.



box and whisker plot.



MMPvsALT correlation.

Conclusions: Our data suggest that patients with hepatic steatosis may metabolise azathioprine differently resulting in higher levels of MMP, consistent with previously published data.[2] We also conclude that the combination of liver steatosis and higher levels of MMP may be a risk factor for hepatitis.

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Clinical feasibility of dried blood sampling for infliximab in IBD patients

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Background: Therapeutic drug monitoring (TDM) is important to optimise outcome of infliximab (IFX) treatment in inflammatory bowel disease (IBD). Dried blood spot (DBS) sampling using capillary blood obtained via a finger prick could facilitate TDM, since patients can administer this finger prick themselves at any time and away from the hospital. We investigated the predictive performance and the feasibility of DBS for measuring IFX concentrations in IBD patients.
Methods: We studied 40 adult IBD patients receiving IFX therapy according to standard guidelines. From each patient blood was obtained simultaneously via venepuncture and DBS via finger prick by a trained employee at 3 different time points (trough, peak, 3–5 weeks after infusion). One week before IFX infusion (time point 4), patients performed DBS at home and the sample was directly sent to Sanquin laboratories, Amsterdam, The Netherlands. The corresponding serum concentration for this time point was estimated using Bayesian pharmacokinetic analysis using the three samples obtained by venepuncture. Capillary blood was obtained by a microsampling device developed by Neoteryx™. Haematocrit (Hct) values of each individual patient were used to convert DBS eluate results to values which can be compared with (venous) serum concentrations. Spearman's correlation coefficient was used to assess correlation and bias was calculated.
Results: Forty IBD patients were included with median [interquartile range] age: 41 [32–50], albumin: 43 mg/l [41–45], and CRP: 1.3 mg/l [0.4–4.4]. IFX concentrations obtained from the DBS method correlated strongly with serum results from the same patient for IFX trough- and mid-interval concentrations (Spearman correlation coefficient >0.88) and moderately for IFX peak concentrations (Spearman correlation coefficient = 0.69). IFX serum concentrations from the DBS performed at home showed strong correlation with the concentrations obtained by Bayesian analysis (Spearman correlation coefficient = 0.71). No structural bias was shown (Table 1).

Table 1. Concentration range and relative bias.

	Concentration range (mg/l)	Relative bias, mg/l (%)*
Time point 1 (before infusion, trough)	0.03–23.0	–3.8 (–15.7 to 8.0)
Time point 2 (after infusion, peak)	72.0–341.7	–4.1 (–10.3 to 2.1)
Time point 3 (3–5 weeks after infusion, mid)	2.0–41.2	–0.1 (–8.2 to 8.3)
Time point 4 (1 week before next infusion)	1.6–32.5	8.5 (–11.9 to 28.9)

*Values are expressed as mean prediction error (95% confidence interval)

Conclusions: DBS via finger prick can be used for the assessment of serum IFX concentrations. More importantly, we showed the feasibility of using DBS via finger prick at home. This method greatly facilitates the use of TDM in the treatment of IBD patients using IFX.

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Comparison of the KU Leuven ustekinumab concentration assay and the antibodies-to-ustekinumab assay with assays developed at Janssen R&D and used in clinical studies of IBD patients

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Background: Monitoring ustekinumab (UST) concentrations and antibodies-to ustekinumab (ATU) during IBD treatment may allow more informed decisions in assessing exposure/response and appropriate dosing. To aid in interpreting results in the context of Janssen's published UST results, the reliability of different assays measuring UST and ATU was compared with those from Janssen. This abstract reports the comparison of the UST and ATU assays from KU Leuven (KUL, Leuven, Belgium) and Janssen (JRD, Spring House, PA, USA). Results from the other companies will be reported at a later time.
Methods: Blinded test samples, prepared by JRD, were sent to the KUL and JRD labs for UST and ATU assessments. Results were reported to JRD for integrated analyses. All assays were tested for specificity, selectivity, accuracy and precision. ATU assays were evaluated for sensitivity, drug interference, and potential interference of IL-12. UST and ATU were tested at KUL using Enzyme-Linked Immunosorbent Assays (ELISA), and at JRD using Meso Scale Discovery electrochemiluminescent immunoassays (ECLIA). The lower limit of quantification was 0.25 µg/ml for the KUL UST concentration assay and 0.1688 µg/ml for the JRD UST concentration assay.
Results: Strong agreement was observed between the JRD and KUL UST assays. Specificity was demonstrated when both UST assays accurately detected 1.0 or 10.0 µg/ml of UST, but did not detect other human monoclonal antibodies (mAb). The presence of ATU titres up to 200 or IL-12 concentrations up to 100 pg/ml did not interfere with the UST assessment in either assay. Accuracy was confirmed by three independent measurements of UST-spiked (0.06–32 µg/ml) human psoriasis (PSO) sera and with UST measured in sera from UST-treated PSO patients. Both UST assays were precise, as determined by inter-occasion reproducibility. Strong agreement was observed between the JRD and KUL ATU assays. Both ATU assays specifically detected anti-UST antibodies; results were not affected by high titre antibodies against other human mAb. The KUL ATU assay was not drug tolerant, while the JRD ATU assay demonstrated drug tolerance to 8.0 µg/ml of UST. Concentrations of free or bound IL-12 (≤100 pg/ml) did not interfere with ATU detection in either assay. Both ATU assays were reproducible.
Conclusions: Our study results indicate that the KUL UST concentration and ATU assays strongly correlate with those from JRD. The substantial agreement between the KUL and JRD assays may provide support to clinicians in their use of these assays, and for understanding their patients' UST and ATU result relative to published data from clinical studies of UST.

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Combination therapy for perianal fistulising Crohn's disease in biological era: What is the optimal time for surgical intervention?

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Background: Management of complex perianal fistulising Crohn's disease (pCD) continues to be challenging. Recent studies have recognised that combined surgery and anti-TNFa therapy could improve clinical outcomes in patients with pCD. However, the optimal timing of surgical intervention after infliximab infusion is still controversial.